2016

Comparison of Thyroid Disease Mortality between Urban and Rural Populations in Southwest Georgia

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Abstract

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MSN, Walden University, 2008

BSN, Albany State University, 2005

Dissertation Submitted in Partial Fulfillment

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Doctor of Philosophy

Public Health

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Abstract

Twenty million people in the United States have some form of thyroid disease. In 2014, there were 62,980 new cases of thyroid cancer and 1,890 deaths. Water source is a known risk factor for thyroid disease. Pollutants that are known to alter thyroid function can find their way into water sources. The effect of various water sources on thyroid-related mortality has not been determined in the state of Georgia. The purpose of this correlational study was to investigate whether invasive thyroid disease mortality differs between urban participants who drank municipal water and rural participants who drank untreated water in Southwest Georgia. Using the ecologic systems theory, secondary data from the Georgia Department of Public Health and the Department of Environmental Services were analyzed for 179 cases of invasive thyroid disease mortality and corresponding water source. According to the Wilcoxon-Rank sum test, there was no statistically significant difference in invasive thyroid disease mortality between individuals who consumed municipal water and individuals who consumed untreated well water. However, a disproportionate number of cases came from Dougherty County, particularly within rural areas and among women. The positive social change implication of this study was to discover an area of disparity for thyroid disease mortality in the state of Georgia. Larger studies need to be conducted to determine if there is a correlation between water consumption and thyroid disease and to explore the geographical, environmental, and demographic factors associated with cases in Dougherty County.

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Dedication

This dissertation is dedicated to my husband Mr. Nathan R. Childs that has stood with me through all and graduated three times over with me. To my children; Denarris, Dajour, Darryan, Triniti, and Nathan, anything is possible once you set your mind to it. I wish each of you the best with your future endeavors. I love you.

D’

Acknowledgments

I would like to take the time to thank everyone that has assisted me on this journey. Specifically, my husband, who would not let me give up. Thank you Dr. Ferrero, Dr. Morrell, and Dr. Amankwaa for mentoring me during this process. I also thank my mom and dad for believing in me throughout my life; as well as my two sisters that saw me through.

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Chapter 1: Introduction to the Study

Background

According to the Centers for Disease Control and Prevention (CDC), the United States has one of the safest water supplies in the world (as cited in Patil, Cates, & Morales, 2005). This safety record is accomplished through a multistep process that communities use to remove disease causing agents from public drinking water systems. The most commonly used steps for municipal water filtration include coagulation and flocculation, sedimentation, filtration, and disinfection (CDC, 2009). However, in the United States, standards and regulations for private water sources are not as stringent as those for municipal water systems (United States Geological Survey [USGS], 2009).

Approximately 43 million citizens in the United States drink untreated water, including water from private wells, whereas the rest rely on municipal water sources (USGS, 2009). The Federal Safe Drinking Water (1974) Act does not currently regulate private wells. Wells may contain both natural and synthetic contaminants. The USGS (2009) gathered approximately 2,000 samples from private wells and found that more than 20% of the samples contained contaminants that could pose a potential health hazard. In addition, regulated public well systems are disinfected using chemicals. Chemicals used during the disinfection process include chlorine, chloramines, chlorine dioxide, and ozone (CDC, 2009). However, chlorine is known to react to certain organic materials to produce harmful chemical byproducts (National Environmental Service Center, 2012). Both treated and untreated water sources can contain pollutants and

contaminants. Contaminants from these water sources may lead to negative effects on thyroid functions. Thyroid hormones are imperative to the normal development of the nervous system, and increased production of thyroid stimulating hormone (TSH) has been associated with elevated blood pressure (Miller, Crofton, Rice, & Zoeller, 2009). Miller et al. (2009) determined that water source was a potential risk factor for invasive thyroid disease mortality, specifically in Southwest Georgia. However, information on the relationships between consumption of treated and untreated drinking water and the potential association with invasive thyroid disease mortality are currently lacking for Georgia.

Problem Statement

The purpose of this study was to examine the relationship between water sources and invasive thyroid mortality cases in Southwest Georgia. Currently, there are few data on thyroid-related cases other than cancer. The study adds to the knowledge base by focusing on the correlation of drinking water source with thyroid mortality in Southwest Georgia. According to the Georgia's Department of Natural Resources, Environmental Protection Division (GAEPD, 2012), "All waters shall be free from toxic, corrosive, acidic, and caustic substances discharged from municipalities, industries or other sources, such as nonpoint sources, in amounts, concentrations or combinations which are harmful to humans, animals, or aquatic life" (para. 2). Chemicals considered to be toxic pollutants in the state of Georgia include 2, 4-dichlorophenoxyacetic acid (2, 4-b); methoxychlor; and 2, 4, 5-trichlorophenoxy propionic acid (TP Silvex). Additional chemicals labeled as

toxic priority pollutants by the EPA are arsenic, cadmium, Chromium III, Chromium VI, copper, lead, mercury, nickel, selenium, silver, zinc, lindane (Hexachlorocyclohexane [g-BHC-Gamma]), cyanide, and over 80 additional elements (GAEPD, 2012). The above referenced chemicals are xenobiotics that can be found in the untreated water of Southwest Georgia and may affect endocrine function.

Multiple steps have been taken by governmental agencies to ensure that the population has safe drinking water. These steps include coagulation and flocculation, sedimentation, filtration, and disinfection (CDC, 2009). However, despite the implementation of the water treatment process, xenobiotics, including herbicides, insecticides, and medications, still find their way into water sources (USGS, 2009). Ingestion of xenobiotics can alter the biological processes of the body, contributing to a number of health-related issues, including weight gain and obesity (Tremblay, Pelletier, Doucet, & Imbeault, 2004) and chromosomal mutations (Gandhi, Dillon, Nikiforov, Pramanik, & Wang, 2010).

Xenobiotics such as lead, mercury, and certain pesticides in drinking water are known to disrupt metabolism, interfere with the human detoxification process, increase insulin resistance and inflammation, and alter thyroid function (Tremblay et al., 2004). Disruption of thyroid hormone metabolism contributes to metabolic dysfunction and thyroid disease (Smeltzer, 2010). Xenobiotics are stored in human adipose tissue, and when released during weight loss, have been associated with a reduction in thyroid hormones (Tremblay et al., 2004). Gandhi et al. (2010) found that when exposed to

xenobiotics, human chromosomes are susceptible to DNA mutations known to contribute to obesity. Furthermore, cancer-specific Receptor Tyrosine Kinase/Papillary Thyroid Cancer (RET/PTC) arrangements were found in human thyroid cells (Gandhi et al., 2010).

Although it is not currently known if xenobiotics in either well or treated municipal water are associated with actual prevalence of invasive thyroid disease mortality in Georgia, scholars have examined xenobiotics in other geographical areas. Aschebrook-Kilfoy et al. (2012) found that nitrate, as a contaminant in agricultural areas, was associated with the development of thyroid cancer. Winquist and Steenland (2014) found that perfluorooctanoic acid (PFOA), released from a mid-Ohio River Valley chemical plant, had exposed the surrounding community through drinking water, leading to higher risks of being diagnosed with a functional thyroid disease. Despite those studies, which are discussed further in Chapter 2, there is a dearth of published studies on the relationship between water source and thyroid mortality in Georgia. This study fills a gap by providing data on the association between well or municipal water consumption and thyroid-related mortality cases in Georgia.

Purpose of the Study

The purpose of this study was to investigate the relationship between drinking water source and thyroid mortality cases in Georgia. There are potential adverse effects on human thyroid function from pollutants that may be found in drinking water. I explored the effects of water source on thyroid cases in Georgia by investigating whether

there was a difference in counts between urban participants who drink municipal water as opposed to rural participants who drink untreated water. This study contributes to the literature on risk factors and the mortality of thyroid disease.

Research Question

The research question and hypotheses for this study were as follows:

RQ1. Is there a difference in invasive thyroid disease mortality between residents in urban areas who consume municipal water and residents in rural areas who consume untreated well water?

H_0: There is no significant difference in the invasive thyroid disease mortality among residents in urban areas who consume municipal water as opposed to residents in rural areas who consume untreated well water.

H_1: Residents in urban areas who consume municipal water have a lower invasive thyroid disease mortality as opposed to residents in rural areas who consume untreated well water.

Theoretical Framework

The theoretical foundation for this study was based on the ecological systems theory, developed by Bronfenbrenner in the 1970s. The development of humans is based upon five environmental systems: the microsystem, mesosystem, exosystem, macro system, and the chrono system (Bronfenbrenner, 1979). Each subsystem details how environmental factors influence development. However, this theory often varies from culture to culture. I discuss this theory further in Chapter 2 to help explain how chronic

exposure to pollutants from the environment (macro system) can affect chronic disease in the individual (microsystem).

Nature of the Study

In this quantitative study, I used secondary data and correlational research. The correlational research design was used to compare the statistical relationships between two variables. Secondary data helped me to determine if there was a relationship between invasive thyroid disease mortality (dependent variable) and type of water source based on urban/rural residence (predictor variable). I compared the median rank of invasive thyroid disease mortality between the urban population who consume municipal water and the rural population who consume private (well) water. I obtained information pertaining to the number of thyroid disease mortality cases from the Georgia Department of Public Health and information pertaining to the location of private wells within the county from the Department of Environmental Services.

Definition of Terms

Municipal water source: A supply that is treated and maintained by a municipality or other governmental entity that supplies water for at least 25 individuals for a minimum of 60 days per year (EPA, 2013). Municipal water can be further defined as a treated water source that has undergone the disinfection process, usually a multistep process that communities use to remove disease causing agents from public drinking water systems (CDC, 2009).

Rural: The United States Census Bureau (2013) stated that rural communities have a population of 2500 individuals or less. Rural was used to further describe individuals who primarily use a private or raw water source for water consumption.

Thyroid disease mortality: Any medical condition that alters the function of the thyroid gland and sends it into a hypo- or hyperactive state leading to death (McDermott & Ridgway, 2001). This definition includes diagnoses from thyroid cancer and any type of thyroid autoimmune dysfunction as reported by the Georgia Department of Public Health. The data provided by the Department of Public Health in the form of datasets provided the invasive thyroid disease mortality counts and rates for Southwest Georgia from 2003-2012. The information was the submitted for use in the form of an Excel spread sheet.

Well (nontreated) water source: A supply that is not treated and maintained by a municipality or other governmental agency that supplies water for residential use (EPA, 2012).

Urban: According to the guidelines set forth by the United States Census Bureau (2013), an urban population consists of a minimum of 1,000 persons per square mile with surrounding areas consisting of a population density of at least 500 persons per square mile. The term urban also describes individuals who primarily use municipal water sources for water consumption.

Assumptions

The study was based on the following assumptions:

1. It was assumed that information drawn from the literature regarding thyroid disease was reliable and accurate.
2. It was assumed that information drawn from the literature regarding the effects of water pollutants was reliable and accurate.
3. It was assumed that the data collected from governmental agencies were reliable and accurate.

Limitations

The limitations of this study were related to the use of secondary data. I used statistical data obtained from the Georgia Department of Public Health (GDPH) for cases of thyroid disease mortality. These data might be considered a convenience sample of the population because I was only able to access data collected by GDPH, and they may not be complete. The biological nature of autoimmune disorders where genetics and other unknown environmental factors that may not be related to the consumption of drinking water play a role in disease onset remains a confounder.

I used correlational research, which also raised the issue of directionality, and may mean that the findings of this study could not prove a causal link between invasive thyroid disease mortality and type of water source. Only correlation between these variables can be determined. Finally, I have attempted to account for the possible third variable problem because there may be other variables that could be related to the association between thyroid- related mortality and type of water source that were not measured in this study.

Scope and Delimitations

The scope refers to the boundaries of the study. The delimitations refer to how the scope may reduce the strength of the study. Participants that suffered mortality from invasive thyroid diseases, including thyroid cancer and autoimmune disorders of the thyroid gland, were included. However, due to limitations of the dataset, only mortality counts greater than five within each zip code were found in the study. The reason for this limitation was that there were no datasets available that included the variables of water source and invasive thyroid disease mortality, and collection of primary data was beyond the scope of an unfunded dissertation study.

The environmental factor examined in this study was limited to drinking water sources, which necessarily limited the findings to pollutants present in water. The study included participants at least 18-years-old living in Southwest Georgia. Because the study was only limited to adults in Southwest Georgia, this delimited the generalizability of the findings.

Significance of the Study

The incidence of thyroid disorders is increasing, especially among women. Twenty million people in the United States have some form of thyroid disease, at a cost of $4.3 billion health care dollars (American Thyroid Association, 2013). Thyroid disease is associated with bio-accumulative organochlorines (OCs) such as polychlorinated biphenyls (PCBs) and polychlorinated dibenzodioxins (PCDDs) that can seep into the water supply (Turyk, Anderson, & Persky, 2007). Thyroid disease is also associated with

other diseases such as obesity, cardiac disease, and decreased neurological development, providing a significant source of morbidity and mortality (Julvez, Debes, Weihe, Choi, & Grandjean, 2011). Although the EPA takes measures to ensure that the municipal water supply only has minimal contamination, there is no way to ensure that the concentrations remain within safe consumption range in private water sources such as wells, or once dispersed within the water supply. There are 43 million individuals in the United States who drink from unregulated private water sources (USGS, 2009).

This study added data to the relationship between the type of water source and number of thyroid mortality cases in the state of Georgia. The evaluation of thyroid disease mortality and the effects of water source obtained from this study can be used to inform health care professionals, public health officials, and the public of the risks associated with water supplies in Georgia. Risk information associated with water source can be used to educate the public about ways to protect against contaminants that come from drinking water that may impact health.

Implications of Social Change

One of the key objectives in conducting research is to bring forth information that will improve society and the environment as a whole. The findings of the study will contribute to the understanding of whether specific water sources may lead to higher risks for thyroid disease, so that necessary precautions and regulations can be established. Examining thyroid disease mortality and the effects of water source can assist chemical

manufacturers, clinicians, health educators, government officials, and community residents to make decisions that will improve the overall health of the population.

Summary

Although the United States may have some of the safest drinking water in the world (Patil et al., 2005), more data are needed to determine the impact of xenobiotics in the water supply on thyroid function. Exploration into thyroid disease mortality and the effects of water source is necessary to assist public health officials and health care providers in maintaining the health of the population. The ecological systems theory framed this study. Chapter 2 includes further examination of these issues through the literature. Chapter 3 provides details about the association between type of water source and thyroid mortality. Chapter 4 will discuss the settings where the research was conducted, the demographics of the participants, the data collection and analysis processes, and the results of the study. Chapter 5 will discuss the interpretations of the findings, the limitations of the study, recommendations for future research, and implications of positive social change.

Chapter 2: Literature Review

Introduction

In the literature review, I identify research studies and information related to thyroid disease and water pollution. The purpose of this study was to investigate the relationship between drinking water source and invasive thyroid disease mortality in Southwest Georgia. The study could lead to increased awareness of the potential adverse effects of drinking water source on human thyroid function. There are several sections in this chapter, including search strategy, theoretical foundation, pathobiology of thyroid disease, and pollutants found in waters and the effects on thyroid health. Well water and treated municipal water are used to categorize contaminants in drinking water. Finally, I discuss the theoretical foundation and methodological framework.

Pollutants found throughout the environment may alter how the thyroid gland operates (Turyk et al., 2007). Environmental pollutants in water sources include organochlorines (OCs), polychlorinated biphenyls (PCBs), and elements such as cadmium and nitrates. Studies included within this literature review provide evidence of how environmental pollutants are associated with thyroid abnormalities such as hyperthyroidism, hypothyroidism, and thyroid cancer. It is estimated that 20 million people in the United States have some form of thyroid disease, amounting to $4.3 billion in health care (American Thyroid Association, 2013). I used the ecological systems theory to investigate any correlation between drinking water source and invasive thyroid disease-related mortality cases in Southwest Georgia.

Bronfenbrenner's (1979) ecological systems theory was originally developed and used in the field of psychology to assist in understanding how human behavior varies in different settings. Stallones (1983) expanded the theory as early as 1982 to include environmental factors that researchers used in public health studies. The theory includes five subsystems that explain how environmental factors influence the development of communities. I used ecological systems theory to focus on how chronic exposure to pollutants from drinking water may correlate with the development of thyroid disease in exposed individuals.

Literature Search Strategy

I conducted searches using the key terms of *water pollution*, *water and thyroid, thyroid disease, thyroid cancer*, *Graves' disease*, *goiter*, *hyperthyroidism, hypothyroidism*, *thyroid disease and pollution,* and *causes of thyroid disease*. I obtained journal articles, governmental reports, and dissertations by accessing the multidisciplinary databases of ProQuest Central, Google Scholar, and EBSCO Content Select. I collected research studies spanning from 2005 to 2015 and obtained them from peer-reviewed journals, governmental websites, and dissertations. Several articles outside of this range provided background information on the biology of the thyroid gland, pathophysiology of thyroid diseases, and background of the ecological systems theory. In this literature review, I highlight the research gap, namely, the lack of focus on thyroid disease and how water sources affected thyroid disease rates outside of the development

of thyroid cancer. The studies selected focused on environmental and industrial pollutants and their effects on the thyroid gland.

Theoretical Foundation

Bronfenbrenner's ecological systems theory provided the theoretical foundation for the current study. Bronfenbrenner's (1979) ecological systems theory was initially developed to explain how everything within the personal environment affects how an individual grows and develops. The theory was used in the field of developmental psychology but has become readily accepted and used in public health. It is often used to examine how family, political structures, and economy impact an individual, and how these aspects of life may affect the health of people, neighborhoods, and communities. Bronfenbrenner explained how the complexity of overlapping ecosystems affects behavioral development. Bronfenbrenner also described how the interactions of environmental ecosystems affect the health and quality of individuals through investigation of environmental systems. The five environmental levels of the ecological systems theory include the microsystem, mesosystem, exosystem, the macro system, and the chrono system (Bronfenbrenner, 1979).

In this study, I focused on the macro system (pollutants from the environment) and the microsystem (the individual). The independent variable (water) was the source for the contaminants, and the individual was the host for the dependent variable of invasive thyroid disease mortality. The microsystem has a direct impact on a person and refers to the closest influences on an individual, such as interpersonal relationships. The

macrosystem is the farthest realm of the ecological systems theory and refers to the ideological and political factors that influence the microsystem (Bryans, Cornish, & McIntosh, 2009).

The ecological systems theory provided a foundation for understanding the factors that lead to the development of thyroid disease. The ecological systems theory has been used to describe the complexity of factors linked to the development of chronic diseases such as cardiovascular disease and cancer (Krieger, 2001). Many factors affect the development of chronic illnesses, ranging from biological to the type of environment in which a person lives, all of which can be examined by implementing the ecological systems theory. This theory provides multiple levels for the analysis of information and data. The ecological systems theory was used in many facets of public health, including health conditions in humans, genetics, health risk reduction, and environmental health. This theory aided in conceptualizing behavioral, physiological, and environmental factors as related to obesity, HIV risk, and water systems. None of these factors can be fully considered without understanding how each layer affects the other in the development of health issues.

Many researchers have applied the ecological systems theory in their studies. Chikwendu (2004) used the ecological systems theory to understand HIV risk. Chikwendu focused on HIV risk reduction activities such as changing individual behaviors, advocacy, organizational change, and policy development in multimethod programs (Chikwendu, 2004). Human behavior is understood through five layers or

levels of influence and interventions. Interpersonal factors, interpersonal processes, institutional factors, community factors, and public policy can explain human behavior (Chikwendu, 2004). Chikwendu showed how an individual's environmental layers affect the correlation of that person developing or contracting a disease.

Bohensky (2006) used a social ecological systems perspective to explain water management in South Africa in a public health study. Bohensky focused on the macrosystem by taking traditional approaches to water management that cover water resources, ecosystems, health services, the people affected, and the institutions governing these water sources. Bohensky proposed that water management in South Africa should be considered a social ecological system. The social ecological system is a coupled and inseparable system of human beings and nature. According to Bohensky, on one end of the spectrum, people are considered in control of the water system; yet, on the other end of the spectrum, social systems as a construct of the human species, are contained within ecosystems, and human control over ecosystems is nonexistent. These two views provide a meaningful position. There is a complicated relationship between humans and ecosystems. Ecological systems theory provided a framework to explain how a person’s environment affects the individual.

Chikwendu (2004) and Bohensky (2006) provided examples of how the ecological system theory was applied in public health. The layers of the microsystem, mesosystem, exosystem, macrosystem, and chrono system are intricately intertwined. Humans and industrial practices that pollute the ecosystem are the result of human

activity that can all affect the ecosystem. This human activity affects human health and was assessed in terms of thyroid-related mortality. The advent of social epidemiology allowed causal models to evolve from just simple binary models (cause and effect) into more complicated, multilevel models. The evolution enabled the inclusion of various determinants of an event or a phenomenon at the molecular and societal levels in order to formulate a foundation for understanding the complex relationship between human health and the environment.

Pathobiology of the Thyroid Gland

The endocrine system is composed of specialized cell clusters, glands, and a number of hormones. The glands included in the endocrine system are the adrenal, pancreas, pituitary, thyroid, and parathyroid glands. The thyroid gland is located in the anterior part of the neck and secretes thyroxin (T4) and triiodothyronine (T3) (Naraynsingh, Cawich, Maharaj, & Dan, 2014). These hormones affect body tissues through protein synthesis and by increasing metabolic activity. The thyroid gland also produces calcitonin, which is essential for calcium metabolism and bone development. Interruptions of these vital functions by xenobiotics may lead to the development of thyroid disorders. Toxicants may bind to thyroid receptors, displacing the biological hormones needed for proper thyroid function (Miller et al., 2009).

Dysfunction of the endocrine system results from deficiencies within the endocrine glands, the release of trophic hormones, hormone transport, or the target tissue where the hormone is expected to react within the body (Aron, Finding, & Thyrell, 2004).

Disorders are also caused by the hypo or hypersecretion of hormones, hyporesponsiveness of receptors, inflammation, or tumors (Franklyn, 2013). Thyroid diseases are typically caused by hormone overproduction, enlargement, inflammation, or deficiency (Bahn et al., 2011). These disorders ultimately lead to the hypersecretion or hyposecretion of hormones; therefore, disease is often diagnosed through the testing of thyroid hormones.

The additional causes of thyroid dysfunction are attributed to inflammation or tumors. Inflammation may be chronic or acute and often results in the endocrine gland secreting additional hormones (Bahn et al., 2011). Although tumors can occur in any part of the body, pituitary tumors cause abnormal hormone production within the endocrine system (Bahn et al., 2011). Therefore, the disruption of thyroid hormones leads to conditions such as hypothyroidism, hyperthyroidism, and goiters (Bahn et al., 2011).

Enlargement of the thyroid gland is known as a goiter (Gao et al., 2012). Goiters may be caused by a lack of iodine intake or the ingestion of certain foods and drugs. Goiters also occur randomly when the demands for thyroid hormone are increased, for example, during pregnancy, menopause, and adolescence. This form of goiter is known as a nontoxic goiter. A toxic goiter may develop if a nontoxic goiter is left untreated and is most often seen in elderly individuals (Tsai et al., 2006).

The toxic goiter occurs when the thyroid gland is unable to produce enough hormones to meet the metabolic demands of the body, which results in increased mass of the thyroid gland. This increased mass can compensate for mild to moderate hormone

impairment (Burton, 2011). Endemic goiters result from insufficient intake of iodine, which results in an inability to synthesize thyroid hormones properly. Endemic goiters are commonly found in areas with iodine deficient soil and water, such as the Midwest, Northwest, and Great Lake regions of the United States (Burton, 2011). Sporadic goiters often result from the consumption of large amounts of goitrogenic foods and drugs (Cao et al., 2010). Goitrogenic foods and drugs contain products that suppress the production of T4. Drugs that are known to be goitrogenic include propylthiouracil, iodides, aminosalicylic acid, cobalt, and lithium (Cao et al., 2010). Clinical manifestations of nontoxic goiters include an enlarged thyroid gland, stridor, dysphagia caused by trachea and esophagus compression, and dizziness (Burton, 2011). Treatments for nontoxic goiters include thyroid replacement hormones, diet, radiation, or surgery. Radiation and surgery both have been associated with hypothyroidism (Srikantia et al., 2011).

Hypothyroidism is a condition presenting with elevated thyrotropin and low thyroxine levels, resulting in the slowing of metabolic processes (Park, Oh, & Jeon, 2013). When cells in the target organ fail to provide appropriate receptors for the hormone, the organ is said to be hyporesponsive (Mehrabian, Khani, Kelishadi, & Kermani, 2011). This hyporesponsiveness means that the organ is unable to detect the released hormones, and the gland is unable to stop the secretion. Individuals who suffer from hyporesponsiveness will present normal or high blood levels but will show clinical manifestations of hyposecretion. Causes of hypothyroidism are thyroid surgery, radiation therapy, autoimmune disease, and treatment for hyperthyroidism. Symptoms that are

noted in adults include easy fatigability, menstrual disturbances, muscle cramps, hair loss, and stiffness (Cyriac, d' Souza, S., Lunawat, Shivananda, & Swaminathan, 2008).

Clinical manifestations of hypothyroidism occur in both children and adults, and children present with several different symptoms. Characteristics of primary hypothyroidism noted in children include the presence of mental retardation and decreased linear growth. Additional symptoms include weight gain and the development of pleural effusions (Gaitonde, Rowley, & Sweeney, 2012). Hypothyroidism affects energy and metabolism, skin and appendages, the nervous system, the musculoskeletal system, the cardiovascular system, the respiratory system, and the urogenital system. Untreated primary hypothyroidism can lead to myxedema coma, which is characterized by "progressive weakness, stupor, hypothermia, hypoventilation, hypoglycemia, hyponatremia, water intoxication, shock, and eventually death" (American Association of Clinical Endocrinologists [AACE], 2012, p. 1). If hypothyroidism goes untreated, individuals also experience dyslipidemia, cognitive impairment, and also possible infertility (Boucai, Hollowell, & Surks, 2011).

Reid and Wheeler (2005) found that autoimmune thyroid disease was most prevalent in the United States, with a higher percentage of women suffering from hypothyroidism than men. There are 7 times more women afflicted with autoimmune hypothyroidism than men (Reid & Wheeler, 2005). Moreover, it is usually a condition that is permanent, resulting in weight gain, fatigue, cold intolerance, and constipation (Cooper & Biondi, 2012).

Hyperthyroidism is the increased secretion of thyroid hormones by the thyroid gland (Burton, 2011). Causes of primary hyperthyroidism include Graves' disease, cancer, solid hyper secreting nodules, and toxic multinodular goiters. Thyroiditis is another form of hyperthyroidism caused by either the excessive ingestion of thyroid hormones or altered synthesis of the hormone in the body. Signs and symptoms of hyperthyroidism include increased metabolism, heat intolerance, and increased stimulation of the sympathetic nervous system (Burton, 2011). Untreated hyperthyroidism leads to conditions such as atrial fibrillation, congestive heart failure, osteoporosis, and thyroid storm.

In the spectrum of thyroid-related diseases, thyroid storm is considered one of the top critical illnesses. Recognizing and managing the life threatening thyrotoxicosis is important to avoid the high morbidity rate and mortality associated with this disorder. Only 10% of patients are hospitalized for thyrotoxicosis, but the mortality rate linked to thyroid storm is as high as 30% (Burton, 2011). The most usual cause of thyrotoxicosis in cases of thyroid storm is Graves' disease. The thyrotrophic receptor antibodies that lead to excessive and uncontrollable thyroidal synthesis and secretion of thyroid hormones or triiodothyronine mediated Graves' disease (Burton, 2011). Thyroid storms also result from systemic insults such as surgery, trauma, myocardial infarction, severe infection, and pulmonary thromboembolism (Panzer, Beazley, & Braverman, 2004). Discontinuing antithyroid drugs, taking too much iodine, whether by ingestion or intravenous administration, as well as using pseudoephedrine and salicylate, also cause thyroid

storms. Salicylates in particular disproportionately increase free thyroid hormone levels (Calis, Berendsen, Logeman, Sarton, & Aarts, 2010).

Epidemiology of Thyroid Disease

Approximately 20 million people in the United States live with thyroid disease, which translates to health care costs reaching as high as $4.3 billion (American Thyroid Association, 2013). The incidence of thyroid disorders is increasing, especially among women (Pinto & Glick, 2002). In 2002, 5% of the U.S. female population had a thyroid disorder, and 6% had detectable thyroid nodules on palpation (Cooper & Biondi, 2012). Moreover, 15% of the general population was found to be suffering from several abnormalities in thyroid anatomy upon physical examination (Cooper & Biondi, 2012). Among those with autoimmune hypothyroidism, 20% display its subclinical form (Cooper & Biondi, 2012). The prevalence of subclinical hypothyroidism can reach as high as 8.5% in general (Cooper & Biondi, 2012). However, for women older than 60 years, the incidence rate may be as high as 20% (Cooper & Biondi, 2012). The incidence of hypothyroidism is common worldwide, but is most notable in iodine deficient areas such as India (Karmarkar, Pandav, Yadav, & Kumar, 2011). Patients are usually treated with lifelong therapy of levothyroxine once autoimmune thyroid disease is diagnosed (Burton, 2011). This medication has to be titrated for the patients to ensure that they do not develop hyperthyroidism.

The most common type of thyroid cancer is papillary thyroid cancer (PTC), making up 80% of all cases. Follicular thyroid cancer makes up the rest of the cancer

cases. Together, these two types of cancer are termed differentiated thyroid cancer (DTC). One of the reasons behind this increasing incidence is the improved detection of smaller tumors through more regular and higher quality ultrasound detection, as well as fine-needle aspiration (FNA) biopsies (Smith-Bindman et al., 2013). Increased incidence of thyroid cancer is also attributed to more frequent pathologic reporting of incidental microcarcinomas or tumors with sizes of less than 1cm in thyroids removed for benign disease. In addition, other explanations for the rising incidence of thyroid cancer include higher radiation exposure, changes in the population's body mass index, increased usage of fertility drugs, and changes in menstrual cycles (Hannibal, Jensen, Sharif, & Kjaer, 2008). Individuals exposed to external radiation to the head and neck region are more vulnerable to having thyroid cancer.

Thyroid-related mortality has been associated with thyroid cancer, hyperthyroidism, thyroid storm, and Graves' disease. The National Cancer Institute (2014) estimated that there were approximately 62,980 new cases of thyroid cancer and 1,890 deaths from thyroid cancer in 2014. Thyroid cancer is the fastest increasing malignancy in the United States, affecting both men and women. Incidence of DTC has increased across the world and a 2.4-fold increase was determined in the United States between 1973 and 2002. The incidence rate has been rising for the past few decades (Howlader et al., 2012).

Based on the statistics provided by the American Cancer Society's Publication (2014) for the year 2014, approximately 62,980 adults (15,190 men and 47,790 women)

in the United States are at risk for thyroid cancer, and approximately 1,890 (830 men and 1,060 women) patients diagnosed with the cancer will die from it. The incidence rates of thyroid cancer in both women and men have been increasing yearly for the past few decades. The five-year survival rate for thyroid cancer is approximately 98%, and the five-year relative survival rate for papillary, follicular, and medullary thyroid cancers that have not spread outside the thyroid is approximately100%. If the cancer has already spread to the regional lymph nodes, the survival rate goes down to 97%. In addition, if the cancer has spread to other parts of the body, the survival rate goes down further, to 55%. Anaplastic thyroid cancer has a much lower survival rate of 7% (American Cancer Society, 2014). Even with aggressive therapy protocols, such as hyperfractionated radiation therapy, chemotherapy, and surgery, survival rate is less than 10% (Endocrine Web, 2014).

Thyroid cancer incidence and mortality numbers are not always straightforward. Some data have shown incidence to be appreciably increasing for the past few decades, but mortality rates have been steadily declining (La Vecchia et al., 2014) globally. However, the recent global trends in thyroid cancer mortality and incidence using official mortality data from the World Health Organization (1970-2012) and incidence data from the Cancer Incidence in Five Continents (1960-2007) showed that in the United States mortality rates have been increasing. In the United States, mortality rates had declined up to the mid-1980s but then started rising in the years that followed. Mortality rates among women declined in most countries considered, except for the United Kingdom, United

States, and Australia. In these countries, mortality declined up to the late 1990s but started to either level off or increase thereafter. The declines in thyroid cancer mortality around the world except for the United States may reflect both variations in risk factor exposure and changes in the diagnosis and treatment of the disease (La Vecchia et al., 2014).

The United States has had an increase in thyroid cancer rates in recent decades. According to Schneider and Chen (2013), thyroid cancer is the fastest increasing malignancy in the United States, for both males and females. The incidence of thyroid cancer increased by 2.4 times between 1973 and 2002 (Schneider & Chen, 2013). Incidental microcarcinomas are often discovered among 10% to 30% of the population by conducting autopsy studies. Better detection of smaller tumors does not adequately account for the overall increasing incidence of DTC. However, even though there is a rising incidence of DTC, the mortality rate remains largely consistent at 0.5 per 100,000 people (Schneider & Chen, 2013).

According to Goldacre and Duncan (2013), both overt hypothyroidism and thyrotoxicosis lead to widespread systemic effects and are related to increasing rates of mortality. However, the majority of the death certificates that include thyroid diseases did not code thyroid disease as the primary cause of death. Goldacre and Duncan described Oxford area (1979–2010) and national (1995–2010) trends in mortality rates for acquired hypothyroidism and thyrotoxicosis, analyzing all certified causes of death (termed "mentions") and not just the primary reason stated on the death certificate. The focus was

acquired hypothyroidism and thyrotoxicosis in the Oxford region only. Findings showed that mortality for acquired hypothyroidism in the Oxford area declined significantly from 1979 to 2010. Mortality rates for thyrotoxicosis decreased significantly as well. This decrease may be explained by improved care of these thyroid conditions.

The studies reviewed in this chapter demonstrate that there are gaps in the monitoring and reporting of the chemical risk factors for various thyroid conditions, leading to a potential underestimation of the real burden of thyroid dysfunction. The current study fills a gap in the literature to determine the number of mortality cases of invasive thyroid disease in Southwest Georgia. I examined a potential link to exposures via water source and included all reported cases of invasive thyroid disease mortality. The following section describes some of the common pollutants that can enter water sources and known associations with thyroid dysfunction. This review was limited in that it could not capture every possible chemical in water that could be associated with thyroid mortality, and it was outside the scope of this study to analyze the water sources for the presence of thyroid disrupting chemicals. However, the following studies highlighted some known key contributors that could potentially be present in the drinking water that residents of Southwest Georgia may consume.

Pollutants in Water Sources and Effects on Thyroid Health

The Environmental Protection Agency (EPA) is charged with collecting data on the many chemicals that are used in the United States. Numerous chemicals have at least some potential to get into drinking water (Aschebrook-Kilfoy et al., 2012; Winquist &

Steenland, 2014). Drinking water primarily comes from either non-treated wells or treated municipal water sources. For the purposes of this study, non-treated water sources were defined as water obtained from aquifers, ponds, lakes, and wells that have not undergone any type of disinfection process. Treated water sources (municipal) are water that has undergone a multi-step disinfection process to remove potentially harmful disease-causing agents and are also known as municipal water sources (CDC, 2009).

There are several ways in which drinking water can become contaminated. Non-treated water becomes contaminated when contaminants dissolve into rainwater and collect into ponds, lakes, and aquifers. Contamination also occurs when liquid hazardous substances are spilled (EPA, 2011). The Federal Safe Drinking Water Act does not currently regulate private wells.

Treated water undergoes a multi-step process that includes the addition of fluoride, chlorine, and the sedimentation process. However, treated water can also become contaminated with pollutants in several ways, such as a compromised filtration process or sewage overflow (CDC, 2012). Treated water may also contain purposeful additives, such as fluoride.

The following sections analyze findings relating to chemicals that have been found in water that may have an impact on thyroid function. Because many of these pollutants may be found in both water sources, it is not always possible to clearly separate the discussion of studies done on non-treated versus treated drinking water. There are several elements, minerals, and chemicals found in drinking water that may

impact the thyroid, including perfluoroalkyl acids (PFAA), perchlorate, nitrates, mercury, arsenic, and lithium. These components are found naturally in the environment and as the byproducts of manufacturing plants, and are discussed in the following sections.

Perfluoroalkyl Acids

PFAAs are a family of chemicals including perfluorooctanoic acid (PFOA), perfluorooctane sulfate (PFOS), and perfluorononanoic acid (PFNA) that have been associated with toxicological effects (Wolf, Zehr, Schmid, Lau, & Abbott, 2010). PFOA is used in the manufacturing of many consumer products and is known to impact thyroid homeostasis and has shown toxicity in animal studies (Melzer, Rice, Depledge, Henley, & Galloway, 2010). PFOA is not a naturally occurring compound, yet it is detectable in the blood of most individuals who reside in industrialized countries (Steenland, Fletcher, & Savitz, 2010). Human exposure to PFOA usually occurs through introduction into the circulatory system primarily through drinking water. PFOA is usually detected in finished drinking water and drinking water sources that have been affected by releases from industrial facilities and wastewater treatment plants, but has been found in waters with no known point sources. The known half-life of PFOA is about three years; it cannot be metabolized and is not readily excreted. Known adverse effects of ingesting PFOA are the formation of various tumors, as well as neonatal death (Steenland et al., 2010). PFOA has been associated with toxicity to the endocrine system, immune system, and liver (Melzer et al., 2010). PFOA inhibits iodide uptake, resulting in the thyroid gland failing to function properly (Schreinemachers, 2011).

In 1951, PFOA was released from a mid-Ohio River Valley chemical plant for over 50 years. The chemical was released into the air and into the Ohio River. The chemical eventually found its way into the ground water and the municipal water supply. Winquist and Steenland (2014) studied 32,354 community members and plant laborers to determine the effects of PFOA exposure on thyroid disease. Adults who consumed contaminated drinking water had 20 times more PFOA levels in their blood as compared to the general United States population. Blood samples obtained from 10,725 children between the ages of 1-17 indicated that they were 1.4 times more likely to develop thyroid disease.

Winquist and Steenland (2014) analyzed health surveys and measured yearly serum PFOA concentrations for each participant starting at birth or in 1952, depending on which came later. They utilized the Cox proportional hazard models, which are categorized by birth year, to evaluate if adult thyroid disease was affected by time-varying yearly or cumulative (sum of annual estimates) estimated PFOA serum concentration. They controlled for sex, race, education, smoking, and alcohol use. They found that 3,633 participants had reported functional thyroid disease, which excluded neoplasm, congenital disease, nodules without functional changes, cysts, and unspecified type. Those with reported functional thyroid disease were validated through the review of medical records. PFOA exposure was linked to both hyperthyroidism and hypothyroidism among female participants, and sub analysis suggested an increased risk of hypothyroidism among men (Winquist & Steenland, 2014). Mortality rates were not

measured in this longitudinal retrospective study, but plant workers who had died prior to the start of the study were included if their information was made available by proxy.

These findings suggested that levels higher than the national average of 4.0 micrograms per liter of PFOA exposure were linked to incident functional thyroid disease, with 85% of the self-reported functional thyroid disease cases being confirmed via medical record review. This large cohort had a PFOA exposure rate of more than 20 nanograms per milliliter via water consumption. Other studies have confirmed the risk of PFOA exposure for thyroid dysfunction.

PFOA and PFOS exposure are confirmed risk associations for thyroid function. Melzer et al. (2010) sought to establish a relationship between PFOA and PFOS concentrations and the prevalence of thyroid disease among the general population in the United States. Melzer et al. found that concentrations greater than four nanograms per milliliter were associated with a 31% prevalence of thyroid disease as diagnosed by a physician or healthcare provider. Individuals in the fourth quartile had PFOA levels greater than 5.7 nanograms per milliliter. There was an association found between thyroid disease and men who had PFOS levels $\geq$ 36.8 ng/mL. However, there was no significant association among women. Even though the findings revealed that higher concentrations of serum PFOA and PFOS were linked to current thyroid disease in the Unites States general adult male population, a limitation of this study was that no details were provided about the specific thyroid diseases that participants were diagnosed with and that only one serum sample was taken to measure the levels of PFOA and PFOS concentrations in

the participants. Further studies should also look at the relationships of these substances to thyroid mortality rates.

A multivariate regression analysis to explore the relationship between PFAAs and reported thyroid disease among environmentally exposed children was conducted by Lopez-Espinosa, Mondal, Armstrong, Bloom, and Fletcher (2012). The investigators used historical information about emissions, pharmacokinetic modeling, and residential histories to model *in utero* concentrations of PFOAs, as well as questionnaires on diagnosed thyroid disease of children living near a Teflon plant in Mid-Ohio Valley in the United States. Subjects were included if they had consumed water from contaminated water districts and private wells, and they were matched to mothers with pregnancy data to model *in utero* exposures, based on data on serum levels of TSH and TT4 from the C8 Health Project in 2005–2006 to substantiate subclinical thyroid disease.

Lopez-Espinosa et al. found an odds ratio of 1.44 for thyroid disease, particularly for hypothyroidism. This study had several strengths, including the large sample size, *in utero* modeling, and serum measurements of some thyroid indicators, but lacked the primary measurements of PFOA concentrations actually consumed in water. Another limitation came from the cross-sectional design, because it hindered the determination of the time sequence between PFAA exposure and outcome, and potential recall bias from self-reported thyroid disease. The estimated fetal thyroid level data provided useful surrogate information about presumed fetal exposures, and their results were in line with other reported correlations with PFOA and thyroid disease (Melzer et al., 2010).

The overall occurrence and population level exposure to PFOAs from drinking water is unknown (Kim et al., 2011), but continued exposure to even relatively low concentrations in drinking water may be significant, particularly for sensitive populations. Infants are particularly sensitive to PFOA's developmental effects because their total exposure through breast milk from mothers drinking contaminated drinking water or preparing milk formula with contaminated drinking water is higher than in adults who drink the contaminated water themselves (Kim et al., 2011).

Findings by Fletcher et al., Kim et al., Lopez-Espinosa et al., Melzer et al., and Winquist and Steenland indicate that consumption of PFOA-contaminated waters could negatively affect thyroid function and increase vulnerability to thyroid diseases. However, there is a dearth of literature establishing the relationship between PFOA and thyroid mortality rates.

Perchlorates, Thiocyanates, and Nitrates

Perchlorate is a naturally occurring and synthetic inorganic salt used to produce products such as rocket-fuel, military explosives, fireworks, and gunpowder. Perchlorate has been found to prevent the uptake of iodide by the thyroid gland (Srinivasan & Viraraghavan, 2009). Iodide is necessary for the synthesis of hormones in the growth of fetuses and neonates and critical to proper functioning of the thyroid gland (Zewdie, 2010). Exposure to perchlorates through drinking water was therefore a risk for thyroid hormone disruption (Zewdie, 2010). Nitrates are naturally occurring and are introduced into water sources through various routes such as animal waste, fertilizer, and human

sewage (EPA, 2012). Once absorbed, nitrates are converted into nitrites. The greatest use of nitrates is as a fertilizer (Ward et al., 2010), and therefore nitrates pose a risk to well water sources. Nitrates alter the uptake of iodide within the thyroid, which leads to alterations in thyroid function (Ward et al., 2010). However, findings on thyroid disruption by nitrates have been controversial. Thiocyanate, found in cigarette smoke and some *Brassica* genus vegetables, can act as an inhibitor of sodium/iodide symporter (Leung et al., 2014). Thiocyanate exposures during pregnancy could reduce thyroidal iodine uptake in the mother, leading to decreased thyroid hormone synthesis (Leung et al., 2014).

Cao et al. (2010) examined the effects of perchlorate, thiocyanate, and nitrates on the thyroid function of 92 infants by examining the correlation between the models of exposure urinary perchlorate, nitrate, iodide, and thiocyanate and T4 and TSH levels. Participant samples came from data obtained from the Study of Estrogen Activity and Development. Urinary samples were obtained via urinary collection bag or compressed diaper. The researchers analyzed the urine samples for levels of determinants for perchlorate (0.05 μg/L), nitrate (500 μg/L), thiocyanate (10 μg/L), and iodide (0.33 μg/L). Then they used a mixed linear model to analyze each chemical independently. Cao et al. found that there was a positive association between perchlorate, thiocyanate, and nitrate with the urinary thyroid levels. Infants who had higher concentrations of perchlorate, nitrates, or thiocyanate in their urine also had higher levels of TSH, which implies that infants exposed to these three things may be at risk for developing hypothyroidism (Cao

et al., 2010). Limitations of the Cao et al. study were its relatively small sample size and focus on children and not adults. Another limitation was that the study did not assess the chemicals in drinking water. The significant correlation between perchlorate, nitrates, thiocyanate, TSH, and T4 in that study provided evidence that perchlorate had the ability to disrupt thyroid hormones.

Aschebrook-Kilfoy et al. (2012) conducted a study with 2,543 participants within the Pennsylvania counties of Lancaster, Chester, and Lebanon to determine any correlation between nitrates found in well water and thyroid disease. Nitrate levels were measured in well water, and the ingestion of nitrates was estimated based on the amount of water that the participants drank. Outcomes measured included clinical hypothyroidism, clinical hyperthyroidism, subclinical hypothyroidism, and subclinical hypothyroidism. Aschebrook-Kilfoy et al. found significant subclinical hypothyroidism in women who ingested nitrate concentrations greater than 6.5 milligrams per liter. There was no correlation found for clinical hypothyroidism and hyperthyroidism among women and no significant correlation subclinical or clinical thyroid disease among men. There were some limitations to this study. The nitrate measurements of wells were not randomized, no residential history was obtained from the participants, and there was no record of participants' daily water intake. However, these results suggest that exposure to nitrates in drinking water may adversely affect the thyroid.

Nitrate has been found in certain vegetables, and this could compete with the uptake of iodide by the thyroid, ultimately affecting thyroid function. Ward et al. (2010)

assessed the effects of nitrate intake from municipal water supplies and from eating nitrate-containing vegetables on thyroid cancer risk, self-reported hypothyroidism, and hyperthyroidism among 21,977 women residing in Iowa. Participants had been drinking from the same water supply for more than a decade. Ward et al. measured nitrate ingestion by utilizing the public database of nitrate measurements in food and a food frequency questionnaire.

Participants experienced a 2.9 % increased risk of thyroid cancer. Longer consumption of water containing over five mg of nitrate was linked to higher risk of thyroid cancer. No link was found between nitrate intake from drinking water and prevalence of hypothyroidism or hyperthyroidism. Increased nitrate intake from consuming cruciferous vegetables such as broccoli, cabbage, kale, and cauliflower was also associated with an increased risk of thyroid cancer (Ward et al., 2010). Additionally, nitrate in vegetables was associated with a higher prevalence of hypothyroidism. These findings indicate that ingestion of nitrates by water or food is a risk for the development of thyroid cancer and hypothyroidism in adult women. Strengths of this study include the retrospective study design and the use of data sample analysis from the same laboratory. Ward et al. focused on drinking water for one year, although participants consumed water from the same drinking source for more than ten years. It was unknown how many participants obtained water and vegetables outside of the study area. These studies indicate that the ingestion of nitrates is a risk for thyroid dysfunction, including thyroid cancer.

Polyhalogenated Chemicals and Phthalates

Phthalates have been associated with thyroid agonist activity in surface waters in China (Hu et al., 2013; Shi et al., 2012). Shi et al. (2012) assessed the existence of phthalate esters and their toxicity in both treated and untreated drinking water from five cities of eastern China. The tests were conducted using an *in vitro* CV-1 cell-based reporter gene assay. They also tested the water from various phases of drinking water processing such as source water, finished water from waterworks, water from the tap, and boiled water from the tap. They used quantitative methods to identify the responsible compounds, concentrations, and toxic equivalents of several phthalate esters including diisobutyl phthalate (DIBP), di-n-octyl phthalate (DNOP), and di-2-ethylhexyl phthalate (DEHP). The majority of the water samples exhibited thyroid antagonistic activities, with phthalate accounting for 84-98% of the antagonistic properties found in the water samples. Approximately90% of phthalate esters and thyroid antagonistic activities can be eliminated through waterworks treatment processes such as filtration, coagulation, aerobic biodegradation, chlorination, and ozonation. Phthalate esters can also be removed by boiling the drinking water (Shi et al., 2012).

Organochlorines (OCs) are polychlorinated chemicals that are commonly found within many herbicides and disinfection agents, some of which can be used in the water-cleaning process (Julvez et al., 2011). Julvez et al. (2011) investigated the relationship between OC exposure and thyroid function during early development using a cohort of 182 children. Julvez et al. determined that exposure to OCs was associated with a

decrease in resin T3 uptake ration, a blood test that measures the transport of thyroid hormone in the blood. The decrease in resin T3was associated with decreased neurodevelopment as measured by neuropsychological tests (Bayley scales and copying block tests) (Julvez et al., 2011).

Turyk et al. (2007) analyzed a random sample of participants who took part in the 1999-2002 National Health and Nutrition Examination Survey to determine associations between thyroid hormones and exposure to polychlorinated biphenyls (PCBs) and polychlorinated dibenzodioxins (PCDDs). Turyk et al. studied the relationships of total T4 and TSH with PCBs, dioxin-like toxic equivalents (TEQs), and p,p'-diphenyldichlorocthene (DDE) in adult participants without thyroid disease who participated in the 1999-2002 National Health and Nutrition Examination Survey. The researchers found inverse associations of total T4 with exposure to TEQs in both sexes, with stronger associations in females. Effects were stronger in older adults, with negative associations of T4 with PCBs and TEQs, and positive associations of TSH with PCBs and TEQs in older women, and a negative association of TSH with PCBs in older men. They also found a dose-dependent decrease in total T4 with exposure to TEQs, especially among women. Those data indicated that older adults were more at risk for disruption of thyroid hormone homeostasis by OCs than younger adults and that females were more at risk than males (Turyk et al., 2007).

Schell et al. (2008) sought to determine an association between chronic exposure via treated water systems and breast milk to POPs including PCBs, DDE, mirex, and

hexachlorobenzene (HCB) and thyroid hormone levels in an adolescent population. Significant changes were noted in thyroid hormones with consumption levels greater than 0.2 parts per million of PBCs.

PCB and HCB had positive correlations with a significance for PCB in non-breast fed adolescents of 0.431and 0.084for HCB. Exposed adolescents had a decrease in thyroid function as evidenced by alterations in thyroid hormone levels, indicating an increased chance of developing hypothyroidism (Schell et al., 2008). These findings were supported by Tillet (2008) who found that POPs reduced the function of thyroid hormones in an adolescent population. Evidence provided by these two studies support the hypothesis that cumulative exposure to POPs negatively affected thyroid function.

OCs have been associated with a dose-dependent decrease of T4, particularly in older adults (Turyk et al., 2007). Turyk et al. analyzed a random sample of participants. Turyk et al. conducted a cross-sectional survey with a random sampling of secondary data of participants with exposure to bioaccumulative OCs, including PCBs and PCDDs primarily through food source. They examined the relationships of total T4 and TSH with PCBs, dioxin-like toxic equivalents (TEQs), and p, p'-diphenyldichlorocthene (DDE). PHC exposure from a primarily seafood diet has been linked to the reduction of circulating T3 and TBG concentrations that lead to the symptoms of hypothyroidism (Dallaire, Dewailly, Pereg, Dery, & Ayotte, 2009).

Dichlorodiphenyltrichloroethane (DDT) is an OC pesticide used throughout the world for malaria control since the 1940s (Delport et al., 2011). Although the pesticide

has been banned in the United States for many years, both DDT and its by-product dichlorodiphenyldichloroethylene (DDE) are still found in soil samples. DDE is then transferred into groundwater as it seeps through the soil and drains into rivers, lakes and ponds. Long-term exposure to OCs may alter thyroid hormone homeostasis through interaction with the proteins that carry thyroxine. Retinol binding protein is transported by transthyretin (TTR), the same protein that carries T4 (Delport et al., 2011). Delport et al. analyzed male subjects, dividing them into exposed and not exposed categories based on serum concentrations of DDT isomers. Findings indicated that long-term exposure to DDT/DDE was associated with decreased retinol-binding protein, TTR, and reduced plasma levels of thyroid hormones.

Polybrominated diphenyl ethers (PBDEs) are used as flame-retardants in the manufacturing of many products and can be introduced into the human system through food, water, and handling products that contain PBDEs (Ibhazehiebo et al., 2011). Ibhazehiebo et al. found that several PBDE congeners could have a disruptive effect on the TH system by partial dissociation of TR from TRE acting through TR-DBD and, consequently, may disrupt normal brain development. The above studies demonstrated that POPs that can be found in water, such as polyhalogenated compounds and phthalates, pose a risk for disruption of thyroid hormones.

Metals and Other Elements

Certain elemental metals are linked to thyroid disruption. Some of these elements and metals are found naturally within drinking waters, and some are deposited in the

water supply through emissions. Mercury is an elemental chemical known to affect the thyroid gland (Mahaffey, Meiller, & Tan, 2009; Schell et al., 2008). Mechanisms of mercury toxicity include cytotoxicity in endocrine tissues, accumulation of mercury in the endocrine system, interactions with sex hormones, up/down regulation of enzymes, and changes in hormone concentration. Sources of environmental exposure to mercury include the burning of coal, alkali and metal processing, agricultural pesticides, and mining of gold and mercury (Mahaffey et al., 2009). The thyroid system of post mortem mineworkers had altered levels of thyroid hormones after exposure to MeHg, HgCl2, or Hg vapors. Although there are no coal or gold mines in Southwest Georgia, exposure to MeHg via agricultural pesticides used in the area may occur (Mahaffey et al., 2009).

Copper and iron have been associated with goiter. Afridi et al. (2010) found that participants with goiters had significantly higher levels of copper and iron in both urine and blood samples. Those participants who had goiters were also found to have lower T3 and T4 levels. Arsenic has been demonstrated to alter the levels of TSH, fT4, fT3, and thyroglobulin (Tg) (Ciarrocca, 2012). Arsenic can occur naturally in well water and has been found in wells in Georgia. In 2009, a new well dug in the city of Cairo, Grady County, Georgia had an arsenic level that was six times the limit set by the Environmental Protection Division (Donahue, Kibler, & Chumbley, 2013). These are all counties in Southwest Georgia. The above studies suggested that elemental metals may be present in drinking water and this may be a risk for thyroid hormone disruption for residents who drink metal-contaminated water.

Cadmium is a mineral commonly used for the manufacturing of steel, plastics, and batteries (Luparello, Longo, & Sirchia, 2011). This contaminant has no beneficial properties to human biology and is readily released into drinking water. Exposure also occurs via smoke from cigarettes. Brzóska, Moniuszko-Jakoniuk, and Pilat-Marcinkiewicz (2008) investigated the effects of cadmium administered to male rats in drinking water for an association with the function and structure of the thyroid and parathyroid glands. The rats were administered water with concentrations between 5mg and 50 mg Cd/dm3 for a period of 12 weeks and 24 weeks. Thyroid and parathyroid function were measured by testing the serum levels of thyroid and parathyroid hormones. Assessment of the glands showed follicular cell changes. Hypertrophy and hyperplasia of the parathyroid glands occurred in rats that ingested the higher concentrations of cadmium compared to those that had ingested lower levels. Although animal studies cannot always be extrapolated to humans, those data indicated that humans who were exposed to cadmium in drinking water may be at risk of thyroid disorders.

Fluoride is an element that can be found in water supplies from plant emissions, natural occurrences, or may be added deliberately for prevention of tooth decay. Basha et al. (2011) administered high-fluoride water orally to assess its effects on the rats' thyroid hormone status, the histopathology of discrete brain regions, the acetylcholine esterase activity, and their learning and memory abilities. They found that the fluoride-treated group showed poor acquisition and retention and higher latency. Changes in the thyroid hormone levels were deemed as the probable cause. That finding was further supported

by evidence found in the early 1900s when physicians began to analyze and dissect goiters. The dissections showed that fluoride has a greater affinity for the thyroid than iodine, and interferes with the manufacture of T3 and T4 by blocking iodide receptors. This process leads to an iodine/iodide deficiency, which in turn, leads to hypothyroidism. The National Research Council (NRC) has found increased fluoride contamination caused by emissions from "coal-fired electricity generating plants" (NRC, 2006, p. 103). The finding on fluoride emissions is important to this particular study because there is a coal-fired electricity-generating plant located in Dougherty County. This implies that residents may be exposed to fluoride contamination not only from added fluoride in municipal water, but also possibly from unintended contamination of well water. Findings by Basha et al. and Brzóska et al. indicate that the consumption of fluorine and fluorides in water may have detrimental effects on the thyroid gland and thyroid hormones.

Medications

Medications, including lithium, have been found in both untreated water sources and municipal water supplies (Fram & Belitz, 2011). High concentrations of lithium were found in untreated drinking water in the Argentinean Andes Mountains(Broberg et al., 2011),and improper disposal of medications may result in detectable levels in water supplies. Further research is needed to determine potential impacts of medications in water supplies on thyroid hormone function.

Lithium has been associated with alteration of thyroid function (Broberg et al. (2011). Broberg et al. studied 202 women from four Andean villages in Northern Argentina, measuring lithium exposure using spot urine samples. Thyroid function was evaluated through the plasma free T4 and TSH. Broberg et al. found that long-term ingestion of drinking water containing 8-1,005 micrograms per liter of lithium was associated with thyroid dysfunction, as evidenced by a negative association with T4 with a significance rate of -0.19 and a positive association with TSH with a significance rate of 0.096. Those findings were consistent with clinical findings on the potential side effects of lithium when used in medical treatment (Broberg et al., 2011). Aside from exposure by improper disposal of medications, which can occur anywhere that lithium is prescribed, there was a pharmaceutical production plant located in Dougherty County Georgia, supporting the potential for residents to be exposed to lithium in their drinking water.

The above studies indicated that many chemicals can be found in drinking water that may impact thyroid function. However, there is still a dearth of information on the relationship between these chemicals in the water and thyroid mortality. The current study will help to fill a gap in the literature regarding thyroid-related mortality associated with drinking water.

Municipal Water

Many industrialized countries throughout the world implement water purification or cleaning processes to provide a fresh water supply to residents. However, filtration and purification does not always remove unwanted chemicals, and some chemicals are

purposefully added. Dichloroacetate (DCA) is a byproduct of chlorinated water and is commonly found in disinfection agents (Julvez et al., 2011). DCA is not only ingested but is also absorbed through the skin during bathing and swimming in chlorinated waters.

Fluoride remains one of the most controversial purposeful additions to drinking water. Since the 1950s, the addition of fluoride to municipal water sources has been debated, with one side arguing that the addition of fluoride would decrease the incidence of tooth decay and the other stating that the risks of such additions have not been adequately studied (Hong et al., 2006). In 2006, the NRC contended that the Environmental Protection Agency's limit of 5mg/L be lowered because of potential health risks posed to both children and adults. Evidence suggested that the exposure to fluoride at the recommended level caused dental fluorosis (discoloration and disfiguring of emerging permanent teeth) in children. Bansal, Jain, Mittal, & Kumar (2014) suggested that the same levels of fluoride also increased the risk of bone fractures and stiffening of joints, known as skeletal fluorosis in adults, and have an adverse effect on the thyroid gland.

In a study carried out in England, water fluoridation was associated with higher rates of hypothyroidism (Peckham, Lowery, & Spencer, 2015). Approximately 10% of residents in England live in areas with community fluoridation schemes. Peckham et al. analyzed hypothyroidism prevalence using general practice data to look for a link between levels of fluoride in water supplies and hypothyroidism prevalence. They gathered 2012 data on fluoride levels in drinking water, 2012/2013 Quality and

Outcomes Framework (QOF) diagnosed hypothyroidism prevalence data, 2013 General Practitioner registered patient numbers, and 2012 practice level Index of Multiple Deprivation scores. They found that the levels of fluoride in drinking water were positively linked with hypothyroidism prevalence. In particular, practices located in the West Midlands (a wholly fluoridated area) were associated with twice the risk of hypothyroidism compared to Greater Manchester, a non-fluoridated area. Those data highlighted the need for additional studies on the safety of community fluoridation and associations with thyroid health, particularly the link between fluoridation and thyroid incidence.

Municipalities take measures to ensure that the individuals they serve have drinking water that is safe and provide health preventative measures for the population. The disinfection process is used to remove bacteria, arsenic, radon, and uranium (CDC, 2014). Municipalities may also add fluoride to the water source to assist with preventing tooth decay. It is likely that untreated well water poses a more significant risk for thyroid hormone disruption than municipal water, based on the literature reviewed in this chapter demonstrating a wide variety of potential exposures and thyroid-related adverse effects. However, the above findings are an indication that municipal water may pose at least some risk for hypothyroidism. This study will help to shed light on the possible associated risks from well water versus municipal water.

Confounders

There were several potential confounders for this study. This study is a secondary data analysis, and it was not possible for me to control the exposure of the participants to any known or potential thyroid disrupting chemicals. Residents of Southwest Georgia may be exposed to toxicants from food or other dietary sources, unintended contamination, factory emissions, or may have occupational exposure. An additional confounder would be the use of water filtration systems, thereby screening out potential exposures that may have otherwise occurred. It is not possible to know whether a person residing at a residence with a well drinks the well water or buys bottled water. In this study, I was limited to the available data and it was not possible to measure actual contaminants in the untreated water or actual water consumption.

There are several types of known risk factors that may or may not have impacted the population under study. Checkoway et al. found a positive correlation between the prevalence of thyroid cancer and those exposed to benzene and formaldehyde for ten or more years (2006). Occupational exposure to arsenic, chromium, and mercury were also linked to thyroid cancer (Lope et al., 2008). Toxicological effects of nonylphenol (NP) on the endocrine system at doses of 50mg/kg were associated with an increase in thyroid weight (Gye-Hyeong et al., 2007). Malondialdehyde (MDA) and nitric oxide (NO) found in paint production chemicals were associated with hyperthyroidism by Saad-Hussein, Hamdy, Aziz, & Mahdy-Abdallah (2011).

The aim of this study was to provide evidence of one type of risk for developing invasive thyroid disease which may be attributable to drinking water through secondary data analysis, but it was not possible for me to control for any potential risks in this type of study. The following section contains a discussion of similar studies and their methodology in order to support the methodology I used in my study.

Methodological Review

This study was a quantitative secondary data analysis that used vital statistics provided by the Georgia Department of Public Health. This section presents a review of studies that used a similar methodology to assess the effects of chemicals in drinking water on thyroid function. Conducting a secondary data analysis assisted with meeting time constraints, was economically feasible, and the data sets were somewhat easily accessible. The two main sources of data for this study were the demographic information and invasive thyroid disease mortality obtained from the Georgia Department of Public Health, and the type of water source, obtained from the Department of Environmental Services (DES). Demographic information collected from the Georgia Department of Public Health included zip codes and invasive thyroid disease mortality cases. Data from DES included each participant's name and the type of water source based on the zip code of the participant.

While I found no similar published studies on invasive thyroid-related mortality using vital statistics provided by a Department of Public Health, there were some key secondary data analysis studies that informed my choice of methodology. Steinmaus,

Miller, & Smith (2010) conducted a quantitative study on perchlorate using secondary data obtained from the California Department of Public Health Drinking Water Program. The data set contained data on 497,458 newborns in California in 1998, including over 800 perchlorate measurements, and more than 200 separate water sources. Participant data were placed in two groups: water sources that had a perchlorate level greater than five micrograms per liter (exposed) and water sources that had perchlorate levels less than five micrograms per liter (unexposed). Bivariate analysis determined the association between TSH and the link between maternal exposure by drinking water to perchlorate during the pregnancy period and newborn thyroid hormone levels. Logistic regression was used to compare TSH levels in communities exposed to perchlorate versus communities not exposed to perchlorate through drinking water.

Steinmaus et al. (2010) found that elevated TSH in neonates was associated with reduced T4 concentration. Results were classified according to age at TSH collection, because a post birth surge in TSH levels is considered normal and because water sources, as well as perchlorate exposure, may not stay the same after birth. Maternal exposure to perchlorate was associated with increased neonatal TSH levels. Weaknesses of the Steinmaus et al. study include possible misclassification of participants because other water sources could have been used, and participants may have also consumed perchlorate in food (Steinmaus et al., 2010). Steinmaus et al. (2010) did examine thyroid incidence, which is of interest in the current study. Those data support that secondary data analysis is a useful methodology to determine whether chemicals in drinking water

are associated with thyroid health, but there are some factors that cannot be controlled for when using secondary data. I was not able to control for cross exposures between municipal and well water and exposures via other means, such as occupational.

Balazs, Morello-Frosch, Hubbard, and Ray (2011) conducted a quantitative correctional study between nitrate levels and communities located in different socio-economic locations. The study used secondary data from the California Department of Public Health Water Quality database and demographic information from the 2000 census. Three measures of interest were estimated nitrate levels, population exposure to nitrate levels, and nitrate concentrations. Balazs et al. originally used a mixed-methods approach that showed an unusual distribution. That finding resulted in Balazs et al. using linear regression between community water system demographics and nitrate levels. Results of the study showed that community water systems that serviced larger Latino and lower socioeconomic communities had a 9% higher nitrate level than individuals living in higher socioeconomic statuses. Comparisons of the different statistical analysis methods used in studies such as Balazs et al. support my choice of the Wilcoxon Rank Sum method for this study.

The literature reviewed in this chapter indicates that quantitative research designs that use secondary data sets were appropriate for answering research questions related to the correlation of invasive thyroid disease and water source. The purpose of this study was to utilize a secondary data analysis to reveal any correlational relationship between drinking water sources regarding invasive thyroid-disease mortality cases. Secondary

data sets from the Georgia Department of Public Health and the Dougherty County Department of Environmental Services were used in this study. The Dougherty County Department of Environmental Services is a division of the Dougherty County Department of Public Health, which oversees the entire GPHD 8-2. The research design will be further described in Chapter 3.

Literature Gap

This literature review indicates that there are multiple chemicals found in water that can contribute to the risk of thyroid disease. The literature reviewed for this study included no published findings to date that specifically associated source of drinking water with thyroid disease mortality, but there were correlations found with drinking water and the development of thyroid disease. I found no studies conducted with data from Georgia that specifically looked at well water versus municipal water. The research question used in the study assisted in determining whether thyroid disease mortality correlates with the consumption of untreated well water or municipal water sources, based on the framework of the ecological systems theory. Although ideally, thyroid-related morbidity would be a useful end point, the study design was limited by the data that existed in the chosen data set. Findings of the study could assist future researchers in building upon this theory and determining whether particular environmental factors found in water are related to thyroid disease mortality.

Summary and Conclusion

Multiple studies have found associations between thyroid function and toxicants found in water, including the outcomes of hypothyroidism (Aschebrook-Kilfoy et al., 2012; Basha et al., 2011; Cao et al., 2010;Dallaire et al., 2009; Lopez-Espinosa et al., 2012; Peckham et al.; Sang et al., 2013; Schell et al., 2008;Ward et al., 2010; Winquist & Steenland, 2014), thyroid cancer (Aschebrook-Kilfoy et al., 2012; Checkoway et al., 2006; Gandhi et al., 2010; La Vecchia et al., 2014; Lope et al., 2008; Ward et al., 2010), and hyperthyroidism (Saad-Hussein et al., 2011; Winquist & Steenland, 2014). The literature reviewed in this chapter concerned the adverse effects of PFAAs, perchlorates, thiocyanates, nitrates, polychlorinated chemicals, polybrominated chemicals, phthalates, metals and other elements, and medications in water supplies on thyroid function. The literature review supported my choice of methodology by demonstrating what others have done using similar datasets and research questions. The completed study was based on the ecological systems theory, which has been used in a myriad of studies assessing the causes and effects of many types of diseases. The findings of this study provide information on the correlation between thyroid disease mortality and treated or untreated water sources. Moreover, the study adds to the knowledge base regarding risks for thyroid disease and can be used as a basis for future research.

Chapter 3: Research Methodology

Introduction

The purpose of this study was to determine if there were any significant differences in invasive thyroid disease mortality between individuals who consume municipal water and residents who consume untreated well water in rural areas. In Chapter 2, I described the various chemicals found in water that are associated with thyroid disease mortality.

This chapter provides information about the research design and the rationale for choosing the design. Information is included about the population examined and the methods used to calculate an appropriate sample size. An in-depth explanation of recruitment procedures and data collection is addressed. The inclusion of an overview of internal and external threats to validity is provided along with how these threats were minimized. In the final section of this chapter, I address any ethical concerns that have arisen during this research process.

Research Design and Rationale

In this study, I compared two groups using two predictor variables: urban/rural residence and type of water source. Residing within an urban or rural location directly influences whether an individual has a municipal water supply or a private water supply. The two comparison groups included (a) urban individuals who consumed municipal water and (b) rural individuals who consumed untreated well water. The dependent variable was invasive thyroid disease mortality.

This study was a quantitative design because I wished to collect numeric data, analyze numbers using statistics, and conduct an investigation in an objective and unbiased manner (Creswell, 2005). The use of the quantitative research method is appropriate when the focus of the research is to determine whether a relationship exists among variables (Cooper & Schindler, 2003). A quantitative method was applied in this study because the focus of the hypotheses was to narrow and concise. A quantitative method was most appropriate for this study because numerical data produced information necessary to study the difference in the mortality from thyroid diseases in individuals who consumed municipal water in the urban areas as opposed to those who consumed in the rural areas (Creswell, 2008). The information collected can help in informing the general public, health care professionals, and health officers about contaminants found in water sources.

Creswell (2009) asserted that quantitative research was viewed as confirmatory and deductive in nature. The philosophical foundation behind quantitative research derived from a positivist perspective and was put forth by Auguste Comte in the middle of the 19th century (Giddens, 1974). According to Johnson, Burke, and Onwuegbuzie (2004), "the major characteristics of traditional quantitative research are a focus on deduction, confirmation, theory/hypothesis testing, explanation, prediction, standardized data collection, and statistical analysis" (p. 18). Because I did not have control over the variables of interest in this secondary data analysis, the study was suggestive rather than rigorously causative.

The quantitative correlational design was appropriate for this study because the objective was to determine whether there was a relationship between invasive thyroid disease mortality among individuals who consumed municipal water in urban areas and those who consumed untreated water in rural areas. With the correlational design, the levels or categories for the independent variable were already defined or classified so that I did not have the ability to manipulate or randomly assign individuals to certain groups. In the context of social and educational research, this research was a retrospective study, in which I used existing conditions to assess comparisons. The nonexperimental research design for this study provided a detailed investigation of information gathered from multiple sources and provided information for those who may be at risk for developing thyroid disease. This study design was susceptible to several possible constraints, including the amount of time needed to review mortality and environmental records, obtaining permission from the Georgia Department of Public Health, and the accuracy of the data provided by both the Department of Public Health and the Department of Environmental Services (Creswell, 2009).

Population

The initial intent of this study was to use the target population of individuals who lived in Albany, Dougherty County, Georgia, because Albany provides many of the most extensive medical and public health services for the Southwest Georgia Public Health District 8-2 (Dougherty County Health Department, n.d.). In addition, I chose the location because there was a good mix of rural and urban participants living in the

county. According to information obtained from the Unites States Census Bureau (2013), the total population for the county was 94,501 individuals. Information pertaining to mortality due to invasive thyroid disease came from the Georgia Department of Public Health. Information pertaining to the location of private wells within the county came from the Department of Environmental Services. The study population was expanded after I received data from the Georgia Department of Public Health showing only 63 cases within Dougherty County. I increased the sample population by sending an additional petition to receive data concerning the counties that make up Southwest Georgia.

The final target population of Southwest Georgia consisted of 14 counties and 32 zip codes. I chose the region of Southwest Georgia in order to improve the sample size of the study. Only individuals 18 years or older participated in the sample. According to information from the Unites States Census Bureau (2013), the total population for this region was 355, 707. Of the 355,707 individuals of Southwest Georgia, 54.4% were female. The expansion of the population allowed for a sample size of 179 cases to be reached.

Sampling and Sampling Procedures

There are four primary sampling strategies for conducting a research study. I used convenience sampling. Convenience sampling is a sample in which the participants are selected, in part or in whole, based on the convenience of the researcher (Stevens, 1996) and encompasses the data readily available to be researched. More specifically,

convenience sampling is typically based on time, money, and availability of sites or respondents (Marshall, 1996). A convenience sampling technique is a nonprobability sampling technique that considers the willingness and availability of participants (Leedy & Ormrod, 2010) or selects a random sample (Leedy & Ormrod, 2010). Convenience sampling is regularly used in exploratory research to collect data generally representative of the population being studied. This method is often used during initial research efforts. However, by its nature, convenience sampling sacrifices generalizability and, therefore, may not provide sufficient representation of the target population (Urdan, 2005). This means that those selected for the study may only partially represent the population being investigated. The sample was obtained from statistics provided by the Georgia Department of Public Health. Only those individuals who lived within Dougherty County were initially used in the sample, but this sample was too small. I then expanded the sample to the entire 8-2 region of Southwest Georgia to increase sample size. Participants with thyroid cancer and thyroid autoimmune disorders were also included. The current study also included participants at least 18-years-old living in Southwest Georgia.

When calculating the sample size for this study, I considered three factors. The first factor was the power of the test. The power of the test measures the probability of rejecting a false null hypothesis (Keuhl, 2000). For the purpose of this study, a power of 80% was sufficient to adequately reject as false the null hypothesis (Moore & McCabe, 2006). A power of 80% ensured that the statistical analyses could provide valid

conclusions with regard to the total population. This provided 80% strength in terms of assessing the validity of the statistical tests.

The second factor was the effect size, which measures the strength of the relationship between the variables in the study (Cohen, 1988). Cohen (1988) categorized the effect size for different tests into three different categories, which included a small effect, moderate effect, and a large effect. For the purpose of this study, a moderate effect size (0.30) provided evidence of a relationship between the independent and dependent variables without being too strict or lenient.

The final factor considered was the level of significance. The level of significance is the probability of rejecting a true null hypothesis and is usually defined as being equal to 5% (Moore & McCabe, 2006). The level of significance was selected before conducting the analysis, such that it could be determined whether there was a significant relationship between the variables. For this study, the level of significance was equal to 5% because this provided a 95% confidence level that the conclusions drawn from the statistical test were true.

The sample size also depends on the type of analysis conducted. Initially, I considered a two-sample *t*-test for this study. The minimum sample size was calculated through G*Power, and considering 80% power and medium effect size, the minimum sample size was 128 total observations with 64 in each group. The data for Southwest Georgia met the required sample size but failed to meet the required assumptions for the two-sample *t*-test. It was determined that the Wilcoxon Rank Sum test would provide the

most accurate analysis of invasive thyroid disease mortality e data because of the small sample size and uneven distribution.

Secondary Data Sources

Data for this research study were solicited from two governmental agencies that provided statistical data on individuals who make up the total population of Southwest Georgia. There were two main sources of data for this study: the demographic information and invasive thyroid disease mortality from the Georgia Department of Public Health and the type of water source from the Department of Environmental Services (DES). Demographic information came from the Georgia Department of Public Health and included zip code and invasive thyroid disease mortality status. Data from DES included each participant's name and the type of water source based on the zip code of the participant.

Research participants were provided an exit statement because I was using secondary information collected and stored by the governmental agencies. Additional permissions came from the local Environmental Services Department and the Georgia Department of Public Health. The letters were signed by the respective facility organizers to ensure that all information was approved to be published through this current study. The Data Use Agreements are shown in the Appendices.

Variables of Interest

Invasive thyroid disease mortality were divided into two groups based on the source of water where the participants resided: (a) urban areas with municipal water and

(b) rural areas with untreated well water. The independent variable in this current study was the source of water. The independent variable was a binary variable, which corresponds to 0 for individuals in urban areas who resided in an area that received municipal water and 1 for individuals in rural areas who resided in an area that received untreated well water. The dependent variable was invasive thyroid disease mortality, also a binary variable (0=*no thyroid mortality*, 1=*thyroid mortality*). Invasive thyroid disease mortality included diagnosis of thyroid cancer, hypothyroidism, and hyperthyroidism. Data provided by the Department of Public Health in the form of datasets were recorded using ICD9 codes. Codes that did not list a form of invasive thyroid disease as the primary diagnosis were excluded from the study.

Data Analysis Plan

I obtained the data in Excel or comma delimited format and analyzed the data through Statistical Package for Social Sciences (SPSS) 17.0. The two-sample *t*-test could not be used for statistical analysis because the data were not normally distributed within the urban and rural populations. Therefore, I used a nonparametric alternative. Poisson and binomial distribution were also considered but were rejected because of the large sample size that would be needed for each. The Wilcoxon Rank-Sum test (Bush, 2012) was the nonparametric alternative used to determine any differences in rank means between the treated and nontreated water sources. The test was used to test two samples that came from the sample size. The Wilcoxon Rank-Sum test allowed for the cases to be ranked within the rural population and the urban population. The mean of ranks was then

calculated and compared to determine if the null hypothesis could be rejected. Therefore, invasive thyroid disease mortality identified from the Department of Public Health data were ranked within two groups: urban cases who drank treated water and rural cases who drank well water. The Wilcoxon Rank Sum test determined whether one group had a larger number of cases of invasive thyroid disease mortality.

Threats to Validity

Validity is the accuracy of what a person is measuring; that is, it is the congruence between an operational definition and the concept it is attempting to measure. From a practical standpoint, validity is the ability to create meaningful and useful inferences from data gathered from scores on a survey instrument (Creswell, 2009). Validity involves both internal and external threats. Internal threats are those related to procedures, treatments, or experiences by the participants of the study that prevent or hinder the researcher from extracting accurate inferences. Internal validity is the ability to draw accurate and consistent conclusions based on the research design. External threats are those that happen when the researcher applies the conclusions of a study incorrectly by generalization (Creswell, 2009).

The extent to which the study's conclusions can be applied beyond the study in other contexts is external validity. Generally, researchers who employ randomization to select participants from the study population have more external validity than those who do not (Leedy & Ormrod, 2010). In the present study, I used convenience sampling of participants to sample the study population, which may have weakened the study's

external validity. This strategy was used because random sampling of the study population was outside the scope of my resources. When convenience sampling is used, repeating the test to compare results may be advised. Reliability is an indication of scores from an instrument being stable and consistent. The reliability of quantitative data is based upon consistency (Creswell, 2009). Because secondary data were gathered in this study, the government agencies involved in data collection used a consistent method in gathering data for the type of water source and the diagnosis of invasive thyroid diseases among the population. The Department of Health made use of standardized ICD-9 codes to determine whether mortality from thyroid disease was diagnosed. Moreover, the type of water source in each area was well-documented in the government data. Installing municipal water sources involves necessary permits, which allow the government to track whether each area has municipal water source or untreated well water.

Ethical Assurances

Before the data collection process, I secured the approval of the Institutional Review Board (IRB). Due to the use of secondary data, there was no contact with human participants in this study. Therefore, the most important ethical concern was maintenance of confidentiality of participant information. No individually identifiable information was disclosed or published, and all results were presented as aggregate, summary data. A copy of an authorization to use disclosed protected health information (PHI) for research purposes is attached.

The information collected from the agencies was kept confidential and secure by design. All aggregate data were stored in a secured file for a minimum of 5 years and will then be permanently destroyed. If any content is published, it will be done only for scientific purposes. That is, data will be used to further the cause of science rather than for personal reasons. The governmental agencies and community partners were given a copy of the results of the analyses for reference. Data Use Agreements were obtained from both government agencies as presented in Appendix C and D. This allowed me to access and use the agencies' data files to fulfill the purpose of this current study.

Paper copies of the data were stored in a locked filing cabinet, which only I can access. By doing this, the confidentiality of collected data was maintained so that no personal information was accessible. Electronic data will be stored in my personal files for a period of 5 years after completion of the research study, after which, it will be destroyed and deleted from the hard drive. Any paper-based information will also be destroyed, by shredding the documents in a paper shredder.

Summary

This quantitative secondary data analysis study was designed to explore the differences in invasive thyroid disease mortality between residents who were exposed to municipal water versus untreated water in both rural and urban areas of Georgia. Individuals in Southwest Georgia were chosen through convenience sampling. Secondary data from the Georgia Department of Public Health and DES were analyzed to determine

if there was a correlation between invasive thyroid disease mortality and exposure to municipal water versus untreated water.

The research question was answered through a Wilcox Rank Sum. Chapter 4 includes a description of the demographic profile of the participants, the data analysis procedures, and the results of the study.

Chapter 4: Data Analysis and Results

The purpose of this study was to investigate the relationship between drinking water source and invasive thyroid disease mortality in Southwest Georgia. The study adds to the body of knowledge regarding the potential adverse effects of pollutants that may be found in drinking water on human thyroid function. Specifically, I explored the effects of water source on thyroid disease mortality in Southwest Georgia by investigating whether there was a difference in frequency between urban participants who drink municipal water as opposed to rural participants who drink untreated water. The results add to the literature on potential risks for thyroid disease. This quantitative study used secondary data and correlational research.

The correlational research design was used to compare the statistical relationships between two variables. I used secondary data to determine if there was a relationship between invasive thyroid disease mortality (dependent variable) and type of water source based on urban/rural residence (predictor variable). I used statistical analyses to examine the data for differences in mortality from thyroid disease between the urban population who consumed municipal water and the rural population who consumed private (well) water. Data were obtained pertaining to the invasive thyroid disease mortality from the Georgia Department of Public Health and information pertaining to the location of private wells within the county from the Department of Environmental Services.

In this chapter, I present the results of the data analysis methods following the collection and organization of the data. A comparison of means test was used to observe

thyroid disease mortality (cases) between drinking water sources. Prior to discussing the results of the statistical test, descriptive statistics of the demographic variables of the participants are presented, followed by a description of the study variables.

Research Question and Hypothesis

The research question and hypotheses for this study were as follows:

RQ1. Is there a difference in invasive thyroid disease mortality between residents in urban areas who consume municipal water and residents in rural areas who consume untreated well water?

H_0: There is no significant difference in the invasive thyroid disease mortality among residents in urban areas who consume municipal water as opposed to residents in rural areas who consume untreated well water.

H_1: Residents in urban areas who consume municipal water have a lower invasive thyroid disease mortality as opposed to residents in rural areas who consume untreated well water.

Data Collection Process

Secondary data came from the Georgia Department of Public Health and the Dougherty County Department of Environmental Services. Data request forms were submitted to both governmental agencies. Information was returned within 4 weeks after receipt of data requests. Data received from the Department of Environmental Services provided information for over 212 wells in Southwest Georgia. Additional information

obtained from the Online Analytical Statistical Information System (OASIS) showed that the total population for this area was over 90,000 individuals from 2000-2013. Women accounted for 53% of the overall population, and men accounted for the remaining 47%. This information was then compared to the data received from the Georgia Department of Public Health.

Initially, the Georgia Department of Public Health provided secondary data related to the mortality from thyroid disease within Albany, Dougherty County, Georgia that included 63 cases. I made a second request to obtain the thyroid disease mortality information for the GDPH District 8-2, which consists of 14 counties within Southwest Georgia and includes Dougherty County, to ensure that there was an adequate sample size. There were over 9,061 cases of invasive thyroid disease mortality within the state of Georgia between the years of 2003-2012. There were 238 cases within Southwest Georgia.

County data were also broken down by zip code and categorized into rural and urban zones respectively. The zip code data were used for analysis, including any zip code with five or more cases of thyroid disease mortality, within rural and urban areas. Those zip codes with fewer than five cases were not used because there was no way to determine the actual number of cases in those areas. There were 32 zip codes within Southwest Georgia, but only 16 zip codes were used for data analysis due to small case count. These zip codes ranged from 31701 to 39842.

I categorized the zip codes into rural and urban areas based on the percentage of land that was classified as being in the city limits. The borders for city and county jurisdiction were determined by using county and city maps used by the Department of Environmental Services. The cases of thyroid mortality could not be traced back to specific wells without using personal identifiable information. Those zip codes that contained greater than 50% of land lying within areas and that used a raw water source for water consumption were placed into the rural category. The remaining zip codes were placed within the urban category. The zip codes 31705, 31721, 31757, 31779, 31792, 39819, 39828, 39837, and 39842 were categorized as rural. The zip codes of 31701, 31707, 31730, 31763, 31791, 39817, and 39828 were considered urban.

Demographic Information

Information collected from the Georgia Department of Public Health contained information on *Invasive Thyroid Disease Mortality* for Southwest Georgia from 2003 to 2012. Table 1 shows a summary of these mortality rates for each area, by males/females, and overall. For analysis, if any rate was not calculated (where counts were less than 5), the data was not used. The overall and total counts for each area were used for statistical analysis, where the count was greater than or equal to 5.

Table 1

Invasive Thyroid Disease Mortality, Southwest Georgia (GDPH 8-2), 2003-2012

		Males		Females		Total	
Zip Code	Area	Count	Rate	Count	Rate	Count	Rate
Zip Code 31705	rural	7	~	20	11.8	27	8.6
Zip Code 31721	rural	<5	~	***	~	15	~
Zip Code 31757	rural	<5	~	***	~	8	~
Zip Code 31779	rural	<5	~	***	~	8	~
Zip Code 31784	rural	<5	~	<5	~	<5	~
Zip Code 31792	rural	<5	~	***	~	14	~
Zip Code 39813	rural	<5	~	<5	~	<5	~
Zip Code 39819	rural	<5	~	***	~	8	~
Zip Code 39823	rural	<5	~	***	~	8	~
Zip Code 39837	rural	<5	~	<5	~	7	~
Zip Code 39841	rural	<5	~	<5	~	<5	~
Zip Code 39842	rural	<5	~	***	~	6	~
Zip Code 39846	rural	<5	~	<5	~	<5	~
Zip Code 39861	rural	<5	~	<5	~	<5	~
Zip Code 39885	rural	<5	~	<5	~	<5	~
Zip Code 31701	urban	<5	~	***	~	12	~
Zip Code 31707	urban	<5	~	***	~	12	~
Zip Code 31716	urban	<5	~	<5	~	<5	~
Zip Code 31730	urban	<5	~	***	~	7	~
Zip Code 31763	urban	5	~	20	18.2	25	11.5
Zip Code 31772	urban	<5	~	<5	~	<5	~
Zip Code 31781	urban	<5	~	<5	~	<5	~
Zip Code 31789	urban	<5	~	<5	~	<5	~
Zip Code 31791	urban	<5	~	<5	~	5	~
Zip Code 31796	urban	<5	~	<5	~	<5	~
Zip Code 39817	urban	<5	~	***	~	7	~
Zip Code 39826	urban	<5	~	<5	~	<5	~
Zip Code 39827	urban	<5	~	<5	~	<5	~
Zip Code 39828	urban	***	~	<5	~	10	~
Zip Code 39845	urban	<5	~	<5	~	<5	~
Zip Code 39859	urban	<5	~	<5	~	<5	~
Zip Code 39862	urban	<5	~	<5	~	<5	~
Zip Code 39866	urban	<5	~	<5	~	<5	~

Zip Code 39870	urban	<5	~	<5	~	<5	~
Zip Code 39877	urban	<5	~	<5	~	<5	~
TOTAL 32		12		40		179	

Note. Average Annual Rate per 100,000, age-adjusted to the 2000 US standard population
~ Rates not calculated where the count is less than sixteen
*** Data suppressed for confidentiality purposes
Suggested Citation: Georgia Department of Public Health, Georgia Comprehensive Cancer Registry, 2015.

There were a total of 179 cases within Southwest Georgia. Data showed that there were 101 cases in rural areas and 78 cases in urban areas. Women were shown to have a higher prevalence of invasive thyroid disease mortality (40) than men (12) within this region. A disproportionate number of cases came from Dougherty County (31701, 31705, 31707, and 31721). There were 24 (35%) cases in urban areas and 42 (65%) cases in rural areas of Dougherty County. Of the 63 cases in Dougherty County, 75% were among women (n=47).

Tests for Normality and Other Model Assumptions

The research question of interest concerned the relationship between drinking water source and invasive thyroid disease mortality in Southwest Georgia. As discussed in Chapter 3, one way to observe this association was through the use of a comparison of means test, specifically a two-sample *t*-test. A requirement of this analysis is that the thyroid disease cases must be normally distributed within the treated/untreated water groups (Bush, 2012). I conducted Shapiro-Wilk tests to help determine whether invasive thyroid disease mortality were normally distributed within the treated/untreated water groups, where a p-value > 0.05 implies a normal distribution. According to the results,

invasive thyroid disease mortality were not normally distributed within the treated (Shapiro-Wilk $p = 0.003$) and untreated (Shapiro-Wilk $p = 0.049$) water groups, which meant that the two-sample *t*-test could not be used for data analysis. The needed sample size was calculated using G*Power for alternative analysis tests (Poisson, binomial distribution, and one-tail). It was found that the sample size for Poisson analysis needed to be 46,000 cases or greater. Sample size calculation for binomial distribution and a one-tail test also needed to be greater than 1,000. Therefore, to observe invasive thyroid disease mortality between treated and untreated water groups, I used a nonparametric Wilcoxon Rank-Sum test.

Statistical Results

I used SPSS version 17 software (SPSS, 2008) to perform statistical analysis. A Wilcoxon Rank-Sum test was used to observe the difference in invasive thyroid disease mortality in urban areas where residents consume treated water, versus rural areas where residents consume untreated water to answer the research question. The Wilcoxon Rank-Sum test is a nonparametric test that can be used as an alternative to the Two-tail Sample *t*-test (Bush, 2012). The test was performed by calculating the counts within all zip codes. These counts were then ranked from 1 to 16. SPSS determined median rank for treated and untreated water groups, and then I compared those values for statistically significant difference. Table 2 presents the results of the Wilcoxon Rank-Sum tests, where results showed the null hypothesis failed to be rejected ($Z = 57.0$, $p = 0.789$). This implies there was no significant difference in invasive thyroid disease mortality within urban areas

where residents consume municipal water as opposed to invasive thyroid disease mortality within rural areas where residents consume untreated well water.

Table 2

Results of Wilcoxon Rank-Sum Tests Rates by Water Group

	Treated Median Rank (IQR)	Untreated Median Rank (IQR)	*Z*	*p-value*
Thyroid Disease Cases	8 (8 – 14)	10 (7 – 12)	57.0	0.789

Summary

The purpose of this research was to investigate the relationship between drinking water source and invasive thyroid disease mortality in Southwest Georgia. Dougherty County accounted for 35% of the total cases within Southwest Georgia. The county also had more cases among woman and more cases than any other county within this region. The difference between invasive thyroid disease mortality cases in urban areas where residents consume treated water versus rural areas where residents consume untreated water was examined through the Wilcoxon Rank-Sum test. From the results of the analysis, there was no significant difference in invasive thyroid disease mortality cases in urban areas with treated water versus rural areas with untreated water. Chapter five will consist of my interpretations of the findings, the limitations of this study, recommendations for future studies, and implications for the study.

Chapter 5: Discussion

Introduction

I explored the presence of a correlational relationship between drinking water sources and invasive thyroid disease mortality using a sample of rural and urban data collected in Southwest Georgia. Thyroid-related ailments continue to rise in the United States (Howlader et al., 2012). In 2002, 5% of the U.S. female population had a thyroid disorder, and 6% had notable thyroid modules (Pinto & Glick, 2002); in 2014, 1,890 deaths were reported due to thyroid cancer (National Cancer Institute, 2014). Burton (2011) found that impaired thyroid function, such as endemic thyroid goiters, are commonly found in areas with iodine deficient soil and water, including the Southeast region of the United States, home to the state of Georgia. Nontreated water, such as water from private wells--a nongovernment regulated water source often found in rural areas, may become exposed to contaminants via rainwater (EPA, 2011). Numerous chemicals and minerals have been known to affect thyroid function including PFAA, perchlorate, nitrates, mercury, arsenic, and lithium. The goal of this study was to explore the effects of water sources on invasive thyroid disease mortality in Southwest Georgia by investigating whether there is a difference in frequency between urban participants who drink municipal water as opposed to rural participants who drink untreated water. A greater understanding of this relationship may assist in increased intervention to reduce water contaminants, regulate previously unmonitored water sources, and reduce rates of problematic thyroid function.

The primary research question and two hypotheses were the following:

RQ1. Is there a difference in invasive thyroid disease mortality between residents in urban areas who consume municipal water and residents in rural areas who consume untreated well water?

H_0: There is no significant difference in the invasive thyroid disease mortality among residents in urban areas who consume municipal water as opposed to residents in rural areas who consume untreated well water.

H_1: Residents in urban areas who consume municipal water have a lower invasive thyroid disease mortality as opposed to residents in rural areas who consume untreated well water.

Methodologically, this was a quantitative study that used secondary data and correlational research. Data pertaining to the number of invasive thyroid disease mortality cases came from the Georgia Department of Public Health, and information pertaining to the location of private wells within the county came from the Dougherty County Department of Environmental Services. A comparison of means test (Wilcoxon rank sum test) was used to observe invasive thyroid disease mortality cases between drinking water sources. The ecological systems theory developed by Bronfenbrenner in the 1970s formed the theoretical foundation of the study. In this chapter, I present interpretation of findings, implications of findings, limitations of this study, and recommendations for future research.

Interpretation of the Findings

According to the results of the study, there was no significant difference in invasive thyroid disease mortality among residents in urban areas with treated water versus residents in rural areas with untreated water. In contrast, previous scholars have supported the link between poor quality, untreated water, and reports of thyroid-related concerns.

Nitrates, which occur naturally and through various routes such as animal waste, fertilizer, and human sewage (EPA, 2012), can pose a risk to rural wells in particular (Ward et al., 2010). Cao et al. (2010) and Aschebrook-Kilfoy et al. (2012) found that a link exists between nitrates and thyroid disease. DDT is another potential well water contaminant associated with reduced plasma levels of thyroid hormones (Delportet al., 2011).

Although I did not find any significant difference in invasive thyroid disease mortality in urban areas with treated water versus rural areas with untreated water, there are several possible reasons for this. As indicated earlier, I used secondary data and did not have direct control over the variables in this study. Moreover, the study's nonexperimental design constrained the study in terms of the amount of time needed to review mortality and environmental records and the accuracy of the secondary data. Another problem is that genetics and environmental factors play a role in autoimmune disorders and are possible confounders. For example, temperature, frequency of reuse, and ultraviolet exposure encountered post development induce the leaching of

plasticizers, such as antimony, bisphenol A (BPA), phethenol, and other xenobiotics, which all contribute to the endocrine-affecting activity (Andra et al., 2011; Makris et al., 2013). Even the consumption of bottled water is a possible confounder and might explain why I did not find any significant differences in the rate of thyroid disease mortality between those who drank untreated water and those who drank treated water. Finally, fluoridation in city water is a possible contaminant that increases the risk of thyroid disease.

Per Bronfenbrenner's (1979) ecological systems theory, there is a bidirectional effect between the varying systems within which human environments and individual humans. Humans can pollute the ecosystem, which can impact human health. The scholars reviewed in Chapter 2 supported this theory. Although I found no correlation between the source of drinking water and thyroid disease mortality, I did find a gender disparity in disease rates within one county in GA. In particular, for Dougherty County, 75% of the reported cases were women. Several scholars have noted that adverse effects vary by gender (Broberg et al., 2011; Melzer et al., 2010; Peng et al., 2014; Turyk et al., 2007). Further studies are needed to determine the source of the disparity, whether that source is water or some other exposure scenario.

Implications of the Findings

Further research is needed to determine whether there is a link between water source and thyroid function in the state of Georgia. Additionally, further research is needed to understand the gender disparity I found in one particular county of Georgia. It

is important to explore the role of other environmental factors such as air pollutants and soil contaminants. Approximately 20 million people are living with thyroid disease in the United States, associated with close to $4.3 billion in health care costs (American Thyroid Association, 2013). Several of the studies reviewed in Chapter 2 (Hu et al., 2013; Shi et al., 2012a) found that thyroid function can be associated with water source. There is a need to better identify sources of risk and vulnerable populations in order for intervention efforts to be efficacious and able to reduce thyroid morbidity and mortality.

Future studies may also benefit from in-depth examination of other demographic variables such as ethnicity, socioeconomic status, and predisposing family history factors. Balazs, Morello-Frosch, Hubbard, and Ray (2011) found a relationship between nitrate levels in California central water systems and social and ethnic disparities. An analysis of the influence of demographic variables, including socioeconomic status, ethnicity, family medical history, and age of Southwest Georgia residents would add to the exploration of risk factors for thyroid disease.

In this study, I used retrospective data. Examination by prospective data may provide additional data, as well as a more specific assessment, of particular chemicals in water sources. PFAAs (Lopez-Espinosa et al., 2012; Kim et al., 2011; Melzer et al., 2010; Winquist & Steenland, 2014; Wolf, Zehr, Schmid, Lau, & Abbott, 2010), perchlorates (Srinivasan & Viraraghavan, 2009; Zewdie et al., 2010), thiocyanates (Cao et al., 2010), nitrates (Ward et al., 2010), polychlorinated chemicals (Julvez et al., 2011), polybrominated chemicals (Ibhazehiebo et al., 2011), phthalates (Hu et al., 2013; Shi et

al., 2012a), metals and other elements (Afridi et al., 2010; Mahaffey, 2009; Schell et al., 2008), and medications (Fram & Belitz, 2011) have all been associated with thyroid dysfunction. However, many of these studies lacked robust results either due to small sample sizes, lack of generalizability, or use of retrospective data. The lack of significant results in this study further intensifies the debate and necessitates deeper investigation of the issue, particularly in Dougherty County where a higher proportion of invasive thyroid disease mortality cases were found, particularly among women.

Limitations

There were inherent limitations to my study. I used secondary data, which consisted of a convenience sample. Convenience sampling is not representative of the larger population, unlike random sampling (Urdan, 2005). This affects the generalizability of the study findings in that it is not certain whether every demographic type of Georgian resident, thyroid dysfunction, and water quality type was included in the original data set. For instance, the dataset is focused on only one region within Georgia; therefore, data findings should not be generalized to the entire state of Georgia. The dataset included individuals who had died from invasive thyroid disease and thyroid autoimmune disorders. Individuals who did not meet this thyroid description were not included in my study, further reducing generalizability. The prevalence of thyroid conditions was necessarily examined primarily through numbers of invasive thyroid disease. Representative population demographics were not available to allow for more generalizable results. When collecting data from any rural setting, distance from

mainstream urban settings may act as a barrier in adequate data collection, further limiting the characteristics of rural participants from being presented. This underrepresentation may occur for a myriad of reasons, including improper transportation, poor access to medical insurance to address health concerns such as thyroid-related concerns, and low resource access to help manage and prevent familial medical concerns (McIlhenny et al., 2011).

The study was further limited by the type of variables available within the data set. Specific populations may be at higher risk than others. Infants may be exposed to higher concentrations of contaminants via breast milk (Kim et al., 2011). My study was limited to individuals who were 18 and older, excluding the examination of whether children and infants from this Georgia-based region were affected. Older adults may be a particularly vulnerable population for thyroid malfunction in relation to poor water quality (Turyk et al., 2007). The findings from this study cannot be generalized to specific age groups, but future studies may benefit from categorizations by age and associated risk level analysis.

Furthermore, confounding variables were not statistically addressed in the present study. Diet may affect thyroid function (Ward et al., 2010). Ward et al. (2010) found that consumption of cruciferous foods such as kale, broccoli, and cabbage increased nitrate intake and risk of thyroid cancer. Fluoridated tap water may also increase the risk, as well as bottled water, which may contain toxic substances. It was not possible for me to identify diet-related variables in the retrospective data set, prohibiting examination of

these confounding relationships. Other confounding factors such as genotypic predisposition were also not assessed.

To address the impact of confounding variables, a future study could complete an analysis of covariance (ANCOVA; Riggs, Haroldson, & Hanson, 2008) in addition to the Wilcoxon rank sum test examination of the research question. ANCOVAs, which are a mixture of regression and analysis of variance statistical methods, allow for the examination of how population means affect one dependent variable as a function of two independent variables or treatment effects. The ANCOVA statistical method in particular would allow for confounders such as diet to be controlled to present more robust results of any potential link between water quality and thyroid disease.

Another limitation of my study was the assumption that those individuals who live in rural settings and have access to private wells actually have access to only one type of water supply. Individuals from rural settings may have their own filtration and water clarification systems or may have access to other water supplies not mentioned in the dataset collected. Thorough prospective data may rectify this concern in future studies.

A measurement limitation existed because the data were collected by the Department of Environmental Services and the Online Analytical Statistical Information System. The validity and the reliability of the measures used was unclear. Cronbach alphas to assess validity and reliability were not available, making the appropriateness of the measurement tools less accessible and discernable. Repetition of the study is limited

in that if the tools were not made public, public and private institutions may find insufficient information for replicating the study and, thus, retrieve varying results.

Recommendations for Future Research

My findings did not indicate with statistical significance a link between poor water quality and impaired thyroid function for southwest Georgia residents. Due to the limitations of the study, a number of recommendations may assist clinical and research personnel in moving forward. It may be useful to include data sets from multisite samples with the option for random sampling. Random sampling would allow for results that can be better generalized to the larger population as well as provide robust support for a correlational link (Stafford, Reinecke, Kaminski, & Gerard, 2006).

A multisite sampling would allow for city, state, and national level statistics to be analyzed to further understanding of whether this issue requires legislative intervention at multiple systemic levels or if localized interference would suffice. For example, Burton (2011) found that endemic goiters commonly occur in areas with iodine deficient soil and water, such as the Midwest, Northwest, and Great Lake regions of the United States. Thus, financial resources may need to be reallocated to help reduce risks and to warn the general public.

Additional demographic variables need to be assessed for continued exploration. For instance, thiocyanate exposures during pregnancy can reduce thyroidal iodine uptake in mothers, leading to decreased thyroid hormone synthesis (Leung et al., 2014).The present study data also reflects a higher number of women with thyroid disease in

Southwest Georgia. Therefore, clinical and research information on gender differences in triggers, interventions, and management of thyroid malfunction may be useful.

Gaining a better understanding of the time sequence of events may shed light on when to intervene. Lopez-Espinosa et al. (2012) found that children exposed to PFAAs in their environment had an increased risk for thyroid disease, in particular hypothyroidism. However, this study did not account for time. Longitudinal studies that aim to understand if water pollutants affect populations over time may clarify the link further and provide information on the best times to intervene to prevent development of severe thyroid conditions.

Finally, it would be useful to decipher which minerals, chemicals, metals, and other elements are present in various sources of water that may adversely affect water quality. The link between PFAAs, minerals, chemicals, metals, and other elements and thyroid malfunction have been provided in this study, as explored in existing research studies. Future scholars may examine which of these elements causes the most harm, how they function in relation to thyroid disease, and provide information on how to best progress technological advances to combat such harm.

Summary and Conclusions

In this quantitative study, I examined the association between water quality and invasive thyroid disease mortality among a rural versus urban convenience sample located in southwest Georgia. Using Bronfenbrenner's (1979) ecological systems theory, I investigated the bidirectional impact of human interaction with the environment. The

null hypothesis was accepted and, therefore, this theory did not fully support the findings of this study. However, there were many potential confounders and limitations that could be explored in additional studies.

According to the literature reviewed in Chapter 2, water can be a source of many contaminants that are a risk factor for thyroid dysfunction. Although I could not confirm a relationship between invasive thyroid disease mortality in urban areas with treated water versus rural areas with untreated water within the study sample for Southwest Georgia, increased risk was found for women in one specific county. Further research is essential to explore this disparity and provide additional information on the risks for women in this county. Future studies may help to establish a connection to thyroid disease for water source or for another exposure route, thereby reducing the morbidity and mortality from thyroid disease in the state of Georgia.

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Appendix A: Confidentiality Agreement

Name of Signer:

During the course of my research entitled Comparison of Thyroid Disease between Urban and Rural Populations in South Georgia, I will have access to information that is confidential and should not be disclosed. I acknowledge that the information must remain confidential, and that improper disclosure of confidential information can be damaging to the participant.

By signing this Confidentiality Agreement I acknowledge and agree that:

1. I will not disclose or discuss any confidential information with others, including friends or family.
2. I will not in any way divulge, copy, release, sell, loan, alter or destroy any confidential information except as properly authorized.
3. I will not discuss confidential information where others can overhear the conversation. I understand that it is not acceptable to discuss confidential information even if the participant's name is not used.
4. I will not make any unauthorized transmissions, inquiries, modification or purging of confidential information.
5. I agree that my obligations under this agreement will continue after termination of the job that I will perform.
6. I understand that violation of this agreement will have legal implications.
7. I will only access or use systems or devices I'm officially authorized to access and I will not demonstrate the operation or function of systems or devices to unauthorized individuals.

Signing this document, I acknowledge that I have read the agreement and I agree to comply with all the terms and conditions stated above.

Signature: **Date:**

Appendix B: Data Use Agreement - Georgia Department of Public Health

March 11, 2014

To whom it may concern,

I have obtained Walden University's support to use data for my research project entitled A Comparison of the Prevalence of Thyroid Disease between Urban and Rural Populations in South Georgia.

I am requesting your cooperation in the data collection process. I propose to collect secondary data from the Georgia Department of Public Health. I will coordinate the exact times of data collection with you in order to minimize disruption to your activities.

If you agree to be part of this research project, I would ask that you allow me to utilize your data pertaining to thyroid disease/cancer. The information will be screened based on the following criteria: (1) whether they have thyroid disease/cancer; (2) based on county of residence; and (3) whether they agree to be a part of the study.

If you prefer not to be involved in this study, that is not a problem at all.

If circumstances change, please contact me via email at dnlchlds@gmail.com.

Thank you for your consideration. I would be pleased to share the results of this study with you if you are interested.

I am requesting your signature to document that I have cleared this data collection with you. You may also respond to this email with "I agree" to document that I have cleared this data collection with you.)

Sincerely,
Donyale Bouie Childs

Printed Name of Public Health Official _____

Date _____

Public Health Official's Written or Electronic* Signature _____

Researcher's Written or Electronic* Signature _____

Electronic signatures are regulated by the Uniform Electronic Transactions Act. Legally, an "electronic signature" can be the person’s typed name, their email address, or any other identifying marker. An electronic signature is just as valid as a written signature as long as both parties have agreed to conduct the transaction electronically.

Appendix C: Data Use Agreement- Dougherty County Department of Environmental Service.

March 11, 2014

To whom it may concern,

I have obtained Walden University's support to use data for my research project entitled A Comparison of the Prevalence of Thyroid Disease between Urban and Rural Populations in South Georgia.

I am requesting your cooperation in the data collection process. I propose to collect secondary data from the Dougherty County Department of Environmental Service. I will coordinate the exact times of data collection with you in order to minimize disruption to your activities.

If you agree to be part of this research project, I would ask that you allow me to utilize your data pertaining to the residents' use of well water. The information will be screened based on the following criteria: (1) whether they have private wells; (2) based on county of residence; and (3) whether they agree to be a part of the study.

If you prefer not to be involved in this study, that is not a problem at all.

If circumstances change, please contact me via email at dnlchlds@gmail.com.

Thank you for your consideration. I would be pleased to share the results of this study with you if you are interested.

I am requesting your signature to document that I have cleared this data collection with you. You may also respond to this email with "I agree" to document that I have cleared this data collection with you.)

Sincerely,
Donyale Bouie Childs

Printed Name of Environmental Service Official _____

Date _____

Environmental Service Official's Written or Electronic* Signature _____

Researcher's Written or Electronic* Signature _____

Electronic signatures are regulated by the Uniform Electronic Transactions Act. Legally, an "electronic signature" can be the person’s typed name, their email address, or any other identifying marker. An electronic signature is just as valid as a written signature as long as both parties have agreed to conduct the transaction electronically.