2020

Impact of Chlorpyrifos Exposure on Colorectal Cancer in Agricultural Communities in Ohio

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2020

Abstract

Impact of Chlorpyrifos Exposure on Colorectal Cancer in Agricultural Communities in Ohio

by

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BS, Kettering College, 2014

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

November 2020

Abstract

Colorectal cancer (CRC) is the third leading cancer diagnosis in the United States, and second in Ohio, for both men and women. In 2019, there were an estimated 145,000 cases of new CRC diagnoses and will lead to more than 50,000 deaths. Results from a systematic review indicate that chlorpyrifos use in agriculture is linked to the incidence of breast and lung cancers and has a possible association with CRC. Grounded in the social-ecological model, this study investigated the association between exposure to chlorpyrifos and CRC rates in agricultural communities in Ohio. The quantitative cohort design method utilized secondary data from the Ohio Cancer Incidence Surveillance System and the Centers for Disease Control and Prevention SEERS database, with a sample of 147,039 CRC cases in Ohio. Mann-Whitney test results ($p = 0.875$) and Kruskal-Wallis results ($p = 0.382$) indicated no statistically significant difference between CRC rates compared to chlorpyrifos usage. Spearman correlation analysis results ($p = 0.709$) showed no statistically significant correlation between chlorpyrifos usage and CRC rates. Wilcoxon Signed Rank test results ($p = 0.000$ and $p = 0.001$) indicated a statistically significant difference between CRC rates for agricultural counties in Ohio and those for the United States and for Ohio overall, respectively. The findings from this study should be used as support for future research in areas with elevated CRC rates. Public policy change should include local health department monitoring and reporting of chemical pesticide usage rates in their respective areas, as well as community education on the risks associated with exposure to pesticides and CRC development.

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Dedication

I dedicate my dissertation to my family for their unwavering support and understanding throughout this journey. My son, Wyatt, who has become my inspiration in life and reason for being. My husband, Eric, for embracing single fatherhood when I was studying. My parents, who instilled an amazing work ethic and symbolized hard work and sacrifice and my sister, for her undying encouragement. Thank you.

Acknowledgments

I would like to acknowledge my family, friends, and Walden faculty for their support and guidance throughout my academic career. I would like to extend a special thanks to my committee chair, Dr. Raymond Panas, my committee member Dr. Bill Sumner Davis, and my University Research Reviewer Simone Salandy. Your guidance and direction have enabled me to navigate the dissertation process with confidence. I could not have accomplished this goal without you. I would also like to acknowledge my employer, Miami County Public Health, and coworkers who have lessened the stress of this journey by providing a quiet and supportive environment to work in and making reaching my goals part of your mission as well.

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Chapter 1: Introduction to the Study

Introduction

In 2019, there was an estimated 145,000 new cases of colorectal cancer (CRC) in the Unites States (American Cancer Society, 2019). CRC has become the third leading cancer cause of death in the United States. Ohio is no exception and is experiencing similar trends. In 2016, 5,760 cases were reported to the Centers for Disease Control and Prevention. The Ohio Cancer Incidence Surveillance System's county information indicates that in some 40 counties CRC is in the top three cancer-related deaths (Ohio Department of Health, 2018). Most of those counties have significant agricultural communities where residents are exposed to various chemical pesticides. With current CRC rates there is a need to investigate risk factors associated with the development of new and existing cancer incidences. By identifying risk factors, community leaders and those living in these areas can be proactive in obtaining CRC screenings and policy makers can implement policies that place restrictions on harmful chemical pesticide use and require chemical pesticide companies to investigate safer alternatives.

This chapter highlights the background of CRC to summarize research that has been conducted on CRC in other agricultural communities as well as the use of chlorpyrifos and any relationship with cancer development. The purpose of the study, along with the research questions, theoretical framework, rationale for the study design, and the study's significance and limitations will also be discussed. The variables being investigated will also be detailed and defined in depth to validate their inclusion.

Background

This research study provided insight on the use of the organophosphate pesticide, chlorpyrifos, and the association with CRC incidences. With research specifically investigating exposure rates to this chemical pesticide, these findings provide information for policy makers, agricultural agencies, and pesticide companies to investigate less harmful pesticide options. Previous studies have linked this chemical to the development of both lung and breast cancer. There have been similar studies conducted in countries such as Brazil and Italy in relation to agricultural workers and CRC rates. None have specifically investigated communities in the United States and exposure to chlorpyrifos specifically.

Cancer Formation

Cancers begin when normal cells undergo a transformation into tumor cells through a multiple stage process (World Health Organization, 2018). There are three potential changes that must occur in the cells for the transformation to begin; these will involve either genetic changes or three external factors that could influence cell mutation. The three external factors include physical carcinogens, chemical carcinogens, or biological carcinogens (World Health Organization, 2018). CRC is not different. It can begin in either the colon or rectum as polyps or growths in the epithelial lining. The most common type of polyp is an adenoma (American Cancer Society, 2017). These polyps can grow for years and often produce few or no symptoms which makes routine screening after the age of 50 very important (Mayo Clinic, 2018). In 2014, roughly 66% of U.S. adults received routine colorectal screening (American Cancer Society, 2017).

Although there are limited symptoms at early stages, rectal cancer is more likely to be diagnosed before colon cancer, as the symptoms appear in this section earlier (American Cancer Society, 2017). Some polyps can turn into cancer, whereas others remain benign and create no serious health issues (American Cancer Society, 2017). Risk factors associated with the development of CRC include age, diet, family history, alcohol and tobacco use, and a sedentary lifestyle (Mayo Clinic, 2018). Some environmental factors, such as chemical pesticides and insecticides, have been linked to other types of cancer, which is prompting researchers to examine potential links to the development of CRC.

Epidemiology

CRC is the third leading cancer diagnosis in the United States for both men and women. In Ohio, CRC is the second leading cause of death due to cancer in Ohio. In 2018, an estimated 140,000 cases of new CRC were diagnosed that will lead to more than 50,000 deaths (American Cancer Society, 2017). Worldwide, CRC is the third leading cancer with 1.8 million cases in 2018 and the second leading cancer cause of death with 862,000 deaths (World Health Organization, 2018).

Gender. There is little difference between men and women as to the risk of developing CRC. For men and women, the risk of a colorectal diagnosis in their lifetime is roughly 4.5% and 4%, respectively (American Cancer Society, 2017). However, the incidence rates between genders are significantly higher for men than women. Colorectal incidence rates for men are 30% higher and mortality rates are 40% higher than women. Gender disparities are not the only differences among different groups.

Race. There are significant racial disparities in terms of CRC diagnoses and mortality rates. From 2009 to 2014, non-Hispanic Black men and women had higher CRC diagnoses and had higher mortality rates (American Cancer Society, 2017). Asians and Pacific Islanders had the lowest rates. From the mid 1980' until the mid- 2000's, there was a gap in CRC rates between the Black and White populations. However, currently, CRC rates are decreasing for all racial groups, except for American Indian/Alaskan Natives. From 2009 to 2013, CRC rates decreased by roughly 3% for non-Hispanic Whites, non-Hispanic Blacks, and Hispanics. Mortality rates have also been on the decline. From 2005 to 2014, death rates for non-Hispanic Whites and Hispanics has decreased by 2% per year and 3% per year for non-Hispanic Blacks (American Cancer Society, 2017).

Geographic disparity. There is a geographic difference in CRC incidence and mortality rates. A shift from higher rates in the Northeast to the South was seen in the later part of the 20th century. This is attributed to racial and socioeconomic changes. Risk factors that contribute to these geographic disparities include regional differences in risk factors, access to CRC screening and treatment, and political variation, all of which are influenced by socioeconomic differences (American Cancer Society, 2017).

Risk Factors

Although there are various environmental factors that contribute to the incidence of CRC, occupational exposures should be examined as well. There are numerous occupations that pose risk factors that could be associated with the higher incidences of CRC. Iron and foundry workers and dockyard workers have a higher relative risk and mortality associated with CRC, respectively, whereas generally CRC rates in farmers or agricultural workers has been low (Oddone, Modonesi, & Gatta, 2014). Historical research has indicated that this could be due to lower levels of smoking and higher levels of physical activity, as lifestyle choices have been significantly associated with the development of CRC (Lee et al., 2007). However, other studies have found that farmers and pesticide workers are at a higher risk for developing CRC due to chemical exposure to pesticides and insecticides.

There have been numerous studies on the potential association of chemical pesticide/insecticides with lung and breast cancer, but more recently researchers are beginning to investigate a potential link to CRC. Chemical pesticides and insecticides are often organophosphates or organochlorines. Organochlorines are chlorinated hydrocarbons that open sodium ion channels in neurons, which causes the nerve cell to continuously fire, leading the cell death. Most organochlorine pesticides, like DDT and methoxychlor, have been banned for all use in the United States (Delaware Health and Social Services, 2015).

Organophosphate insecticides kill insects and other animals, including birds, amphibians, and mammals, by phosphorylation of the acetylcholinesterase enzyme, an enzyme needed for acetylcholine uptake (Environmental Protection Agency, 2018). Acetylcholine plays a vital role in nerve impulse transmission and when left unchecked nerve endings are over stimulated causing cell death. Although some organophosphates have been banned for use in the United States, parathion for example, others have only been banned for household use, such as chlorpyrifos (Environmental Protection Agency, 2018). Chlorpyrifos, though discontinued for household use, is still being used in a commercial setting, such as in large-scale agriculture and farming. Some experimental studies examining the effects of chlorpyrifos on human cells have indicated that the organophosphate can directly alter gut bacteria and increase adenocarcinoma cell viability (Reygner et al., 2016; Suriyo, Tachachartvanich, Visitnonthachai, Watcharasit, & Satayavivad, 2015).

Problem Statement

In Ohio, CRC is the second leading cause of death due to cancer (Ohio Department of Health, 2018). Although there are various risk factors associated with the development of CRC, further investigation into certain potential environmental risk factors is necessary. Historically, CRC rates in farmers or agricultural workers have been low (Oddone et al., 2014). However, other studies have found that farmers and pesticide workers are at a higher risk for developing CRC, due to chemical exposure to pesticides and insecticides (Salerno, Carcagni, Sacco, Palin, Vanhaecht, Panella & Guido, 2016). Chlorpyrifos, an organophosphate, was discontinued for household use but is still used in commercial corn and soybean farming (Environmental Protection Agency, 2018). Experimental studies on the carcinogenic effects of chlorpyrifos on human cells indicate that organophosphates increase adenocarcinoma cell viability (Suriyo et al., 2015). Exposure to chlorpyrifos has been found to be associated with breast cancer in farmers' wives; however, future research with larger samples from a broader geographic area is necessary to examine possible associations with different cancer types (Engel et al., 2017;

Ilgaz & Gozum, 2018). This research provided additional information on the risk factors associated with the development of CRC.

Purpose of Study

The purpose of this study was to investigate the association between the independent variable, exposure to the organophosphate chlorpyrifos, and the dependent variable, incidence of CRC in agricultural populations in Ohio. Covariates investigated included age, gender, and race. In this quantitative study, I utilized secondary data on the incidence rates of CRC in these geographic areas and examined chlorpyrifos application rates for a possible statistical association. This study addressed the need for examination in specific geographic areas of limited research for target populations (Salerno et al., 2016).

Research Questions and Hypotheses

RQ1: Is there a statistically significant association between chlorpyrifos exposure and incidence rates of CRC, after controlling for gender, age, and race, for Ohio agricultural communities?

H_o1: There is no statistically significant association between chlorpyrifos exposure and the incidence rates of CRC, after controlling for gender, age, and race, for agricultural communities in Ohio.

H_a1: There is a statistically significant association between chlorpyrifos exposure and the incidence rates of CRC, after controlling for gender, age, and race, for agricultural communities in Ohio.

RQ2: Is there a statistically significant difference between CRC incidence rates, after controlling for gender, age, and race, in the United States and agricultural areas in Ohio?

H_o2: There is no statistically significant difference between CRC incidence rates, after controlling for gender, age, and race, in the United States and agricultural areas in Ohio.

H_a2: There is a statistically significant difference between CRC incidence rates, after controlling for gender, age, and race, in the United States and agricultural areas in Ohio.

RQ3: Is there a statistically significant difference between CRC incidence rates, after controlling for gender, age, and race, for the state of Ohio and the agricultural areas within Ohio?

H_o3: There is no statistically significant difference between CRC incidence rates, after controlling for gender, age, and race, for the state of Ohio and the agricultural areas within Ohio.

H_a3: There is a statistically significant difference between CRC incidence rates, after controlling for gender, age, and race, for the state of Ohio and the agricultural areas within Ohio.

Theoretical Framework

The theoretical framework I chose for my study was the social-ecological model, which is used to examine the potential associations between individuals and their environment. There are five levels examined in the social-ecological model: (a) the individual, (b) the interpersonal or social network, (c) the organizational and environmental level, (d) the community and cultural norms level, and (e) the public policy level (Okoye, 2016). This model best fits the study, as it was the goal to investigate the association between CRC incidence rates for those living in agricultural communities and exposure to the chemical pesticide chlorpyrifos, while considering the different levels of influence that impact an individuals' health and health related behaviors.

Nature of Study

I used a quantitative approach with a cohort design. The cohort design allowed for the examination of a specific group with the same outcome variable, CRC diagnosis, but differed in their exposure variable, which was exposure to the chemical pesticide chlorpyrifos. This study provided insight on the impact exposure to chlorpyrifos has on the development of CRC.

Definitions

Variables I chose for my study included an independent variable of exposure to chlorpyrifos, a dependent variable of CRC incidence rates, and the covariates age, gender, and race. Exposure to chlorpyrifos was categorized based on county of residence and its classification as low agriculture, moderate agriculture, high agriculture and industrial. The covariate age was categorized into groups of ≤ 35 years, 36-45, 46-55, and ≥ 55; gender was male or female; and race was categorized as non-Hispanic White, non-Hispanic Black, Hispanic, or other. Also included in the covariates were the annual sales estimates of chlorpyrifos in specific areas in Ohio, which was measured in pounds per acre.

Assumptions

Certain aspects of this study were assumed but could not be demonstrated as true. One specific aspect was that those living in agricultural communities are in close proximity of farmland or that chlorpyrifos was actually being used on the crops in these areas. The chlorpyrifos usage rate data and the millions of pounds in sales records helped support this assumption.

Scope and Delimitations

The research problem addressed the association between exposure to chlorpyrifos and the high prevalence of CRC incidence rates in agricultural communities in Ohio in relation to those communities that were not categorized as agricultural. The population that was included in the research was all CRC incidence in Ohio; therefore, the entire state was accounted for not just specific areas. However, this study only investigated Ohio, and other states that have a prevalent agricultural presence may not be experiencing the same level of CRC rates or exposure to chlorpyrifos. Therefore, the generalizability of this study result can only be applied to the population that was investigated.

Limitations

Limitations for this study were estimated to be the covariate gender, which was also assumed to be a confounding variable. Generally, more men are diagnosed with CRC than women, and men, on average, are the ones farming and using the pesticides in agricultural communities. The women in these areas may not develop CRC at any higher rate than men or women living outside these areas. The increased incidence for men may not have been due to chlorpyrifos exposure but due only because men are more often diagnosed. Also, the demographic of male and female population in agricultural areas as opposed to nonagricultural areas might have created a limitation. To address the potential limitation of population bias, the entire CRC dataset was used instead of a random sample.

Significance

The results of this study provided information on the amount of chlorpyrifos exposure and the potential impact this has on population health as it relates to CRC development. Results from the study provided information that could be used to aid public health officials and medical healthcare professionals in educating these target populations and others living in agricultural communities, on the possible negative health effects from exposure to chlorpyrifos. Educating the target population and those around them about the impact certain chemicals can have on their health will help decrease illness. It was also the hope that this population, as well as health care providers and local public health officials in these areas, would be more proactive regarding CRC screenings and overall general health. Educating communities on environmental health impacts can increase the opportunity to be proactive and increase their health literacy.

Chlorpyrifos is the leading pesticide used on corn and soybeans (Environmental Protection Agency, 2018). Corn and soybeans are the two largest yielding crops for Ohio agriculture, and this study provided needed information for those living in these areas regarding the use of chlorpyrifos and the health impacts associated with continued exposure. Continued research and information are necessary for the foundation and creation of new public health education programs that promote colorectal health initiative in these populations in Ohio and throughout the United States. The findings from this study help provide the potential foundation to enable those living in agricultural communities to make educated decisions regarding their health and environment. It was also the hope that this study would drive public health officials and policy makers to implement more stringent policies against the use of hazardous chemicals on food crops and collaboration between agricultural agencies and chemical pesticide companies to investigate safer alternative pesticide options. The potential community health improvements and more strict public policies on harmful chemical pesticide use that could be produced from this study promote significant positive social change

Summary

CRC rates continue to increase in the United States, Ohio included. While some risk factors have been identified, like smoking and other lifestyle choices, there are potential environmental factors that may contribute to the development of CRC. One specific environmental factor is the chemical pesticide, chlorpyrifos. At first glance, the rates for CRC appeared to be higher in agricultural counties than nonagricultural counties in Ohio. It was in the top three cancer-related deaths for nearly 50% of all counties in Ohio. In this study, I investigated the possible association between exposure to chlorpyrifos and the development of CRC in agricultural communities in Ohio. In previous studies conducted in other countries, such as Brazil and Italy, researchers investigated exposure to chlorpyrifos and other pesticides in relation to various cancer types. Although my study's focus was on the relationship between exposure to chlorpyrifos and CRC for entire population in Ohio, other researchers have investigated associations between exposure to chlorpyrifos and other cancer types, such as breast cancer in women living in agricultural communities. The research was built on the foundation these previous studies have provided and included CRC.

Chapter 2: Literature Review

Introduction

In Ohio, CRC is the second leading cause of death due to cancer (Ohio Department of Health, 2018). Although various risk factors are associated with the development of CRC, further investigation into certain potential environmental risk factors is necessary. Historically, CRC rates in farmers or agricultural workers have been low (Oddone et al., 2014). However, other studies have found that farmers and pesticide workers are at a higher risk for developing CRC, due to exposure to chemical pesticides and insecticides. Chlorpyrifos, an organophosphate pesticide, was discontinued for household use but is still used in commercial corn and soybean farming in the United States and Ohio (Environmental Protection Agency, 2018). Experimental studies on the carcinogenic effects of chlorpyrifos on human cells indicated that organophosphates increase adenocarcinoma cell viability (Suriyo et al., 2015). Exposure to chlorpyrifos has been found to be associated with breast cancer; however, future research with larger samples from a broader geographic area is necessary to examine possible associations with different cancer types (Engel et al., 2017; Ilgaz & Gozum, 2018). My study provided additional information on the environmental risk factors, specifically exposure to chlorpyrifos, associated with the development of CRC.

This chapter will provide an in-depth review of the current literature on the topic of CRC related to exposure to environmental chemical hazards associated with agriculture. The theoretical foundation and conceptual framework of my study, which were based on previous studies and the variables under investigation, will also be discussed at length. I provide an extensive review of current research findings to examine popular methods, the strengths and limitations in previous research study approaches, and the rationale for variables of choice. Finally, the chapter includes a review on the relationship between historical research studies and their impact on this study and how the variables were chosen for investigation.

Literature Search Strategy

I used various research methods to conduct this systematic literature review. Multiple databases were searched to locate peer-reviewed research on the topic of CRC as it relates to environmental and chemical exposures and other potential contributing risk factors for those living and working in agricultural communities. The databases used were MEDLINE and CINAHL, EBSCOhost, and Google Scholar. The MEDLINE and CINAHL search produced 1,204 articles and the Google Scholar search produced 308 articles. Key search terms included *cancer, colon cancer, colorectal cancer, rectal cancer, organophosphate, organophosphate insecticides, pesticides, Chlorpyrifos, agricultural, farming,* and *Ohio*. The search terms were used independently and in various combinations to identify appropriate literature. Additional search requirements included research date ranges from 2014-2019, peer-reviewed full text articles in English. From these database searches, I found a total of 1,512 articles, of which I chose14 to include in the systematic review, with 1,498 discarded. Those articles not chosen for inclusion in this review involved research conducted on other types of cancer, genetic risk factors, screening and treatment barriers, studies conducted on animals, and industrial risk factors. There was one exception regarding different cancer types. One specific research article examined the link between chlorpyrifos, specifically, and breast cancer development in wives of farmers in Iowa and North Carolina. This study was included due to the direct link between the pesticide of interest, chlorpyrifos, and the target populations of agriculture communities. Research conducted on animals was not included as the dietary and lifestyle difference between humans and animals plays a role in the development of CRC and the impact of specific environmental risk factors could vary significantly.

Theoretical Foundation

Fourteen current research articles met specific criteria pertaining to exposure to chlorpyrifos and CRC and were therefore appropriate for inclusion in the systematic literature review for this study. Although none of these articles mentioned any specific theoretical or conceptual framework, various frameworks were implied, and multiple research design methods were used. Those frameworks included the health belief model, life course model, biopsychosocial model, and social-ecological model. The health belief model suggests that a person's belief in the threat of an illness or disease along with their belief in the effectiveness of the recommended health behavior will predict the likelihood the person will change a behavior (Boston University of Public Health, 2018). The life course theory is a multidisciplinary approach that suggests the mental, physical, and social health of individuals throughout their life span and life stage determine health (Association of University Centers on Disabilities, 2011). Life course theory or perspective is another multidisciplinary approach that considers the relationship between a person’s history, social relationships, geographic demography, developmental psychology, biology, and economics as they relate to health and decisions about one's health. The biopsychosocial model considers biological, psychological, and social factors and their complex interactions in understanding health, illness, and health care delivery (University of Rochester Medical Center, n.d.). The social-ecological model considers the complex relationship between the individual, relationships, community, and societal factors (Center for Disease Control and Prevention, 2018)

An example of how the biopsychosocial model was implicated came from the study conducted by Ilgaz and Gozum (2018), who examined colorectal screening and influential factors associated with seeking health care as related to CRC. Factors that contributed to potential screening included having associates in the same agricultural occupation who have sought CRC screening options and health care pertaining to CRC. It was also indicated that those with higher risks for the development of CRC had lower screening rates.

An example of life course theory was implicated by Engel et al. (2017) in their study on chlorpyrifos pesticide exposure rates for wives of farmers in Iowa and North Carolina. The researchers examined individual pesticide exposures over time, as reported though questionnaires. Engel et al. also examined factors associated with women's life span living in areas of higher levels of pesticide exposure being married to farmers. Another example in which life course theory was implied is the study conducted by Lee et al. (2017), who investigated occupational risk factors associated with the development of CRC. These studies associated demographic, social, and economic factors with CRC risk.

The social-ecological model is implicated in multiple studies and was chosen as the theoretical model for this study as well. Salerno et al. (2016) examined communities in Vercelli, Italy where rice cultivation was a primary source of economic stability. Due to the significant economic gain that came from rice paddies, farmers are using higher volumes of pesticides to increase crop yields. This economic gain creates a system of increasing environmental exposures to pesticides for financial gain. Farmers are making decisions that affect the health of not only themselves but those living in the community for economic purposes. Martin et al. (2018) also examined the relationship between increased pesticide usage for the purpose of increasing crop yield, as agriculture is a main source of income for the region. Sritharan et al. (2014) examined regional differences between two communities in Ontario. The communities had different disparities that contributed to the incidence of CRC. The area of Timiskaming had a lower socioeconomic status than the town of Peel. The communities also had varying occupations and population demographics that influenced risk factors associated with CRC.

Conceptual Framework

Although the social-ecological theoretical model was appropriate for my study, there were certain conceptual aspects that could not be explained based on this theory. The social-ecological model has five levels of influence, which include the individual, the interpersonal or social network, the organizational and environmental level, the community and cultural norms level, and finally the public policy level (Okoye, 2016). The concept that socioeconomic status may influence the incidence of CRC should also be included in this study. Those living in agricultural areas depend on crop yields for their livelihood and therefore a bountiful crop yield made possible with the use of chemical pesticides, which may outweigh the potential dangers associated with exposure to chlorpyrifos and other harmful pesticides. Various factors influence this specific population's exposure to chlorpyrifos. Living in an agricultural community and/or farming as an occupation is the main source of exposure to the chemical, but other factors such as age, gender, race, and social influence could also impact the CRC incidence rate.

Those living and working in these areas may know of the possible health hazards associated with exposure to chlorpyrifos, but they may not understand the significance of long-term exposure or how to manage their health accordingly. Studies have found that even though a person may not be working directly with chlorpyrifos they may still develop cancer, as found by Engel et al. (2017), who investigated breast cancer development in the wives of farmers.

Literature Review Related to Key Variables

Based on the topic of CRC incidence for those living in agricultural communities, the literature search key variables that were investigated included CRC, chlorpyrifos, pesticides, organophosphates, agriculture, and farming. Combinations of these variables were found in previous literature and were chosen for investigation in this study for the specific geographic region of agricultural areas in Ohio. Key variables for this study included geographic location or area of residence in Ohio, age, gender, occupation, and CRC incidence. The 14 peer-reviewed research articles identified, on the association between key variables, specifically the organophosphate chlorpyrifos and CRC incidence, were summarized and utilized as a foundation for this research study.

Systematic Review of Research Findings

In reviewing the articles, I found that all the research supported other studies on the key variables. According to Reygner et al. (2016), chlorpyrifos residue found on food is a public health issue. These findings supported the literature review study conducted by Uyemura et al. (2017), which indicated that the most likely route for carcinogens to cause CRC is through ingestion. From the cohort studies, there were significant associations found between chlorpyrifos exposure and the development of breast cancer among farmers' wives, hazard ratios between 1.3-1.9 with 95% confidence interval, as well as increased CRC incidences in agricultural workers (Engel et al., 2017; Oddone et al., 2014). From database research studies, it was found that the amount of pesticide sold in a region had a significant effect on standard mortality rates associated with CRC in agricultural regions of Brazil (Martin et al., 2018). Among organophosphate pesticide exposure, age and tobacco use were found to be significant risk factors also associated with CRC risk (Lee et al., 2017).

The experimental design studies provided new insight on the pathophysiology of CRC. The study conducted by Reygner et al. (2016) indicated that chlorpyrifos exposure directly alters human gut microbiota and Sabarwal et al. (2018) found that organophosphate cause oxidative stress on cells which can lead to cancer formation. Suriyo et al. (2015) conducted an experiment that produced results providing insight on the cell survival signaling pathway that promotes adenocarcinoma growth. It was found that the EGFR/ERK1/2 signaling pathway is involved in chlorpyrifos inducing adenocarcinoma cell H508 growth. When examining the association between chlorpyrifos pesticide exposure and different cancer types, Salerno et al. (2016) found that CRC was the most frequent site of cancer development.

Chlorpyrifos Impact on Cells

Few studies have been done to investigate the effects of chlorpyrifos on specific cells. One experimental study examined six different reactor samples that represented different sections of the human colon. Chlorpyrifos in oil form was introduced to these reactor samples to determine the human gut microbiota response. A non-parametric Kruskal-Wallis test and a Mann-Whitney test were conducted with results indicating that CPF oil exposure was associated with increase in bacteroides and prevoella groups. Bacteria diversity was affected specifically for each section. Results indicated that the strongest effects were seen in the transverse and descending colon and chronic exposure to chlorpyrifos can directly alter human gut microbiota (Reygner et al., 2016). Another experimental study conducted involved an invitro study on the effects of chlorpyrifos on the growth of human colorectal adenocarcinoma. Cell cycle analysis and EdU Incorporation assays were conducted with results indicating that chlorpyrifos increases the phosphorylation of epidermal growth factor receptor which promotes adenocarcinoma growth (Suriyo et al., 2015). In 2018, a study was conducted by Thankur and Mantha, to examine the relationship between pesticides, monocrotophos and chlorpyrifos, and their impact on cell proliferation and free radical production. Chlorpyrifos was found to cause free radical production which leads to oxidative stress, and DNA damage and mutation. It is the oxidative stress and cell mutation that lead to the development of cancer (Thankur & Mantha, 2018).

Pesticide Association with Colorectal Cancer Incidence

Limited studies have been conducted to investigate the association between pesticide, specifically chlorpyrifos, and the development of cancer. One cohort study included 30,594 wives of farmers in Iowa and North Carolina where the wives answered questionnaires regarding pesticide exposure. Of the 30,594 participants, 1,081 women were diagnosed with breast cancer during the follow up period of the study (Engel et al., 2017). A Cox Proportional Hazard regression was conducted with results indicating that long term exposure to chlorpyrifos and other organophosphates is associated with the development of breast cancer. After researchers adjusted for diagnosis in the first five years the estimates were stronger. Although this was a different cancer type the article was chosen due to the direct association with the specific pesticide, chlorpyrifos, for women living in an agricultural environment. In 2017, a literature review on occupational toxicants was conducted by Costa, Miozzi, Teodoro, Briguglio,Raposarda & Fenga to examine roughly 63 studies and many of the findings indicated a correlation between pesticides and the development of cancer. A large cohort study, included in the review, utilized self-administered questionnaires given to 56,816 pesticide applicators to gather detailed information on pesticide exposure and cancer incidence. Of the 50 pesticides identified as occupational toxins examined two, chlorpyrifos and aldicarb, were found to have significant association with CRC (Costa et al., 2017). Another population-based case control study included 887 cases and 11,491 controls to examine cancer development among farmers and non-farmers. Data was collected using medical record admission data and social security filing status data. Crude analysis and crude odds ratios along with generalized linear mixed models and *t* tests were utilized for data analysis. Results of the analysis showed that there were 241 (27.2%) new cancer cases in the farmer case category and 646 (6%) in the non-farmer cases with the single most frequent cancer site being colorectal (Salerno et al., 2016). Another literature review of both historical and current research on chemical pesticides effect on human health, as related to cancer development and other disorders, included three exposure methods, five cancer types, and eight disorders. Crude analysis and crude ratios with 95% confidence intervals were conducted as well as linear mixed models and *t* tests, which resulted in a significant association between pesticide poisoning and oncogenic modulation and exposure causing oxidative stress. Chlorpyrifos, specifically, was found to have a significant association with rectal cancer (Sabarwal et al., 2018). An increase in age was also associated with cancer frequency and CRC cancer was found to be the most frequent site.

Chlorpyrifos Exposure a CRC Risk Factor

The mechanisms of action for these pesticides were that they cause free radical formation that, in turn, lead to mutations and the possible development of cancer. It is because of these mechanisms that farmers are at an increased risk of developing CRC (Kaur & Kaur, 2018). Another recent study included agricultural workers and their CRC risk levels, participation in screening, and influential factors. Results indicated that 89% of the participants have risk levels above or very above average (Ilgaz & Gozum, 2018). Individuals with high risk had low rates of CRC screening and the rates for agricultural workers are influenced by associates in the same field. If a worker knows someone who has gotten a screening test, they would more likely seek screening than a worker who did not have an associate who had obtained a CRC screen. Colorectal screening is lowest among agricultural workers, but when offered information on screening the rates increase (Ilgaz & Gozum, 2018). A population base study in 2014 included 10 health districts and 34,206 cancer cases and 1,832,929 controls using conditional logistic regression analysis methods. Results indicated that those living in areas with high levels of pesticide use have an increased risk of all cancer types, including CRC (Parron et al., 2014). This hazard is not limited to agriculture occupations only but poses a health hazard to the general public as well. A literature review of 83 articles on occupational exposure and CRC indicated that, overall, agricultural workers have a borderline significant increase risk of CRC. One study's results indicated that pesticide applicators have a statistically significant increase risk of CRC (Oddone et al., 2014). Another study conducted the same year included 114 participants from Timiskaming and Peel, Ontario, who were given a questionnaire on previously identified environmental risk factors. These risk factors were obtained through NHANES, JCUSH, Cape Cod Breast Cancer study, Canadian Community Health Study, and Genes and Environment on Lung Cancer Study (Sritharan et al., 2014). The questionnaire was offered to visitors at a community center, with the majority of participant being female. Data analysis was conducted using independent sample *t* tests, One Way ANOVA, and Kolmogorov-Smirnov tests. Results indicated that non-nutritional modifiable risk factors associated with CRC development included tobacco use, alcohol consumption, exposure to pesticides and toxic metals from mining were factors for those living in Timiskaming but different for those living in Peel.

Chlorpyrifos and CRC Mortality

There have been limited studies that have investigated the potential association between chlorpyrifos exposure and colorectal mortality rates. Researchers from a population-based study in Brazil, examined data from the Brazilian Government database and the Ministry of Health. The data was analyzed using a Bayesian model for the determination of standard mortality rates. The results indicated that the amount of pesticide sold in each state had a significant effect on the standard mortality rate (Martin et al., 2018). A literature review conducted by Uyemura et al. included 88 research articles on the relationship between pesticide use and the incidence of CRC in Brazil. Results from this review indicate that, due to the application methods for pesticides, the most likely route for carcinogens to cause CRC is through ingestion. It was also suggested that there was an association between increased chlorpyrifos use in the country and the increase mortality rate for CRC (Uyemura et al., 2017).

Systematic Review of Research Method

Engel et al. (2017), conducted a cohort study to investigate breast cancer association with chlorpyrifos exposure in 32,126 women married to farmers. Lee et al. (2007) utilized the Agricultural Health Study cohort of 56,816 pesticide applicators with no history of cancer

Strengths associated with a cohort design study included that multiple outcomes could be measured, and selection bias could be avoided. Limitations for this type of study design are that they can be expensive and time consuming which make them challenging to reproduce.

Salerno et al. (2016) used a population-based design for their case-control study, that included both farmers and non-farmers and their potential pesticide exposure in Vercelli, Italy. The study included a sample of 11,578 with 887 cases and 11,491 controls. Parron, Requena, and Hernandez (2014) also used a population-based sample method. The sample included 10 health districts where long term pesticide exposure in occupational settings was associated with cancer risk. The study included 34,205 cases and 1,832,969 controls from a population-based sample.

A strength for this type of study is that they are usually less costly and less time consuming. Limitations include possible selection bias. Ilgaz and Gozum, (2018) conducted the only cross-sectional study where CRC risk levels and screening factors were investigated. This study included a sample of 244 agriculture workers ages 50-70 years living in Turkey.

There were numerous data/literature review study designs. Martin et al. (2018) collected data from the Brazilian government on mortality associated with colon cancer and exposure to pesticides. Once data was collected it was analyzed using a Bayesian method to determines standard mortality rates associated with pesticide exposure linked to CRC for the Brazilian population. Oddone et al. (2014) conducted a systematic review of 83 articles from 1976-2012 on CRC and occupational and environmental determinants. Sabarwal, Kumara, and Singh (2018) conducted a review of 16 items including childhood cancer, CRC, breast cancer, Parkinson’s, Alzheimer’s, genetic modification and oxidative stress, and examined their association with pesticide exposure. Sritharan et al. (2014) examined predetermined risk factors and geographic disparities between Timiskaming and Peel Ontario as they pertained to CRC. Uyemura, Stopper, Martin, and Kannen (2017) conducted a systematic review of 88 research articles related to pesticide exposure, as its use had increased over the past three decades, along with an increased incidence of CRC in Brazil. Strengths associated with this type of research design method were the potential large number of studies that could be included and analyzed.

There were multiple experimental study designs included in this systematic review. Suriyo et al. (2015) conducted an experimental study that examined the effects of chlorpyrifos on human adenocarcinoma cell growth. Reygner et al. (2016) designed an experiment that examined six reactor samples that represented each part of the human colon and how chlorpyrifos exposure affects gut microbiota. Thakur, Dhiman, and Mantha (2018) examined A549 cancer cells and oxidative damage due to chlorpyrifos and monocrotophos. Strengths for experimental design studies include a controlled environment and the design can be tailored to specific exposures and outcomes. Limitations for experimental studies include a lack of generalizability and they are usually costly.

Strengths and Limitations of Literature

There were many strengths associated with this systematic review. For the cohort studies all exposure information was collected prior to cancer diagnosis and they had large sample sizes. All the studies included offered an extensive amount of data on individual insecticide use and confounding factors were considered in most of the studies.

The experimental design studies offered new insight on CRC cell growth and development as well as proliferation and signaling pathways. Many of the studies used large sample sizes and multiple instruments and analysis methods to properly analyze all data. The study conducted in Ontario was the first study of its kind in Timiskaming and provided insight on modifiable risk factors associated with CRC development.

Limitation for this review included some studies not considering confounding factors. For the reviews included, most of the studies were cohort designs therefore results were limited to this type of design method. This was similar to the limitation in the Ilgaz and Gozum (2018) study where only those in the age range between 50-70 years were included. The studies that examined specific geographical areas were only able to generalize the results for those populations. Another limitation involved low dose chronic exposure which is difficult to study in humans (Sabarwal et al., 2018). This was similar to other studies with limitations associated with man-made pollutants requiring protracted exposure rates that do not always have immediate carcinogenic effects, thus making it difficult to study (Martin et al., 2018; Uyemura et al., 2017).

Limitations for studies that utilized questionnaires or surveys included potential recall bias. Those studies with a limited number of cases could produce results that were due to chance. Cohort studies used only new cancer cases so those with a previous diagnosis, while it may have been linked to pesticide exposure, were not included in the results. The experimental design studies had unique limitations as they pose difficulty replicating the experiment and results.

Policy Implications

The implications for practice and policy change were fairly straight forward. In the studies conducted on agricultural regions of Brazil, it was suggested that government should create a monitoring system to monitor exposure of certain pesticides that pose human health risks like colon cancer (Martin et al., 2018). Risk evaluations should be conducted to examine the risk for CRC based on occupational exposures (Oddone et al., 2014). There is a need for stricter regulations against the usage of insecticides and other chemicals that are found to be carcinogenic to humans and currently banned in other countries. Many studies imply that education is the key to reducing CRC and other disorders associated with chlorpyrifos pesticide exposure. Education should include the risk factors, both modifiable and non-modifiable, that are associated with CRC, as well as the importance of routine screening for at risk populations.

Key Stakeholders

Key stakeholders involved in the topic of CRC and its association with exposure to chlorpyrifos and other pesticides included residents in farming and agricultural communities, public health agencies, health care professionals, agricultural societies, chemical manufacturing companies, state and national cancer registries, local, state and national government agencies, and agricultural workers and their families.

Summary and Conclusions

CRC rates are increasing worldwide with certain populations posing greater risk factors for the development of CRC as well as other disorders and cancers types. Some of the risk factors identified in association with CRC are tobacco use, age, dietary choices, obesity, and various environmental agents.

Environmental risk factors including pesticides and insecticides have been found to be linked to the development of certain types of cancers. The organophosphate pesticide chlorpyrifos is used in numerous commercial and large-scale agricultural areas throughout the world. Studies have indicated that exposure to this pesticide could be associated with the increase incidence of CRC. Experimental studies have shown that chlorpyrifos is associated with CRC cell growth as well as breast cancer cell proliferation.

The risk factors identified from this systematic review, along with practical implications, should be used by public health professionals and health care providers to create education programs for at risk populations. Key stakeholders associated with the topic of CRC should be educated on these risk factors and prevention measures. Future research should investigate chlorpyrifos residue on foods consumed by humans as well as animals as a possible route for exposure as it relates to CRC development.

Along with community education, government agencies should create surveillance programs that monitor the use of hazardous pesticides, like chlorpyrifos, so that cancer rates and other disorders can be investigated in high usage areas. Governmental agencies, chemical production companies and agricultural workers should also work together to create and/or identify alternative pesticide options that do not have the same harmful health effects that have been found with organophosphate pesticides, like chlorpyrifos.

As was indicated in the literature review, there were various design methods used in previous studies, which were dependent upon the variables being investigated. Based on the results provided from previous studies and the chosen variables for investigation, which included chlorpyrifos exposure, incidence rates of CRC, gender, age, race, and geographic location of residence, I used a quantitative cohort design method. My study design method also included multiple data analysis tests to help answer research questions based on the relationship between the key variables identified.

Chapter 3: Research Method

Introduction

The purpose of my quantitative, cohort study was to examine the environmental factors associated with CRC incidence rates among those living in agricultural communities in Ohio. In the study, I examined the association between the independent variable, exposure to the organophosphate chlorpyrifos, determined by county of residence, and the dependent outcome variable, CRC. Additional covariates included age, gender, and race. The study population included Ohioans diagnosed with CRC, with a target population of those living in agricultural communities. People living in agricultural communities are exposed to different environmental chemicals such as pesticides and herbicides. Although some pesticides have been labeled as carcinogenic and associated with various other cancer types, chlorpyrifos is still widely used commercially on corn and soybean crops in Ohio (Environmental Protection Agency, 2018). With the increasing CRC incidence rates, it is important to identify risk factors for at-risk populations.

This chapter focuses on the study's quantitative methodology and the cohort design. The research design and rationale, internal and external validity, population, sampling methods, inclusion methods, and variable data collection and analysis methods are discussed. The study design alignment with the research questions and problem statement is also presented.

Research Design and Rationale

The secondary data for the study population was obtained from the Ohio Cancer Incidence Surveillance System and the Centers for Disease Control and Prevention SEERs database. Data on chlorpyrifos usage rates were obtained from the U.S. Geological Survey. The database on specific pesticide usage rates is updated annually with estimates in millions of pounds based on crop and year (U.S. Department of Interior, 2016). The U.S. Department of Agriculture also conducts surveillance on pesticide usage and produces a report on specific pesticide use and number of acres treated per state. This information was examined with the variable Ohio county of residence. The cohort study design was appropriate because I examined a group where all members have the same outcome but may have different risk factors. The population in question for this study consisted of individuals who had all been diagnosed with CRC, but there were two different groups within the population, those exposed to chlorpyrifos and those not exposed to chlorpyrifos. A cohort study also allows researchers to examine incidence rates among specific groups.

Methodology

Population

The population under investigation included Ohioans diagnosed with CRC with the target population being those living in agricultural communities. This target population was under investigation due to their exposure to the chemical pesticide chlorpyrifos. Those living outside of agricultural communities would not be exposed to this chemical and therefore served as a control group to compare differences in CRC incidence rates between the two groups.

Sampling and Collection Methods

There were more than 147,000 entries in the data set obtained from the Ohio Cancer Incidence Surveillance System. The entire data set was used for analysis to adequately determine the relationship between exposure to chlorpyrifos and CRC incidence. The dataset included residents from all counties in Ohio, thereby providing the ability to compare CRC rates between agricultural and nonagricultural counties. By utilizing the entire data set, I was able to compare the CRC rates for agricultural counties to overall rates for Ohio and to national rates.

Data Collection

I collected data for this study from the secondary source of the Ohio Department of Health's Cancer Incidence Surveillance System (2019) and the Centers for Disease Control and Prevention, SEER's (2019). Data on the usage rates of chlorpyrifos were collected from the U.S. Geological Survey Estimated Annual Agricultural Pesticide Use (2018).

Data Analysis Plan

The data analysis plan included descriptive statistical analysis. Because I analyzed the entire Ohio CRC population, instead of just a sample, this statistical analysis method was appropriate. The descriptive statistical analysis provided information on the relationship between exposure to chlorpyrifos and CRC incidence rates in agricultural communities in Ohio. It also provided information on any differences between CRC incidence rates for agricultural communities and Ohio as a whole, as well as between Ohio agricultural county rates and national incidence rates. I used various data analysis methods in the investigation into the relationship between exposure to chlorpyrifos and the incidence rates of CRC for those living in agricultural communities. For the quantitative study design, I utilized SPSS (Version 24) to conduct the appropriate data analysis tests. The data obtained from the secondary sources were recoded and examined as needed for appropriate analysis. The independent variable, county of residence, was coded as a continuous variable, number of CRC cases in each county. The counties were then categorized into one of two groups, agriculture or nonagricultural. The two groups were then compared using a Wilcoxon Signed Rank Test to analyze the difference between the two means. The number of cases of CRC in each county were compared to the number of pounds of chlorpyrifos using a Spearman correlation. Results from this test will range from -1 to 1 indicating the strength of the correlation. The closer to -1 indicates a strong negative correlation and closer to 1 indicates a strong positive correlation and zero indicating no correlation (Laerd Statistics, 2018). This provided information for RQ1 "(i.e., Is there a statistically significant association between chlorpyrifos exposure and incidence rates of CRC after controlling for gender, age, and race, for Ohio agricultural communities?)" The incidence of CRC for agricultural counties in Ohio was compared to the Ohio CRC rates mean as well as national rates mean using a Wilcoxon Signed Rank Test. This provided information for RQ2 "(i.e., Is there a statistically significant difference between colorectal cancer incidence rates, after controlling for gender, age, and race, in the United States and agricultural areas in

Ohio?)" and RQ3 "(i.e., Is there a statistically significant difference between colorectal cancer incidence rates, after controlling for gender, age, and race, for the state of Ohio and the agricultural areas within Ohio?)"

The Wilcoxon Signed Rank Test examined the differences between CRC group means. A Mann-Whitney test was conducted to investigate the relationship between the continuous dependent variable, CRC incidences and chlorpyrifos group usage rates. I conducted a Kruskal-Willis test to examine Ohio agricultural county rates and chlorpyrifos usage groups. A Chi-square test for association was conducted to examine the possible association between agricultural county rates and chlorpyrifos usage rates. Logistic regression analysis and simple liner regression analyses were not conducted as the data failed to fit the assumptions required in order to utilize those analysis methods.

Threats to Validity

External Validity

External validity refers to factors that reduce the generalizability of the results. In this study, potential threats to validity could have been caused by selection bias and/or confounding variables. The selection procedures for the sample being investigated included all incidences of CRC in Ohio. A potential confounding variable issue stemmed from the county of residence listed. Although some counties in Ohio are not necessarily considered agricultural, some may have significant farming communities. These counties CRC incidence rates could be related to exposure to chlorpyrifos, but if they are listed as "non-agriculture" they could have been mislabeled and skewed the results. To address this issue, I created a third category to include non-agriculture with farming communities to account for incidence rates in these counties.

Internal Validity

Internal validity refers to how sound the research methods of the study are and how well the research results provide evidence that there is a cause-and-effect relationship between the independent and dependent variables. This threat increases with the number of confounding variables. With the variables being investigated in this study only one presented a possible confounding issue and it was addressed by recoding variables appropriately.

Ethical Procedures

Once the study proposal was approved, an application to move to the data collection phase was submitted to the Walden Institutional Review Board (IRB) for review of the proposed research and methods ethics. In addition to IRB approval, a Data User Agreement for Research Access form for the Ohio Department of Health Ohio Cancer Incidence Surveillance System was completed and submitted to the Ohio Department of Health. After approval was granted by both the Walden IRB (approval reference number 12-23-19-0492032) and Ohio Department of Health IRB (approval reference protocol number 2020-03; 012820), data were accessed and examined.

Any data collected were used for the purpose of this study and accessible to me. Data and analysis results storage was done on private password protected devices. The data being used for analysis were confidential, but any data that had not been so were de-identified so that there would be no potential ethical issues concerning the privacy of those in the cancer registry.

Summary

The methods outlined for my quantitative study included a cohort design using secondary data that were obtained from the Ohio Cancer Incidence Surveillance System. The data used for the variables in question were accessed only after IRB approval from both Walden University and the Ohio Department of Health, and de-identified to ensure ethical standards were met. The variables to be investigated included a dependent variable, CRC incidence, independent variables of county of residence and exposure rates of chlorpyrifos, and covariates of age, gender, and race. These variables were recoded appropriately to accommodate the assumptions for Mann-Whitney test, Kruskal-Wallis test, Wilcoxon Signed Rank test, and a Spearman correlation test. I used various analysis methods identify the relationship between exposure to chlorpyrifos and CRC incidence rates, with the target population being those living in agricultural counties in Ohio. The data analysis testing provided information on research questions “Is there a statistically significant association between chlorpyrifos exposure and incidence rates of CRC, after controlling for gender, age, and race, for Ohio agricultural communities?”, “Is there a statistically significant difference between CRC incidence rates, after controlling for gender, age, and race, for the state of Ohio and the agricultural areas within Ohio?” and “Is there a statistically significant difference between CRC incidence rates, after controlling for gender, age, and race, in the United States and agricultural areas in Ohio?”

Chapter 4: Data Analysis & Results

Introduction

CRC is the second leading cause of death due to cancer in Ohio. CRC is in the top three cancers for almost half of the counties in the state of Ohio. My purpose in this study was to examine the risk factors associated with the development of CRC and whether there was a difference between counties. The research questions were as follows: RQ1 "Is there a statistically significant association between chlorpyrifos exposure and incidence rates of CRC, after controlling for gender, age, and race, for Ohio agricultural communities?" The null hypothesis: "There is no statistically significant association between chlorpyrifos exposure and the incidence rates of CRC, after controlling for gender, age, and race, for agricultural communities in Ohio." The alternative hypothesis "There is a statistically significant association between chlorpyrifos exposure and the incidence rates of CRC, after controlling for gender, age, and race, for agricultural communities in Ohio." The second and third research questions were variations of RQ1. RQ2 "Is there a statistically significant difference between CRC incidence rates, after controlling for gender, age, and race, in the United States and agricultural areas in Ohio?" With a null hypothesis: "There is no statistically significant difference between CRC incidence rates, after controlling for gender, age, and race, in the Unites States and agricultural areas in Ohio." The alternative hypothesis: "There is a statistically significant difference between CRC incidence rates, after controlling for gender, age, and race, in the Unites States and agricultural areas in Ohio." RQ3: "Is there a statistically significant difference between CRC incidence rates, after controlling for gender, age, and race, for the state of Ohio and the agricultural areas within Ohio?" The null hypothesis: "There is no statistically significant difference between CRC incidence rates, after controlling for gender, age, and race, for the state of Ohio and the agricultural areas within Ohio." and the alternative hypothesis: "There is a statistically significant difference between CRC incidence rates, after controlling for gender, age, and race, for the state of Ohio and the agricultural areas within Ohio."

This chapter will highlight the data analysis and results. I used various data analysis methods, including a Spearman correlation, a Kruskal Wallis test, a Mann-Whitney test, a Chi-square test, and Wilcoxon Signed Rank tests.

Data Collection

The data on CRC rates for Ohio counties individually and Ohio as a whole were obtained from the secondary data source, the Ohio Cancer Incidence Surveillance System and CRC rates for the United States were obtained from the Centers for Disease Control and Prevention SEERs database. The chlorpyrifos usage rates were obtained from the U.S. Geological Survey. The dataset for CRC rates for Ohio included 147,039 cases. Table 1 presents the descriptive statistics, outlining county cases, chlorpyrifos levels, gender, race, and age.

Table 1

Descriptive Statistics: County Cases, Chlorpyrifos Levels, Gender, Race, and Age

	N	Minimum	Maximum	Mean	Std. deviation	Variance	Kurtosis	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. error
CountyAGCase	147039	1	3	1.93	.849	.721	-1.598	.013
GenderCode	147036	0	1	.49	.500	.250	-1.999	.013
RaceCode	145208	1	5	1.12	.392	.153	34.306	.013
Chlorpyrifos	147039	1	4	2.02	.879	.773	-.806	.013
Valid *N* (listwise)	145205							

Utilizing all CRC cases in Ohio ensured that the sample was representative of the population and addressed external validity. The data obtained from the Ohio Cancer Incidence Surveillance System included years 1996-2017; however, the data obtained from SEERS included years 1996-2016. When analyzing the differences between Ohio agricultural rates, Ohio rates, and U.S. rates, the cases were transformed into cases/100,000. The U.S. rates data obtained from the SEERS site was already in this format; therefore, I converted Ohio agricultural county rates and Ohio rates to cases/100,000 for ease of analysis by dividing the case counts by the population (Ohio agricultural county combined population and Ohio State population, respectively), then multiplied by 100,000.

Analysis Results

Analysis testing conducted included descriptive statistics (see Table 1), for the entire Ohio CRC case counts, chlorpyrifos usages categories, race, gender, and age at diagnosis, descriptive statistics for Ohio agricultural county CRC case counts and chlorpyrifos usage rates for each county in Ohio (see Table 2).

Table 2

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. deviation	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. error	Statistic	Std. error
Cases	88	160.00	18089.00	1602.0455	2549.88158	4.198	.257	21.663	.508
Chlorpyrifos	88	152.25	82076.70	23919.2676	17722.10140	1.054	.257	1.370	.508
Valid *N* (listwise)	88								

Additional descripting statistics were conducted to investigate the frequencies of gender (see Figure 1), race (see Figure 2), and age (see Figure 3) as they related to the different agricultural groups.

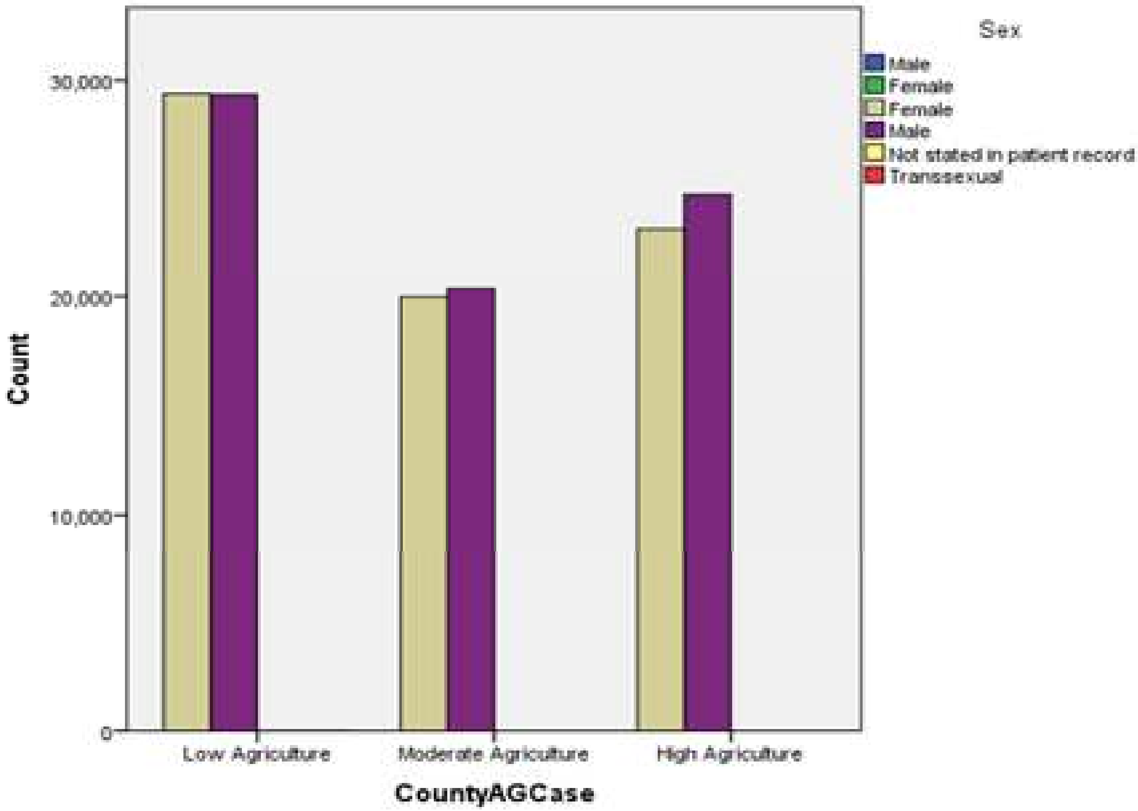


Figure 1. Gender frequency for different county Ag case groups.

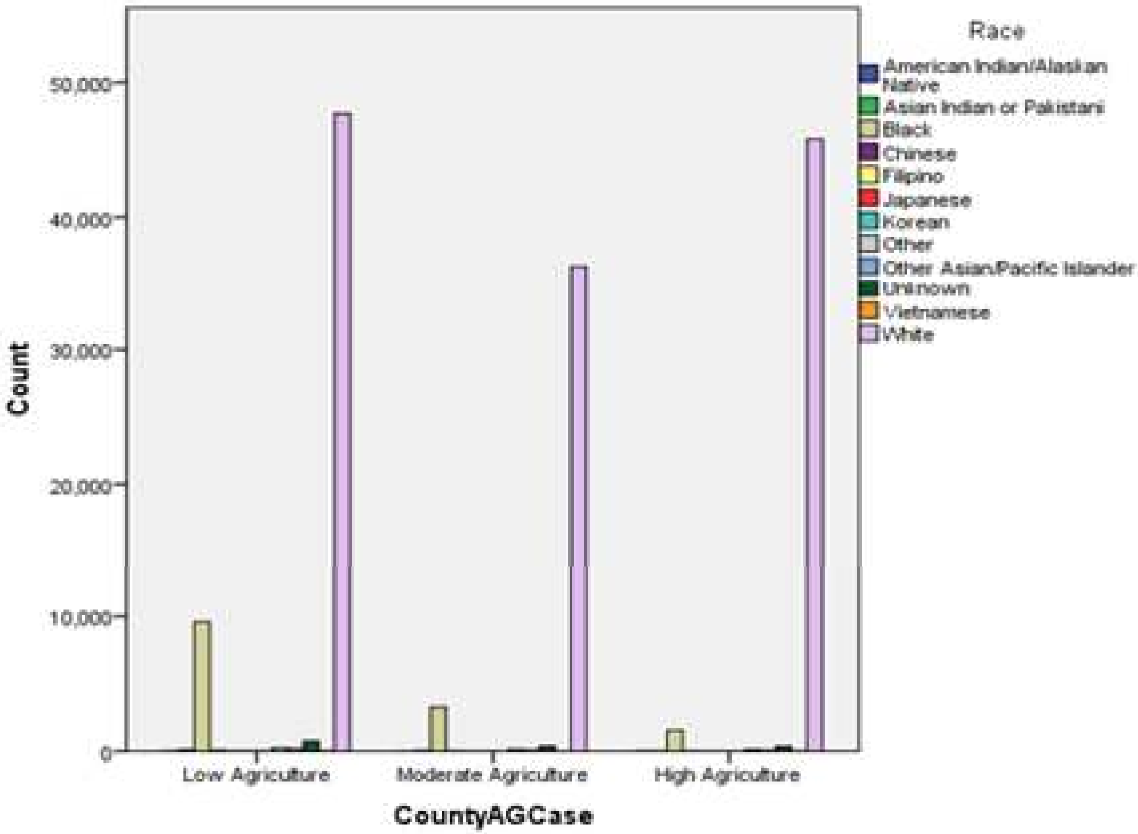


Figure 2. Race frequency for different county Ag case groups.

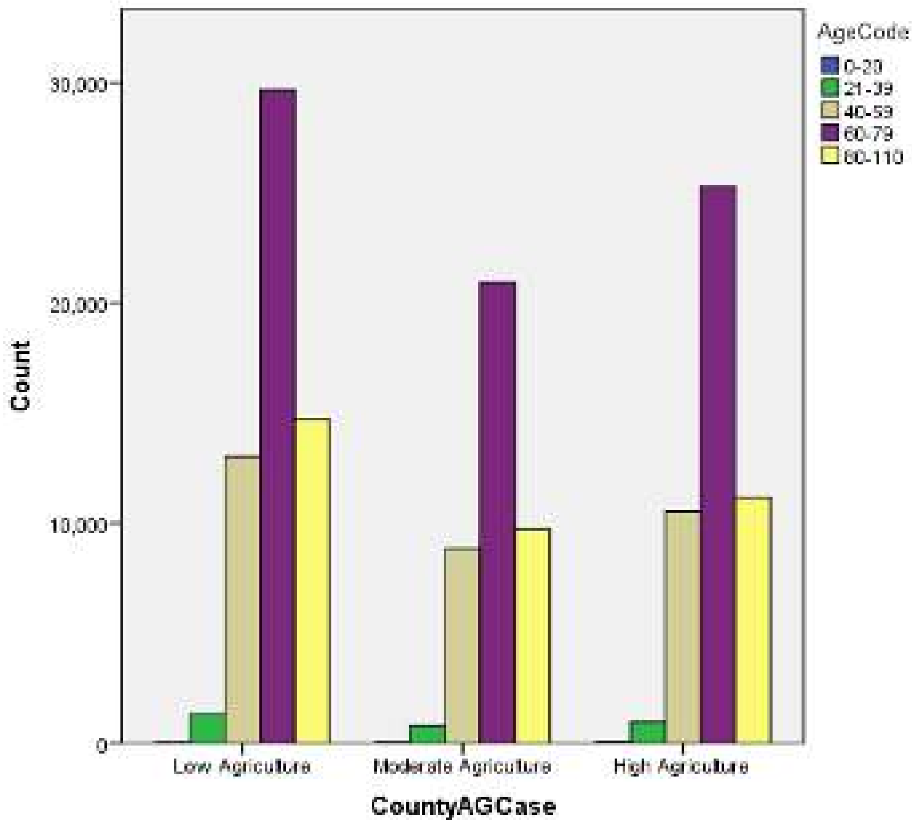


Figure 3. Age group frequency for different county Ag case groups

Also included in the analysis testing were a Mann-Whitney Test (continuous dependent variable and a dichotomous independent variable) to examine the differences between the Ohio county CRC cases and chlorpyrifos groups of high usage or low usage and a Kruskal-Wallis (continuous dependent variable and categorical independent variable) to examine differences between Ohio agricultural county CRC rates and four chlorpyrifos usage groups. A Chi-square test for association was utilized to examine the possible association between agricultural county rates (categorical) and chlorpyrifos usage rates (categorical). A Spearman correlation test was conducted for Ohio county cases (continuous) and chlorpyrifos usage (continuous), to investigate the possible association between chlorpyrifos usage in a county and the county's CRC rates. This test was utilized due to significant outliers in the data that could not be removed. Finally, Wilcoxon Signed Rank test was conducted to examine the possible differences between Ohio agricultural county CRC rates, Ohio CRC rates, and United States CRC rates.

Mann-Whitney Test

A Mann-Whitney test was conducted to help answer the first research question: Is there a statistically significant association between chlorpyrifos exposure and CRC incidence rates for those living in agricultural communities in Ohio? The test allowed me to investigate the association between the continuous dependent variable, Ohio CRC rates, and the dichotomous independent variable, chlorpyrifos usage rates groups of high usage and low usage. This nonparametric test was utilized for its ability to analyze data that is not normally distrusted. The data analyzed in this study failed the normal distribution assumption for a standard *t* test, however it met the assumptions for the Mann-Whitney test for a continuous dependent variable and a dichotomous independent variable, independence of observations, and the distribution of scores for both groups.

The continuous dependent variable was comprised of all 88 Ohio counties and their corresponding CRC rates for the time frame of 1996-2017. The dichotomous independent variable was comprised of the total combined chlorpyrifos usage amounts from 1996-2017 for each county. These totals were then divided into two groups, high usage of 26000lb/acre-100klb/acre and a low usage rate of 0-25999lb/acre. The 88 different county case counts were analyzed with the corresponding chlorpyrifos usage rates. The Hypothesis Test Summary (see Figure 4) lists a significance value of $p = 0.875$ and the decision of retain the null hypothesis.

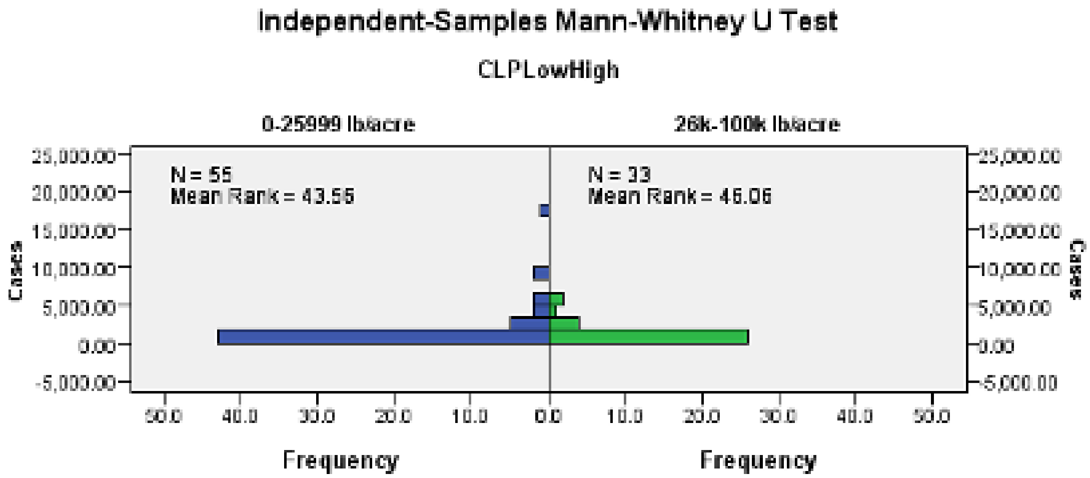
Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of Cases is the same across categories of CLPLowHigh.	Independent-Samples Mann-Whitney U Test	.875	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

Figure 4. Mann-Whitney Hypothesis Test Summary: county cases vs CLPLowHigh

Visually inspecting the histogram results in Figure 5, the data followed the assumption of the distribution of scores. It also provided means for the two groups, with the Low Usage mean at 43.57 and the High Usage mean at 46.06.



Total N	88
Mann-Whitney U	959.000
Wilcoxon W	1,520.000
Test Statistic	959.000
Standard Error	116.022
Standardized Test Statistic	.444
Asymptotic Sig. (2-sided test)	.657

Figure 5. Mann -Whitney Test histogram and output

Kruskal-Wallis Test

The Kruskal-Wallis test was also conducted to further aid in answering the first research question by investigating the difference between groups of chlorpyrifos usage rates and CRC rates. The Kruskal-Wallis test is the nonparametric equivalent of an ANOVA used to determine a statistically significant difference between two or more groups. It was utilized as it met all four assumptions, a continuous dependent variable, an independent variable with two or more groups, independence of observations, and the distribution of scores over the groups. This analysis examined four different chlorpyrifos usage groups, 0-10999lb/acre, 11k -25999lb/acre, 26k-50999lb/acre, and 51k-100k lb/acre with the total CRC county case counts for the 88 counties. The Hypothesis Test Summary results output, in Figure 4, list a significance value of $p = 0.382$ and the decision to retain the null hypothesis.

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of Cases is the same across categories of CLP Groups.	Independent-Samples Kruskal-Wallis Test	.382	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

Figure 6. Kruskal-Wallis: Hypothesis Test Summary

The Kruskal-Wallis report list medians for the four groups, 0-10999lb/acre, 11k - 25999lb/acre, 26k-50999lb/acre, and 51k-100k lb/acre at 617.5, 1018.00, 749.0, and 705.0, respectively. A post hoc test was not necessary as the significance value was above the threshold at $p = 0.382$.

Chi Square Test for Association

A Chi-square test for association was conducted to investigate the association between chlorpyrifos usage rates and county CRC rates. This analysis test was conducted to provide additional information pertaining to the first research question. The Chi-square test for association was appropriate as it met the assumptions of analyzing two categorical variables, the observance of independence or no relationship between the observations in the groups, and all expected cell counts were greater than five (see Table 3).

The variables investigated were county CRC rates in three categories of low agriculture, moderate agriculture, and high agriculture and chlorpyrifos usage rates in four different groups of 0-10999lb/acre, 11k-25999lb/acre, 26-50999lb/acre, and 51k-100k lb/acre. Results for the Chi-square for association test list a Pearson Chi-square significance value of $p = 0.000$ (see Table 4).

Table 3

*Chlorpyrifos * CountyAGCase Crosstabulation*

			CountyAGCase			
			Low agriculture	Moderate agriculture	High agriculture	Total
Chlorpyrifos	0-10999 lbs/acre	Count	46964	1059	699	48722
		Expected count	19468.7	13354.9	15898.4	48722.0
		% within Chlorpyrifos	96.4%	2.2%	1.4%	100.0%
		% within CountyAGCase	79.9%	2.6%	1.5%	33.1%
		% of total	31.9%	0.7%	0.5%	33.1%
	11k-25999 lbs/acre	Count	10267	26419	17108	53794
		Expected count	21495.4	14745.2	17553.4	53794.0
		% within Chlorpyrifos	19.1%	49.1%	31.8%	100.0%
		% within CountyAGCase	17.5%	65.5%	35.7%	36.6%
		% of total	7.0%	18.0%	11.6%	36.6%
	26k-49999 lbs/acre	Count	405	12826	24449	37680
		Expected count	15056.5	10328.2	12295.3	37680.0
		% within Chlorpyrifos	1.1%	34.0%	64.9%	100.0%
		% within CountyAGCase	0.7%	31.8%	51.0%	25.6%
		% of total	0.3%	8.7%	16.6%	25.6%
	50k-100k lb/acre	Count	1119	0	5724	6843
		Expected count	2734.4	1875.7	2232.9	6843.0
		% within Chlorpyrifos	16.4%	0.0%	83.6%	100.0%
		% within CountyAGCase	1.9%	0.0%	11.9%	4.7%
		% of total	0.8%	0.0%	3.9%	4.7%
Total		Count	58755	40304	47980	147039
		Expected count	58755.0	40304.0	47980.0	147039.0
		% within Chlorpyrifos	40.0%	27.4%	32.6%	100.0%
		% within CountyAGCase	100.0%	100.0%	100.0%	100.0%
		% of total	40.0%	27.4%	32.6%	100.0%

Table 4

Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	114965.230[a]	6	.000
Likelihood Ratio	132751.312	6	.000
Linear-by-Linear Association	77542.811	1	.000
N of Valid Cases	147039		

[a]0 cells (0.0%) have expected count less than 5. The minimum expected count is 1875.69.

The Cramer's V reported value is the measure of the strength of the association between chlorpyrifos usage and county CRC cases. The generated value from the Chi-square for association test is 0.625 (see Table 5).

Table 5

Symmetric Measures

		Value	Asymptotic Standard Error[a]	Approximate T[b]	Approximate Significance
Nominal by Nominal	Phi	.884			.000
	Cramer's V	.625			.000
Interval by Interval	Pearson's R	.726	.002	405.048	.000[c]
Ordinal by Ordinal	Spearman Correlation	.755	.001	441.383	.000[c]
N of Valid Cases		147039			

[a]Not assuming the null hypothesis.

[b]Using the asymptotic standard error assuming the null hypothesis.

[c]Based on normal approximation.

Spearman Correlation

A separate Spearman correlation test was conducted to examine the continuous variables for CRC rates and chlorpyrifos usage rates. The Spearman correlation test calculates a coefficient that is the measure of the strength and direction of an association between two continuous variables and provided information pertaining to the first research question. This test met the assumptions of two continuous variables that represent paired observations. A scatter plot of the variables can be seen in Figure 7.

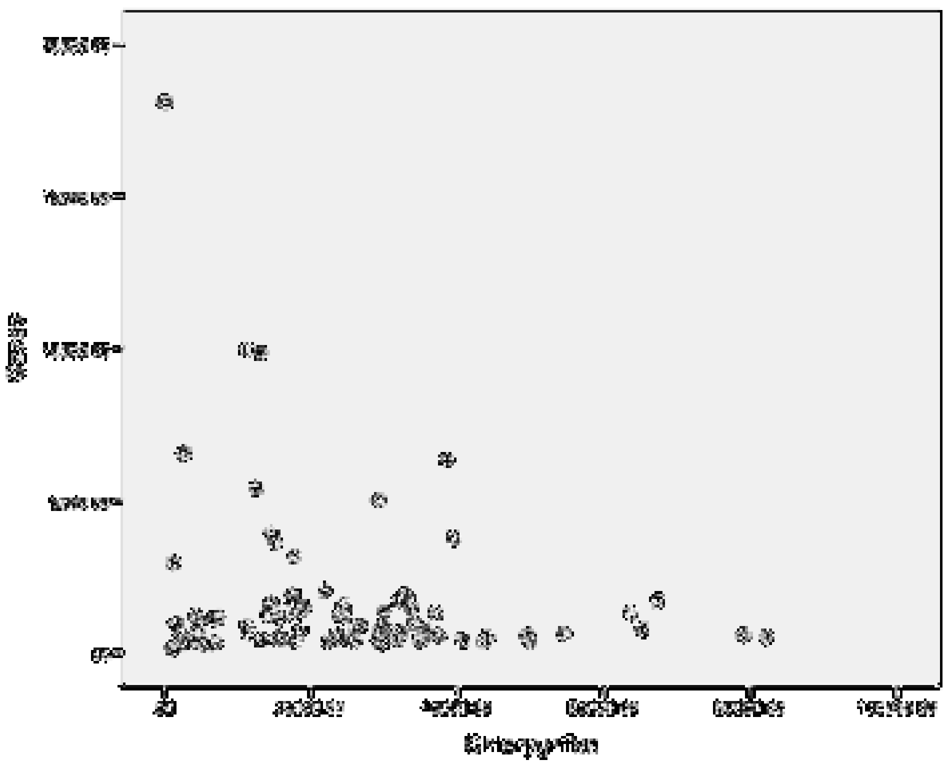


Figure 7. Scatter Plot: county cases & chlorpyrifos usage rates

Table 6 provides the results output from the Spearman correlations test and list a significance value of $p = 0.709$ and a correlation coefficient of 0.040.

Table 6

Correlations: Spearman Correlation CRC Cases vs Chlorpyrifos Usage

			Cases	Chlorpyrifos
Spearman's rho	Cases	Correlation coefficient	1.000	.040
		Sig. (2-tailed)		.709
		N	88	88
	Chlorpyrifos	Correlation coefficient	.040	1.000
		Sig. (2-tailed)	.709	
		N	88	88

Wilcoxon Signed Rank Test

A Wilcoxon Signed Rank Test was conducted to provide information pertaining to research questions two and three: Is there a statistically significant difference between CRC rates in the United States and rates for agricultural areas in Ohio? Is there a statistically significant difference between CRC incidence rates for the state of Ohio and agricultural areas? The Wilcoxon Signed Rank test examines the difference between CRC rates for the United States and CRC rates for agricultural counties, and Ohio CRC rates and rates for agricultural counties. The CRC rates for each year from 1996-2016, were coded as cases/100,000 for Ohio Ag county rates, Ohio CRC rates, and U.S. CRC rates. Rates, if not already in cases/100,000, were calculated by dividing the total number of cases by the population then multiplying by 100,000. In regard the Ohio agricultural counties, the total population was calculated by using the sum of the agricultural counties combined. Ohio rates were based on the population of Ohio for the corresponding year.

Case counts for Ohio total and Ohio Ag counties were obtained from the Ohio Cancer Incidence Surveillance System and the population was obtained by the United States Census Bureau. The U.S. CRC rates, already in cases/100,000, were obtained from the Centers for Disease Control and Prevention SEERS database.

A Wilcoxon Signed Rank test was conducted to examine the possible difference between CRC rates for agricultural counties in Ohio and CRC rates for the United States. Results, shown in Figure 6, list the Hypothesis Summary Test with a significance value of $p = 0.000$ and a decision to reject the null hypothesis, in lieu of the alternative hypothesis, that the difference between the medians is zero.

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The median of differences between CRCRatesUS96_2016 and CRCRatesAGOhio96_2016 equals 0.	Related-Samples Wilcoxon Signed Rank Test	.000	Reject the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

Figure 8. Wilcoxon Signed Rank Test: Ohio Ag rates vs U.S. rates

The Wilcoxon Signed Rank test report lists the median for Ohio agricultural CRC rates at 62.04 and the median for U.S. rates at 46.89, with a median difference of 14.18.

A second Wilcoxon Signed Rank test was conducted to investigate possible difference between CRC rates for agricultural counties in Ohio and CRC rates for Ohio overall. The Hypothesis Summary Test in Figure 9 lists a significance value of $p = 0.001$, with the decision to reject the null hypothesis that the difference between the medians is zero.

Hypothesis Test Summary

	Null Hypothesis	Test	Sig.	Decision
1	The median of differences between CRCRatesAGOhio96_2016 and CRCRatesOH96_2016 equals 0.	Related-Samples Wilcoxon Signed Rank Test	.001	Reject the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

Figure 9. Wilcoxon Signed Rank: Ohio Ag rates vs Ohio rates

The Wilcoxon Signed Rank test report lists the median value for Ohio agricultural county CRC rates as 62.04 and the median for Ohio overall CRC rates as 60.07, with a median difference of 1.86.

Summary

Various statistical analysis tests for association and differences between groups were utilized to answer the research questions: Is there a statistically significant association between chlorpyrifos exposure and CRC incidence rates for those living in agricultural communities in Ohio? Is there a statistically significant difference between CRC rates in the United States and rates for agricultural areas in Ohio? Is there a statistically significant difference between CRC incidence rates for the state of Ohio and agricultural areas? The data collected from secondary datasets was coded into both continuous and categorical variables. The data were not normally distributed therefore nonparametric analysis tests were required. A Mann-Whitney test, a Kruskal-Wallis test, a Chi-square test for association and a Spearman correlation test were all conducted to provide information on the first research question.

The Mann-Whitney test was conducted to determine if there were differences in CRC rates for Ohio counties between dichotomous chlorpyrifos groups of high use or low use. Media rates, 46.06 for high usage and 43.47 for low usage were not statistically significant ($p = 0.875$). The Kruskal-Wallis was conducted to determine if there was a difference in Ohio county CRC rates between chlorpyrifos groups that differed by various levels of usage, 0-10999lb/acre, 11k -25999lb/acre, 26k-50999lb/acre, and 51k-100k lb/acre at 617.5, 1018.00, 749.0, and 705.0, respectively. The results indicated that there was no statistically significant difference in CRC rates for the different chlorpyrifos usage rate groups.

Chi-square test for association and Spearman correlation test were conducted to provide information on the first research question. A Chi-square test for association was conducted between county CRC groups and chlorpyrifos usage groups. All expected cell frequencies were greater than five. Results indicated that there was a statistically significant association between CRC rates and chlorpyrifos exposure, $\chi2(6) = 114965.23$, $p = 0.000$. The association was strong, Cramer's V = 0.625. This supports the alternative hypothesis for the first research question, that there is a statistically significant association between CRC rates and chlorpyrifos exposure. These results were contradictory to the Mann-Whitney, the Kruskal-Wallis, and the Spearman correlation test. The Spearman correlations test was conducted to assess the relationship between the continuous county CRC rates and the continuous chlorpyrifos usage rates. Visual inspection of the scatter plot indicated a non-monotonic relationship. There was no statistically significant correlation between county CRC rates and chlorpyrifos usage rates, $p = 0.709$. The null hypothesis could not be rejected.

Wilcoxon Signed Ranks tests were conducted to help answer the second and third research questions regarding the difference between CRC rates for agricultural counties in Ohio, Ohio overall CRC rates, and U.S. rates. The Wilcoxon Signed test comparing the medians between Ohio Agricultural counties and U.S rates listed a significance value of $p = 0.001$, a decision to reject the null hypothesis that the median difference is zero, and a median difference of 14.18. The Wilcoxon Sign Rank test conducted on Ohio agricultural rates and Ohio overall CRC rates listed a significance value of $p = 0.001$, a decision to reject the null hypothesis that the difference in medians between the two groups, and a median difference of 1.86. These tests support rejecting the null hypothesis in lieu of the alternative hypothesis for both research questions two and three, there is a statistically significant difference between U.S. rates and rates for agricultural areas in Ohio and the alternative hypothesis was there is a statistically significant difference between Ohio rates and rates for agricultural area, respectively.

The proposed covariates, race, gender, and age were also examined, however, the gender ratio for all CRC cases in the data set were approximately equal, 49.3% female and 50.7% male and evenly distributed among the agriculture classifications as they were associated with chlorpyrifos usage rates. Race and age categories among the different groups indicated equal distributions among the different agriculture and chlorpyrifos groups as well.

While the analysis testing conducted provides information to offer answers for the posed research questions, a more in-depth interpretation of the analysis results is needed. In addition, the data collected from secondary datasets and the nonparametric statistical analysis tests, like the Chi-square test for association and Spearman correlation, presented opposing results and both strengths and weaknesses that should be addressed.

Chapter 5: Discussion & Conclusion

Introduction

The main objective of this study was to investigate the relationship between exposure to the chemical pesticide chlorpyrifos and CRC incidence rates in Ohio. CRC is the second leading cause of death due to cancer in Ohio. Chlorpyrifos is the leading pesticide used on corn and soybean crops, which are the largest produced crops in Ohio agriculture. Previous research has provided information indicating that chlorpyrifos is linked to the development of both lung and breast cancers; however, few studies have been conducted to investigate the potential link to CRC. To examine this relationship, I used secondary data from the Ohio Cancer Incidence Surveillance System, the Centers for Disease Control and Prevention's SEERs database, and the U.S. Geological Survey on Pesticide Usage. Quantitative analysis testing, for the chosen variables, was conducted to examine CRC rates in Ohio and chlorpyrifos usage from 1996-2017.

For the first research question, Is there a statistically significant association between Chlorpyrifos exposure and incidence rates of CRC, after controlling for gender, age, and race, for Ohio agricultural communities?, correlation analysis results indicated that there was not a statically significant relationship between chlorpyrifos exposure and CRC rates. This led to the acceptance of the null hypothesis there is no statistically significant relationship between chlorpyrifos exposure and CRC rates in agricultural communities in Ohio. However, the Chi-square for association provided contradictory results indicating that there was a statistically significant relationship between county CRC rates and chlorpyrifos usage in Ohio. These conflicting results could be due to Type

I error. The continuous county CRC rates and continuous chlorpyrifos usage rates were coded into groups to satisfy data assumptions of analyzing categorical variables. Coding continuous variables into categorical variables can increase Type I error, leading to a false positive association and erroneously rejecting the null hypothesis. The Chi-square test was the only analysis test that indicated a rejection of the null hypothesis in lieu of the alternative was appropriate and that there is a statistically significant relationship between county CRC rates and chlorpyrifos usage rates. It is possible that these results were the product of a Type I error due to categorizing continuous variables.

Results also indicated that there was not a gender difference in relation to colorectal cancer incidence throughout Ohio. However, results from means analysis testing that was conducted to help answer RQs 2 and 3 (i.e., Is there a statistically significant difference between CRC rates, after controlling for gender, age, and race, in the United States and agricultural areas in Ohio? Is there a statistically significant difference between CRC incidence rates, after controlling for gender, age, and race, for the state of Ohio and agricultural areas within Ohio?) led to the rejection of the null hypothesis in lieu of the alternative that there is a statistically significant difference between CRC rates in agricultural areas of Ohio and CRC rates for the United States and for Ohio overall.

Interpretation of Findings

After extensive statistical data analysis investigation between the variables of chlorpyrifos usage rates and CRC incidence rates in Ohio counties, results indicate that there is not a statistically significant relationship between exposure to chlorpyrifos and the development of colorectal cancer in agricultural communities in Ohio. These results offer contradictory findings when compared to experimental studies that found chlorpyrifos exposure promotes adenocarcinoma cell growth. However, the experimental study utilized chlorpyrifos oil, which is at higher concentration levels than what would be found in pesticides used in agriculture. This could explain the effects on adenocarcinoma cells. Additional studies that examined exposure to chemical pesticides, such as chlorpyrifos, and the impact on cancer development produced results indicating a correlation with the development of other cancer types like breast and lung cancer. These results were used as a foundation for this research study to examine the possible correlation in the development of CRC. Although for my study, I only examined CRC rates and chlorpyrifos usage rates for counties in Ohio, the analysis results indicate that chlorpyrifos exposure is not correlated with increased CRC rates.

Historically, CRC rates in farmers and/or agricultural workers have been low. Although Martin et al. (2018) found an association between the amount of pesticide sold and mortality rates associated with CRC, this study produced results that indicate that there is not a statistically significant association between chlorpyrifos usage and CRC rates in Ohio counties. Martin et al. examined mortality rates associated with CRC, not the development of CRC. This study should lend support for studies such as that of Martin et al. in that it provides a different perspective and additional information regarding CRC and its relationship with exposure to chemical pesticides such as chlorpyrifos. Salerno et al. (2016) found that when examining the association between chlorpyrifos exposure and cancer rates, colorectal was the most frequent location.

Although these studies do not provide concrete evidence of a direct correlation between chlorpyrifos exposure and the development of CRC, they provide information needed for a foundation for future research. The findings from this study, while indicating that there is not a statistically significant association between chlorpyrifos exposure and CRC rates in Ohio counties, does provide information that will be useful in future research. This study provides statistics for only one agricultural state, which should lend to the foundation for research in other high agriculture states as well as multi-state research.

Results from this study did indicate a statistically significant difference between Ohio agricultural CRC rates and CRC rates in the United States. CRC rates for Ohio agricultural counties have a median difference of more than 14 when compared to CRC rates for the United States. This should lead to additional research into other risk factors potentially associated with CRC within Ohio. Other research should investigate CRC rates and pesticide usage in states with high agriculture, as well as using large amounts of chlorpyrifos, and compare them with those of other states. These results should also warrant examination of potential risk factors that differ for agricultural communities that could be leading to higher CRC rates in these areas when compared to U.S. rates.

Theoretical Framework

The theoretical framework used for this study was the social-ecological model. There are five levels examined in the social-ecological model, which include the individual, the interpersonal or social network, the organizational and environmental level, the community and cultural norms level, and finally the public policy level. The variables investigated included the amount of chlorpyrifos used in each county in Ohio, as well as all CRC cases from 1996-2017. Age, gender, and race were also examined to identify any differences among the different agricultural county groups and chlorpyrifos usage groups. The results indicated that there were no differences among agricultural areas or low, moderate, or high chlorpyrifos usage areas, in regard to age, race, or gender.

Investigating the different environmental aspects of the CRC cases, I found that there was not a statistically significant relationship between CRC rates and the environment in which an individual lived, low agricultural, moderate agriculture, or high agriculture. These variables fit the social-ecological model levels of individual, social network, community and cultural norms, and environment. The final level of public policy is impacted by the results. Although the results indicated that there was not a statistically significant relationship between chlorpyrifos usage and CRC rates in agricultural counties in Ohio, the results did indicate a statistically significant difference between CRC rates for agricultural communities in Ohio and CRC rates for the United States. Policy makers in Ohio should investigate personal and environmental risk factors associated with CRC in Ohio. Public policy and health education promotion on risk factors should focus on reducing CRC rates in Ohio.

Study Limitations

There were limitations in this study. The generalizability of this study is limited in that only one state was examined; therefore, the results cannot be applied to all states with considerable agricultural communities. Also, the appearance of higher CRC rates in agricultural counties, in preliminary investigation, was not found to be accurate. When

CRC rates were investigated relative to population size, the rates for agricultural counties were not statistically significantly different from other counties in Ohio.

Although significant racial disparities have been identified among those diagnosed with CRC, the results from this study did not indicate any racial disparities in Ohio and cannot be applied to other states. Also, this study's results did not indicate a difference between gender and CRC rates in Ohio, which also contradict national statistics. By including all the CRC cases in Ohio from 1996-2017, the results are valid for Ohio only.

Recommendations

This study did not indicate a statistically significant relationship between CRC rates and chlorpyrifos exposure; however, results did indicate a difference between CRC rates in Ohio agricultural communities and CRC rates for the United States. This should be utilized as a foundation for future research to investigate differences between Ohio CRC rates and other state CRC rates, as well as chlorpyrifos usage and other potential risk factors specific to these states. These results warrant a more in-depth look at the different risk factors impacting those living in Ohio and/or other agricultural states.

Future research in Ohio should investigate other potential risk factors, additional pesticide usage as Ohio has significant agriculture, as well as environmental factors associated with manufacturing. Areas with higher rates of CRC, within Ohio, should be investigated at length to determine if there are risk factors unique to these areas.

Study Implications

The results from this study should serve as a foundation for positive social change in each of the social-ecological levels. With analysis results indicating that Ohio CRC rates are higher than U.S. rates, there is a significant need for change in Ohio. Health education programs on known risk factors are imperative and should be created and implemented at both the state and community level. Individuals need to be informed in order to make educated decisions on health. Policy makers need to examine current policies on environmental risk factors unique to their regions, to evaluate areas that could be improved upon. Community input should be considered in these policies to ensure support at all levels. Unless there is support by all levels within a community, policies that impact these areas will not be successful. New strategies will include more stringent policies on environmental waste products produced by both agricultural and manufacturing industries.

Transparency between policy makers, agriculture/industrial partners and community members, regarding environmental wastes and policy regulations should be of the utmost importance. Community members need to be informed and educated on any and all possible risk factors associated with industries in their respective areas.

Implications for positive social change at the individual level will include education programs on CRC risk factors for respective areas. State and local health professionals need to create campaigns that highlight the difference between Ohio CRC rates compared to U.S. rates and potential risk factors specific to respective areas. A focus on why Ohio CRC rates are higher and more investigation on risk factors specific to Ohio is necessary to ensure that CRC rates do not continue to increase. Local health department, in agricultural areas, should create programs that monitor and report pesticide usage and the impacts on health associated with exposure. Communities need to be informed about various cancer rates and hazardous chemical use in their areas. These strategies will create much needed positive changes within communities and cultural norms that impact CRC rates and overall health of community members. Public Health care professionals, medical professionals, and community members will be able to take a more proactive approach to health.

Conclusion

Preliminary investigation into CRC rates in Ohio indicated that there may have been a difference in CRC rates between counties. The focus of my study was to identify risk factors that could be unique to areas with perceived higher CRC rates and the strength of that association between risk factors, contributing to these differences. The results from data analysis for all counties in Ohio, over a 20-year period with a sample of more than 147,000 cases, did not indicate that there is a statistically significant difference between CRC rates for different counties in Ohio. Data analysis results did, in fact, indicate that there is a statistically significant difference between CRC rates for agricultural areas in Ohio and the United States. This poses many questions: what is different about Ohio? Why are CRC rates in Ohio higher? Are there different risk factors for Ohio than other states in the United States? If there are risk factors unique to Ohio, or other states similar to Ohio, it is imperative that they be identified and addressed through improved public health programs and community involvement. If risk factors unique to

Ohio and similar states are not identified, CRC rates will continue to increase, which could lead to CRC becoming the first leading cause of death due to cancer.

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Appendix: Ohio Department of Health IRB Approval

Protocol Number 2020-03
Original Review 01/28/2020
Continuing Review

THE OHIO DEPARTMENT OF HEALTH
HUMAN SUBJECTS INSTITUTIONAL REVIEW BOARD
(FWA00001963, IRB00002180)

ACTION OF THE REVIEW BOARD
(CERTIFICATION)

With regard to the employment of human subjects in the proposed research entitled:

ODH IRB 2020-03: "Impact of Chlorpyrifos Exposure on Colorectal Cancer in Agricultural
Communities in Ohio"

CDC of HHS Federal Project Number (if any):
Principal Investigator: Raymond Panas, PhD
Agency: Walden University

The Institutional Review Board has taken the following action:

☑ Approved ☐ Expedited Review ☐ Waiver of Written Consent
☐ Disapproved ☑ Full Board Review ☐ Exempt
☐ Tabled

Requirements:

Any publication resulting from the approval of this protocol must state the following "This study includes data provide by the Ohio Department of Health which should not be considered an endorsement of this study or its conclusions."

This application has been approved for the period of one (1) year and will expire on January 27, 2021. Renewals are the sole responsibility of the principal investigator. No reminders will be sent.

Additionally, it is the responsibility of the principal investigator to:

1) obtain approval before making procedural changes;

2) maintain the confidentiality of the research participants' identities; and
3) retain a copy of each signed consent form for at least three (3) years beyond the termination of the subject's participation in the proposed activity.

Date: ______________________ January 28, 2020

Signed: ____________________________

CC: Investigator, Division Chief/Bureau Chief