AN ABSTRACT OF THE THESIS OF

Harmony S. Fleming for the degree of Master of Science in Environmental Health and Occupational Safety Management presented on April 24, 2007.
Title: Groundwater Arsenic Concentrations and Cancer Incidence Rates: A Regional Comparison in Oregon.

Abstract approved:_____

Anna K. Harding

Arsenic contamination of groundwater is a global issue with national and local implications. Chronic exposure to arsenic in drinking water has been linked to both carcinogenic and non-carcinogenic health outcomes. The primary exposure route of inorganic arsenic is ingestion from drinking water due to natural contamination in groundwater from dissolution of natural mineral deposits and anthropogenic sources.

The purpose of this study was to determine if there is a spatial relationship between groundwater arsenic concentrations and cancer incidences within two regions of Oregon. The objectives of this study were to: (1) determine if there is a spatial relationship between arsenic concentrations in the Willamette Valley and Southeast Oregon and incidence rates of bladder, kidney, liver and lung cancers; (2) contribute to the Centers for Disease Control and Prevention's development of the Environmental Public Health Tracking network by using secondary data to investigate linkages of arsenic in groundwater and associated health effects; and (3) serve as an exploratory tool for identifying a public health concern that can be followed up with comprehensive analytical studies of the region.

The study used four secondary data sets: Cancer data from the Oregon State Cancer Registry; community water system arsenic data from the Oregon Department of Human Services Drinking Water Program; groundwater arsenic data from the U.S. Geological Survey National Water Inventory System; and population data from the U.S. Census Bureau. Data set were combined and then analyzed with statistical and spatial analysis methods. This study did incur challenges of data compatibility and required extensive data preparation activities of several of the data sets. One such data manipulation was the integration of two independent sources of water quality data

which had not been done before in Oregon and may not have accurately defined the exposure risk of sub-populations. Another limitation was that missing cases due to geocoding were more likely to be in rural census tracts due to the P.O. Box and Rural Route addresses, thus possibly contributing to an underestimation of the number of cancer cases used in the study analyses.

Results indicate several significant differences of risk between demographic and arsenic concentration intervals. However, the inherent limitations of secondary data have produced some unexpected results. Using the arsenic Quintile 1 (0 - 0.9 μg/L) as a reference point, the results showed that arsenic concentration levels in groundwater do not impact the incidence rates of bladder, kidney, liver or lung cancer in populations over the age of 40 in regions with arsenic concentrations above 1 μg/L. Further, although cancer incidence rates might be expected to increase with increasing groundwater arsenic concentrations in Quintiles 3, 4 and 5, the results in this study show otherwise.

Maps of the study regions depicting arsenic concentration levels in groundwater show that arsenic is widely distributed but concentration levels can vary greatly between census tracts located in close proximity. The distribution of arsenic in the region may be affected by geological formations that are known to be associated with higher arsenic levels. Follow-up studies are recommended for regions of the state that were found to have arsenic concentration at or above the current MCL regulated by the Safe Drinking Water Act. Rural regions of the state that rely on private groundwater wells not regulated by the federal standard would also be appropriate.

Results of this study will be shared with the Oregon Environmental Public Health Tracking network, their research partners and other interested state and local agencies.

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Groundwater Arsenic Concentrations and Cancer Incidence Rates: A Regional Comparison in Oregon

by
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APPROVED:

Major Professor, representing Environmental Health and Occupational Safety Management

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Chair of the Department of Public Health

Dean of the Graduate School

I understand that my thesis will become part of the permanent collection of Oregon State University libraries. My signature below authorizes release of my thesis to any reader upon request.

Harmony S. Fleming, Author

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TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

Groundwater Arsenic Concentrations and Cancer Incidence Rates:
A Regional Comparison in Oregon

INTRODUCTION

The acute toxicity of arsenic (As) in its inorganic form has been known for centuries. Today, the chronic exposure to arsenic is also known to have an adverse effect on human health. Chronic arsenic ingestion from drinking water has been found to cause carcinogenic and non-carcinogenic health effects in humans (Basu et al., 2001; Mandal & Suzuki, 2002; Morales et al., 2000; Rahman et al., 2001; Steinmaus et al., 2003). This relationship has been well established in epidemiological studies, most commonly case-control studies, in which the health effects of populations exposed to inorganic arsenic are compared to those who are not exposed. The primary exposure route of inorganic arsenic is ingestion from drinking water due to natural contamination in groundwater from dissolution of natural mineral deposits, industrial effluent and drainage problems (Mandal & Suzuki, 2002).

Long-term chronic exposure to arsenic increases health risks ranging from skin and internal cancers to diabetes, and vascular, reproductive, and neurological effects (Florea et al., 2005; Mead, 2005). Arsenic has been determined to be a class A human carcinogen by the Environmental Protection Agency (EPA), the Department of Health and Human Services (DHHS), and the World Health Organization (WHO) from evidence substantiated from global studies (Agency for Toxic Substances and Disease Registry [ATSDR], 2000; Morales et al., 2000). Arsenic, however, has also been both beneficial to human health and the economy in a wide variety of fields such as medicine, agriculture, livestock, electronics, industry and metallurgy (Mandal & Suzuki, 2002).

In the United States, the current regulation or maximum contaminant level (MCL) set for arsenic by the EPA via the Safe Drinking Water Act (SDWA) is 10 parts per billion (ppb) or 10 micrograms per liter (μg/L). The current MCL was put into effect in January 2006, and is a considerable reduction from the previous MCL of 50 ppb which was established in 1942 without toxicological evidence (EPA, 2005a). The new MCL was established following publications by the National Academy of Sciences (NAS) and National Research Council's (NRC) assessments evaluating 50

years of epidemiologic studies conducted on a world wide basis (NRC, 1999; NRC, 2001).

Groundwater studies conducted by the United States Geological Survey (USGS) show that arsenic is present at varying concentrations across the country (USGS, 2005) (Figure 1). The SDWA was designed to protect public health by regulating the nation's public drinking water supply and sources (EPA, 2006). While this Act protects the drinking water for the majority of Americans, it does not regulate private drinking water sources. Approximately 15 percent of the US population using a self-supplied domestic source; and ground water is the primary source for 98 percent of this population (Hutson et al., 2000).

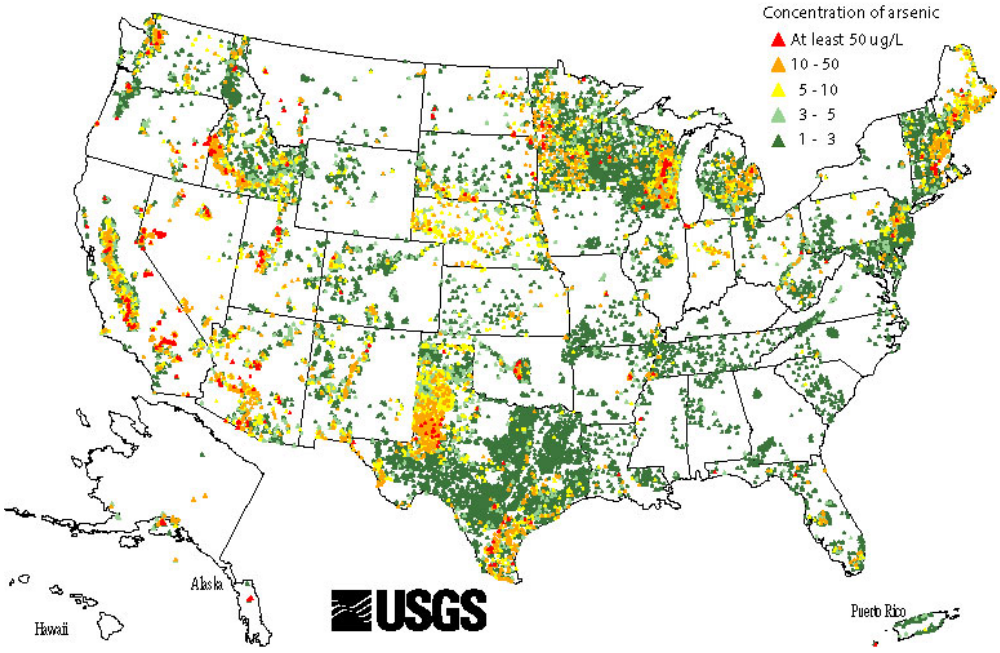


Figure 1. Arsenic Concentrations in Groundwater in the United States, (USGS, 2005).

The responsibility for health and environment in the United States has historically been divided among various government agencies, which often have limited interactions (National Academy of Sciences [NAS], 2004). A poll conducted for Pew Charitable Trusts in 2000 found that 86 percent of the U.S. population

believed that environmental factors are important or very important in causing diseases and, further, inaccurately believed that government agencies were tracking these disease and other environmental incidences (NAS, 2004). In 2001 the Centers for Disease Control & Prevention (CDC) implemented the Environmental Public

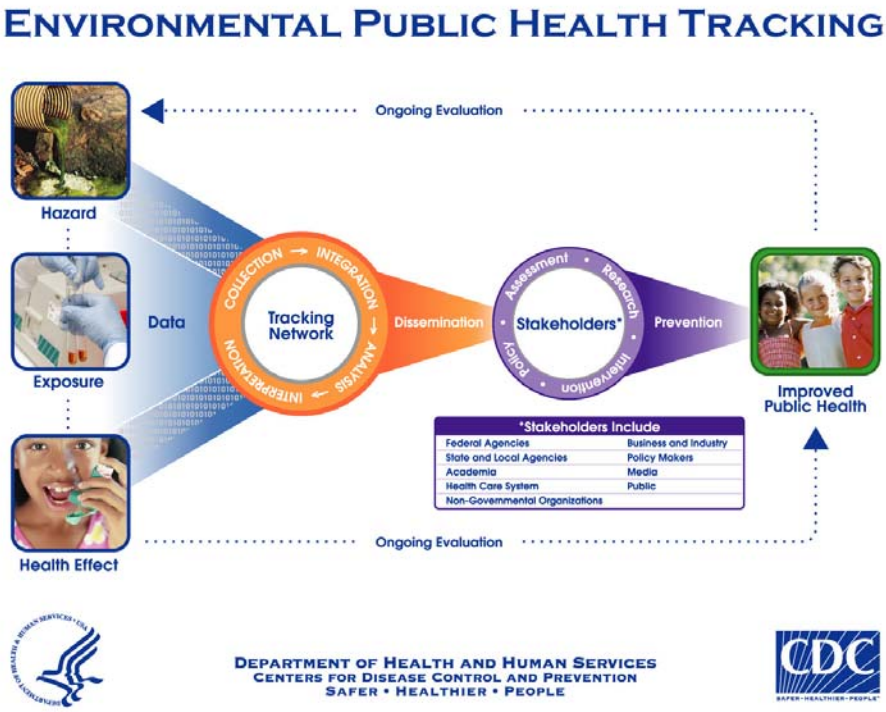


Figure 2. CDC Environmental Public Health Tracking Diagram, (CDC, 2006).

Health Tracking (EPHT) network in response to the report released by the Environmental Health Commission of Pew Charitable Trusts (Figure 2). The network was created to develop a standards-based program to aid states and federal agencies in linking environmental hazard data with health outcome data (McGeehin et al., 2004). The goal of the EPHT network is to improve the health of communities, accomplished by the collaboration and partnership of agencies collecting and analyzing environmental data and health data. The EPHT Program often uses geographic information systems (GIS) to aid in investigating environmental causes of illnesses.

Geographic information systems are spatial analysis tools, which have been extensively used in natural resource management, public works, transportation and government. Only recently however, have public health researchers explored its

capabilities to generate and investigate spatial hypotheses for analyzing relationships from previously static and cross-sectional data (Khan, 2003). GIS software provides the technological platform for environmental and epidemiologic data to be stored, analyzed, and spatially displayed. GIS is comprised of the following elements (Khan, 2003):

- Technology that is used to analyze features that make up the earth's surface
- System that includes software, hardware, data, and personnel
- Use of the relative location of features in x, y, and z space to establish relationship between features

GIS provides valuable information regarding the spatial information of environmental hazards, and the population proximity for exposure and distribution of mortality and morbidity statistics. Study design and data selection are of importance when using a GIS to analyze and produce meaningful research results, as is selection of scale an important factor when creating and analyzing GIS databases for exposure assessment. Homogeneity and heterogeneity of spatial data are affected by scale, and the scale chosen may affect the ability of the study to detect a relationship between the environmental exposure and health outcome (Nuckols, 2004).

Spatial studies of arsenic concentrations, with health outcomes associated with chronic exposure to low-levels of arsenic and populations in proximity for exposure has not been done in Oregon using GIS. Studies evaluating the risk of chronic low-level exposures to arsenic are also needed to gain a better understanding of the mortality and morbidity of health effects resulting from such exposure. No study has been conducted in Oregon to investigate the geographic relationship between groundwater arsenic concentrations and cancer rates.

Purpose of Study

The purpose of this study was to determine if there is a spatial relationship between groundwater arsenic concentrations and cancer incidences within two

geographical regions of Oregon. The objectives of this study were to: (1) determine if there is a spatial relationship between arsenic concentrations in the Willamette Valley Basin and Southeast Oregon and incidence rates of bladder, liver, lung, and kidney cancers; (2) contribute to the Centers for Disease Control and Prevention's development of the Environmental Public Health Tracking network by using secondary data to investigate possible linkages of arsenic in groundwater and associated health effects; and, (3) serve as an exploratory tool for identifying a regional public health concern that can be followed up with comprehensive analytical studies of the region.

Research Questions

The following research questions guided the study.

1. What are the spatial relationships between groundwater arsenic concentrations and age-specific cancer incidence rates within the two study areas in Oregon?
2. Are the overall age-specific cancer incidence rates higher within census tracts that have higher concentrations of arsenic when compared to overall state cancer rates?
3. Are age-specific incidence rates of bladder, kidney, liver and lung cancers higher within census tracts with arsenic concentrations in groundwater at or above 10μg/L?

Significance of Study

A considerable proportion of the population in the Pacific Northwest relies on private wells for their domestic water supply, when compared to other regions of the United States. In Oregon nearly one fourth of the population uses private wells as the primary source of drinking water. This population has been identified as a population with a greater exposure risk to arsenic as a drinking water contaminant due to the lack of an enforceable MCL. The data linkage goal of this study will provide environmental hazard and health outcome data based on surrogate exposure to arsenic found in the groundwater. This contributes to the stated initiatives of the CDC's Environmental Public Health Tracking network to better evaluate effective public

health actions to prevent or control chronic and acute diseases linked to hazards in the environment.

This descriptive study may provide the framework for follow-up analytical studies of chronic low-level arsenic exposure and cancer incidence in the defined study area, and identify potential populations at risk to exposure from private drinking water sources. Spatial description of data may then be used to educate private well owners about the importance of testing for arsenic in their groundwater.

Limitations

There are several limitations inherent in using secondary data that will be important in interpreting the results of this study. The data collected from existing databases have not been collected for the purpose of identifying causal relationships between arsenic concentrations and cancer rates. Rather, arsenic exposure is inferred by the presence of arsenic in groundwater that is used for drinking water purposes. It is also recognized that an implied surrogate exposure may not accurately represent the actual exposure of the population.

In addition, limitations of health outcome data such as that collected by cancer registries have inherent limitations. The registry data reflect cancer cases at time of diagnosis which may not be the time of onset. The study area has predominantly rural population that regularly postpone visits to their healthcare providers.

Inherent problems that exist when individual-level data are substituted with aggregate data must be anticipated, such as making causal inferences about individuals based on findings from group data with both statistical and spatial analyses. In addition, the study has a regional rather than national scope and the results may not be generalizable beyond the study area.

Abbreviations/Acronyms

ATSDR: Agency for Toxic Substances & Disease Registry,

DHS: Department of Health and Human Services
CDC: United States Centers for Disease Control and Prevention
EPA: United States Environmental Protection Agency
GIS: Geographic Information Systems
MCL: Maximum Contaminant Level
NAS: National Academy of Sciences
NRC: National Research Council
USGS: United States Geological Survey

Definition of Terms

Age-Adjusted Incidence Rate : Incidence rates measure the number of new invasive cancer diagnoses per 100,000 population during a defined time period. Age standardization, often referred to as "age-adjustment" is used to eliminate the confounding effects of differences in the age composition among different populations across time, which allows for statistical comparison of rates in these different populations and over different time periods.

Anoxic wells: Groundwater wells that are depleted of oxygen.

Arsenic: A trivalent and pentavalent metalloid poisonous element that is commonly metallic steel gray, crystalline, and brittle.

Community Water System: A public water system that serves year-round residents of a community, subdivision or mobile home park that has >15 service connections or an average of >25 residents for >60 days/year.

Genotoxic: Chemical compounds capable of causing genetic mutation and of contributing to the development of tumors.

Groundwater: Water found in the spaces between soil particles and cracks in rocks underground (located in the saturation zone). Groundwater is a natural resource that is used for drinking, recreation, industry, and irrigation.

Inorganic arsenic: The oxides and other non-carbon compounds of the element arsenic included in particulate matter, vapors, and aerosols.

Maximum Contaminant Level (MCL): The maximum permissible level of a contaminant in water which is delivered to any user of a public water system. MCL levels take into account feasibility and cost but are set as close as possible to the level at which no adverse health effects occur.

Organic arsenic: Arsenic compounds combined with carbon and hydrogen.

Rural: All areas not classified by the Census Bureau as urban are defined as rural and generally include places of less than 2,500 persons.

LITERATURE REVIEW

The literature review is organized into the following sections: (1) Health effects and epidemiological studies; (2) Chemical forms of arsenic; (3) Drinking water regulations; (4) Geographic information systems; and, (5) Environmental Public Health Tracking Program.

Health Effects and Epidemiological Studies

Epidemiologic studies conducted globally have provided a large body of evidence regarding the adverse health effects from the ingestion of inorganic arsenic. Studies within and outside of the United States in countries such as Bangladesh, Taiwan, Chile and West Bengal link both non-cancerous and cancerous outcomes to arsenic exposure. Adverse health effects result from both acute and chronic exposure to inorganic forms of arsenic (National Research Council [NRC], 2001; Steinmaus et al., 2003).

The health effects associated with inorganic arsenic exposure include: tumors of the bladder, kidney, liver, and lung; blood vessel damage; reproductive and developmental effects; neurological effects; peripheral vascular and cardiovascular disease; numbness in the hands and feet; diabetes mellitus; and, dermal effects such as diffused and spotted melanosis, leucomelanosis, keratosis and basal cell cancer of the skin (Basu et al., 2001; Mandal & Suzuki, 2001; NRC, 2001; Physicians for Social Responsibility [PSR], 2005; Rahman et al., 2001; Zierold et al., 2004).

The dose-response relationship of arsenic ingestion is dependent upon many factors. Health effects are believed to be exacerbated with possible synergistic reactions with other environmental exposures such as ultraviolet light, smoking and individual nutritional status (Basu et al., 2001; Rahman et al., 2001; Steinmaus, et al., 2003). The NRC (2001) points out that when assessing the risks from arsenic, it is nearly impossible to rule out the possibility that genetics, lifestyle differences, and exposure to other environmental factors might play a role in explaining variability in the risks of individuals. Other key factors relating to the latency periods and development of adverse health effects from arsenic ingestion in humans are the dose amount, chronic or acute exposure, the frequency of exposure of arsenic, genetics, age and health status or other unknown risk factors (Agency for Toxic Substances &

Disease Registry [ASTDR], 1998; NRC, 2001; Physicians for Social Responsibility [PSR], 2005).

At high doses, at or above the World Health Organization's (WHO) previous maximum permissible limit of 50 μg/L, arsenic ingestion has been reported to result in clinical symptoms of arsenic toxicity within six months to two years (Rahman et al., 2001). In 1993, WHO lowered their recommendations for arsenic exposure to what the agency terms a 'realistic limit' of 10 μg/L, based upon evidence that inorganic arsenic is a documented human carcinogen and is in accord with their goals to reduce the burden of disease worldwide (WHO, 2004).

Long-term chronic exposure to lower concentrations of arsenic may have a prolonged latency period of at least five years (PSR, 2005; WHO, 2001). A definition for low dose arsenic exposure has not been finalized because there is insufficient knowledge on the mode of action of arsenic to justify any specific dose-response model. Currently, the NRC (2001) reports that the increased risks for bladder and lung cancers combined at arsenic concentrations between 3 μg/L and 20 μg/L in the United States are estimated to be between 9 and 72 per 10,000 people. Physicians for Social Responsibility (2005), reported that the previous arsenic drinking water standard of 50 μg/L based upon previous research may have had an excess cancer risk beyond the EPA's 1/1000000 excess cancer risk.

There are a number of uncertainties regarding the latency period of arsenic exposure induced diseases. The prolonged latency period of cancers associated with low-level chronic exposure to arsenic has made it difficult to quantify the amount of arsenic and time required to cause a genotoxic response in humans (Florea et al., 2005; Morales et al., 2000). Recent studies have contributed to better understanding of the association between low-dose arsenic exposure and health.

A study by Steinmaus et al. (2003) investigated the link between lower arsenic concentration exposures and cancer with a case-control study conducted in six counties in western Nevada and Kings County, California. The authors report these counties to have the largest populations historically exposed to drinking water arsenic concentrations near 100 μg/L in the United States. For several populations in the United States who have been exposed to arsenic concentrations near 100 μg/L,

however, risk estimates for these exposures have involved extrapolations from the results of other international highly exposed populations. This study collected individual data on water sources, water consumption patterns, length of residency, education level and smoking, were collected for 181 cases of bladder cancer and 328 frequency matched controls. Overall, there were no increased risks identified in the study population for arsenic intakes greater than 80 μg/day. A major limitation of the research was the long latency period between arsenic exposure and bladder cancer diagnosis for the study population. However, analyses of subgroups in this study found a positive association consistent with other studies to support that exposure to arsenic and cigarette smoke act synergistically in causing cancer.

A second study by Morales et al. (2000) is a risk assessment for mortality due to several internal cancers, based on the reanalysis of data reported from several villages in Taiwan by Chen et al. (1989; 1992). The USEPA has used these data to assess the risk of skin cancer as evidence for revising the current standard for arsenic in drinking water. The authors argue that the methods used in this paper for assessing the risk of bladder, liver and lung cancer produce more convincing results than the USEPA's prior assessment. The current study calculated excess lifetime risk estimates using several variations of the generalized linear model and for the multistage-Weibull model. Risk estimates were sensitive to the model choice and several factors of uncertainty existed. However, despite the sources of uncertainty, such as individual arsenic exposure values, the analyses conducted suggested that a drinking water standard of 50 μg/L for arsenic is associated with a substantial increased risk of cancer and is not sufficiently protective of public health.

Another group of researchers, Zierold et al. (2004), set out to evaluate the prevalence of nine chronic diseases in adults who drink water from privately owned groundwater wells at risk of arsenic contamination in Wisconsin. The nine chronic diseases investigated were bypass, angina, heart disease, heart attack, high blood pressure, stroke, circulatory problems, diabetes, and depression. They analyzed well-water samples and questionnaires from 1,185 people who reported drinking their water for at least 20 years. Significant findings of the study were that respondents with arsenic concentrations of 2 μg/L or greater were statistically more likely to report a

history of depression, high blood pressure, circulatory problems, and bypass surgery than were respondents with arsenic levels less than 2 μg/L.

A recent study by Walker et al. (2006), explored the health risk perception of residents in Churchill County, a rural region in western Nevada whose drinking water supplies were known to contain varying concentrations of arsenic. The researchers solicited study participants who relied on a private drinking water well to complete a survey regarding their perceptions of health risks associated with exposure to drinking water contaminants, with an emphasis on arsenic. They also investigated if the presence of arsenic in their groundwater supply influenced their consumption habits. Overall, the results indicated that private well owners may be unaware that drinking water standards that apply to public water supplies do not apply to private well supplies, and of the potential health effects of contaminants in their drinking water.

Chemical Forms of Arsenic

Arsenic is a naturally occurring metalloid that is usually found in the environment combined with other elements. Arsenic combined with carbon and hydrogen in called organic arsenic. Organic forms are usually less harmful than the inorganic forms. Inorganic forms are combined with elements such as oxygen, chlorine, and sulfur. The major inorganic forms are arsenate [As(V)] or arsenite [As(III)], or a mixture of the two.

A review article by Basu et al. (2001) describes arsenic as naturally occurring and widely distributed in air, water and soil, in the form of either metalloids or chemical compounds. It is the 20th most abundant element in the earth's crust, and is a component of more than 245 minerals. The trivalent form [As(III)] of inorganic arsenic is more toxic then the pentavalent [As(V)] form.

Chemical forms and oxidation states of arsenic are more important to consider with regard to human toxicity (Mandal & Suzuki, 2002). The toxicity of arsenic is also dependent on other factors such as physical state, gas, solution, or powder particle size, the rate of absorption into cells, the rate of elimination, the nature of chemical substituents in the toxic compound, and the pre-existing susceptibility of the individual. Arsenic is not broken down or destroyed in the environment, but most

arsenic compounds dissolve in water (ASTDR, 2005). Inorganic arsenic occurs naturally in many kinds of rock, especially in ores that contain copper or lead.

A USGS report found that in the Willamette Basin of Oregon, high arsenic concentrations have been correlated with two regionally extensive associations of rocks the Fisher and Eugene Formations, and the undifferentiated tuffaceous sedimentary rocks, tuffs, and basalts (Hinkle et al., 1999) . At land surface, these two rock associations cover 24 percent of Willamette Basin. These associations of rock include extensive volumes of silicic volcanic rock, commonly associated with high concentrations of arsenic. Also reported were high concentrations of arsenic in the Tualatin Basin associated with regional alluvial deposits. In addition, there are numerous anthropogenic uses of arsenic, as it has been used as a wood preservative, pesticide and for pharmaceutical purposes.

Drinking Water Regulations

Drinking water is one of the primary routes of exposure of inorganic arsenic (Basu et al., 2001; Morales et al., 2000; NRC, 2001) giving great importance to the regulations protecting the public's health. Overall, groundwater systems have been found to have higher levels of arsenic than surface water supplies (Frey & Edwards, 1997).

The United States Environmental Protection Agency (EPA) has recently revised the drinking water standard for arsenic from 50 μg/L or parts per billion (ppb) to 10 ppb. The EPA (2006a) set the new standard at a level that "maximizes health risk reduction benefits at a cost that is justified by the benefits," in accordance to the 1996 Safe Drinking Water Act (SDWA) Amendments.

This revision, of the arsenic rule, according to the EPA (2006a) will provide additional protection to 13 million Americans against cancer and other health problems, including cardiovascular disease and diabetes, as well as neurological effects. The lowered maximum contaminant level (MCL) of arsenic allowed in public drinking water is based upon the review of decades of research and the comprehensive report by the National Research Council in 1999 and the 2001 update. Although the

MCL was adopted in January of 2001, community water systems were required to comply with the standard on January 23, 2006 (EPA, 2005b).

Drinking water standards apply to public water systems, which provide water for human consumption through at least 15 service connections, or regularly serve at least 25 individuals (EPA, 2006b). Private water supplies, such as groundwater wells are not subject to the regulations and management requirements of the SDWA (EPA, 2006b; Walker et al., 2005). A report commissioned by the USGS states that 15 percent of the U.S. population, or 43.5 million, people have a self-supplied water source (Hutson et al., 2001).

Geographic Information Systems (GIS)

There is increasing interest in research investigating relationships between the health characteristics of populations and physical environmental characteristics. Using a GIS, environmental public health researchers are able to analyze health effects in proximity to environmental hazards, which is important for public health intervention activities (Cromley & McLafferty, 2002; Hassan et al., 2003).

For example, Brody et al. (2004) used GIS analysis to examine breast cancer risk considering historical residential proximity to wide-area pesticide use and the exposure of women residing in Cape Cod. The prolonged latency periods and genetic polymorphisms that exist in the population hinder identifying specific causal factors for breast cancer. This study, however, incorporated environmental modeling of pesticidal chemical movement after application and geo-coded residential data of cases and controls to draw relationships between possible exposure and breast cancer. Study findings did not find an overall pattern of association between pesticide use and breast cancer but did find modest increases in risk associated with aerial application of pesticides.

Cromley and McLafferty (2002) devote an entire chapter in their book, *GIS and Public Health* on the analysis of environmental hazards. The authors suggest that using a hazard-exposure-outcome model with a GIS aids in the description of the process in which an agent in the environment may produce an adverse health outcome. The model process is as follows: (1) hazard surveillance identifies the presence of the

hazardous agent in the environment and route of exposure, (2) exposure surveillance identifies if the host is exposed to the agent, if the agent reaches target tissue and if the agent produces an adverse effect; and, (3) outcome surveillance are records of the effect being clinically apparent. These data are rarely available from one source and are usually drawn from multiple sources and integrated in the surveillance system. Accuracy of this model for environmental epidemiology is dependent upon the quality and geographic scale of the data. For example, modeling point sources and non-point sources of environmental contaminants for evaluating risk of exposure to surrounding populations, fate and transport models, should be used to further investigate what happens to agents released into the environment. Also, the analysis of health outcome data in a GIS is most effective with large populations and the use of individual case and control data to provide the means to analyze outcome to proximity of hazard and exposure sites. In conclusion, the authors warn that the maps generated by a GIS should be carefully viewed because their reliability depends on the modeling criteria used for analysis. The limitations of data and the understanding of the data by the user and maps generated from the same data can take on different appearances, ultimately portraying different levels of risk.

Nuckols et al. (2004) reviewed recent literature on the use of GIS in exposure assessment for environmental epidemiology. They concluded that the use of GIS in exposure assessments can enhance the understanding of the association between contaminants in our environment and disease. Further, it is preferable to estimate and validate levels of the contaminant of interest in the environment of the study population. Finally, when the levels of the contaminant cannot be measured or accurately predicted, GIS provides the optimal technology for using proximity to contaminant source in an environmental epidemiology study. The article reviews four recent studies utilizing GIS as an investigative tool to link environmental hazards, contamination levels and exposure to health outcomes of epidemiologic study populations. The first study reviewed Elliott et al. (2001), in which GIS was used to classify a study population born with birth anomalies living within 2 kilometers of landfill sites in Great Britain. Geocoding of both the cases reported in the health registry data and locations of past and current landfill sites were imperative to

illustrate proximity of cases to the perceived environmental hazard. Shortcomings contributing to the inaccuracy of this type of study can exist when address data is ungeocodable for individual cases because they are incomplete, inaccurate or are located in rural areas that do not list actual place of residency for address records.

The second study reviewed by Nuckols et al. (2004) was Reif et al. (2003), in which GIS was used to identify the potential routes of exposure to trichloroethylene through a municipal water supply known to be released from a superfund site in Denver, Colorado. The researchers paired this environmental hazard data with randomly selected study participants testing for neurobehavioral effects associated with the exposure of trichloroethylene. This study integrated a chemical transport model into the GIS and was able to better refine the path of exposure, improving sensitivity and specificity beyond a simple proximity metric. This method is advanced and assists researchers with problems associated geographical extent which can affect analysis results.

The third and fourth studies reviewed by Nuckols et al. (2004) were Bellander et al. (2001) and Nyberg et al. (2000), which showcased the use of GIS to estimate environmental levels of target contaminants in two epidemiologic studies examining lung cancer incidence in Stockholm. The studies combined dispersion models of air pollution data for three points in time to replace other lesser methods of classifying surrogate exposures to pollutants. The results from these studies indicated that GIS can be successfully used for exposure assessment in environmental epidemiology studies, provided that detailed geographically related exposure data are available for relevant time periods.

In an article by Hassan et al. (2003) the researchers utilize a GIS to identify the spatial pattern of the health risks associated with arsenic exposure in Bangladesh. A primary goal of this research was to explore the spatial pattern of arsenic concentrations in groundwater in Bangladesh for analyzing and mapping ‘risk zones’ for arsenic hazard information by using a GIS, spatial analysis and state-of-the-art decision making techniques. Arsenic measurements associated with tube wells in the region were imported as point data into the GIS to assist spatial analysis of health risks of the local population. The point data for the arsenic concentrations were

interpolated over the landscape resulting in a spatial arsenic risk pattern. Based upon identified risk factors and risk assessment and spatial risk zoning associated with the arsenic concentrations, the researchers concluded that a widespread awareness campaign is needed to save the people in the study area from mass arsenic poisoning.

An exploratory study by Ayotte et al. (2003) characterized the regional occurrence and distribution of arsenic in drinking water wells in parts of Maine, New Hampshire, eastern Massachusetts and Rhode Island. The research team conducted a spatial analysis with a GIS of arsenic concentrations found in the groundwater of the region to identify the potential magnitude of the regional population that may be exposed to arsenic via their water supply. The purpose of estimating the population ingesting groundwater from private wells was to identify possible human health implications of exposure to concentrations of inorganic arsenic at or above 10μg/L.

Water quality studies of groundwater and surface water utilizing GIS for assessing population exposure to drinking water contaminants through time and wellhead protection areas have also become popular. For example, Cohn et al. (1999) mapped water systems that varied in water quality due to source differences using GIS applications to estimate the size of the population exposed to contaminants over time. Water systems with a known history of volatile organic compounds contamination were especially of interest to the study. The study's results demonstrated a decrease in exposure to the population after the New Jersey Safe Drinking Water Act was signed in 1984.

In a second study done in Whatcom County, Washington, GIS was utilized to model differences among four accepted methods used to delineate wellhead protection areas around public supply wells (Miller, 2005). The study specifically compared the delineation results of the calculated-fixed-radius method to the more advanced delineation methods of analytical, hydrological and numerical models. Results of the study concluded the calculated-fixed-radius model compared best to the most advanced hydrological model. Mapping wellhead protection areas in GIS also has proven to be superior over paper maps due to GIS capabilities to compile, display, recognize and compare wellhead protection area for a given region.

Environmental Public Health Tracking Network

The responsibility for health and environment in the United States has historically been divided among various government agencies, which often have limited interactions (Institute of Medicine [IOM], 2004). The driving force behind the creation of a nationwide Environmental Public Health Tracking (EPHT) network is to connect environmental and health data collected over the past 100 years and in the future by these agencies (CDC, 2006; IOM, 2004).

McGeehin et al. (2004) state that the success of a national EPHT network is dependent upon the availability, quality, timeliness, compatibility and utility of existing hazard, exposure, and health effect data. With these it may be possible to find associations between the environment and the risk of noninfectious health effects. Standardizing hazard, exposure and health effect data collected on the national, state and local level is a primary challenge of the EPHT network and must improve data utility for the end user. The authors compiled a comprehensive list of program components essential for the success of the EPHT network's vision and strategy:

- Data systems that use compatible data standards and vocabularies
- High quality, timely mortality and morbidity data with high resolution geographic coordinates
- A wide range of exposure information based on bio-monitoring, personal monitoring, and exposure modeling
- Relevant high-quality, and timely emissions data and monitoring data for air, water, soil, food, and other environmental media as well as geographic and temporal characteristics
- Access to population data, including information on migration and socio-demographic factors
- Tools to link data geographically
- Tools for descriptive and small area analyses
- Tools for data dissemination
- Support for public health action

Twenty-one state health departments, three local health departments, and three Schools of Public Health were initially funded by CDC to form the basis of a

nationwide tracking network (CDC, 2006). A variety of EPHT pilot studies have been done by these public health agencies.

The State of Oregon was one of the states originally funded for planning and capacity building activities and has since been awarded a five-year grant to implement a tracking network that meets Oregon's specific needs while meeting the CDC's requirements for the national program (CDC, 2006; Oregon Environmental Public Health Tracking Program [OREPHT], 2006). Below are the Oregon EPHT Program's operational goals as listed on their website (OREPHT, 2006):

- Implement an EPHT Network that will be a part of the National EPHT Network
- Increase awareness of the EPHT program in Oregon
- Foster collaboration among health and environmental agencies
- Support the development of a State of Oregon EPHT Network that is interoperable and compatible with the National CDC Networks standards and architecture
- Evaluate and provide feedback to the CDC to improve and advance the National EPHT Program

One study conducted in Washington State by Laflamme and VanDerlice focuses on the EPHT goal of linking environmental data and chronic disease data. The authors examine the Behavioral Risk Factor Surveillance System (BRFSS) and its ability to be used to estimate individual exposure. The BRFSS is used in all 50 states and consists of a core health survey designed by the CDC, which can be added to by individual states. Washington State Department of Health has been collecting data on environmental health topics since 1990. Although many states have added environmental health-related questions for state specific issues, the core survey for the BRFSS does not contain a standardized section regarding environmental behaviors and perceptions. Three cases studies of environmental survey modules were examined--drinking water, perceptions of environmental risk, and radon awareness and testing. A key finding of the study was that data on exposure-related behaviors were useful for population exposure assessments and program evaluation. Other

findings indicated that questions about knowledge and attitudes of environmental issues were not as useful because they lacked sufficient detail from which to improve existing educational efforts and in some cases data collected in the survey had not been used at all indicating the need for the data had not been well established. In conclusion, a primary point of the research is the importance of designing a nationwide systematic data collection program that effectively tracks population exposure levels at the state or local level.

A second study by Mather et al. (2004) explores the research limitations of aggregating environmental hazard and exposure data when individual exposure data is not available. Data sets for hazard, exposure and health outcomes are diverse making it imperative for researchers to consider the limitations of data uses outside of its original purpose. The article compiles a list of existing limitations to be considered for all three types of data--completeness of data, timeliness of reporting, availability of access to data, geographic resolution of the data (scale), frequency of data collection, and lack of data collection standards. The authors conclude that newer spatial analysis and proper statistical methods are being developed and used to amend these limitations but require repeated use with various data linkages.

MATERIALS & METHODS

Study Area

The study area includes census tracts from eleven counties within two regions of Oregon that have known arsenic concentrations in the groundwater. These regions are the Willamette Valley Basin and Southeastern Oregon (Figure 3). Counties in the Willamette Valley Basin include Benton County, Clackamas County, Lane County, Linn County, Marion County, Multnomah County, Polk County, Washington County, and Yamhill County. Harney County and Malheur County are located in the southeastern corner of Oregon, in a primarily rural area of the state (Table 1).

Table 1. Counties and Census Tracts Included in Study Area

Willamette Valley Basin Counties	**Number of Census Tracts**
Benton County	8
Clackamas County	36
Lane County	36
Linn County	16
Marion County	30
Multnomah County	31
Polk County	7
Washington County	29
Yamhill County	8
Southeastern Counties	
Harney County	2
Malheur County	7
Total Number of Census Tracts	**210**

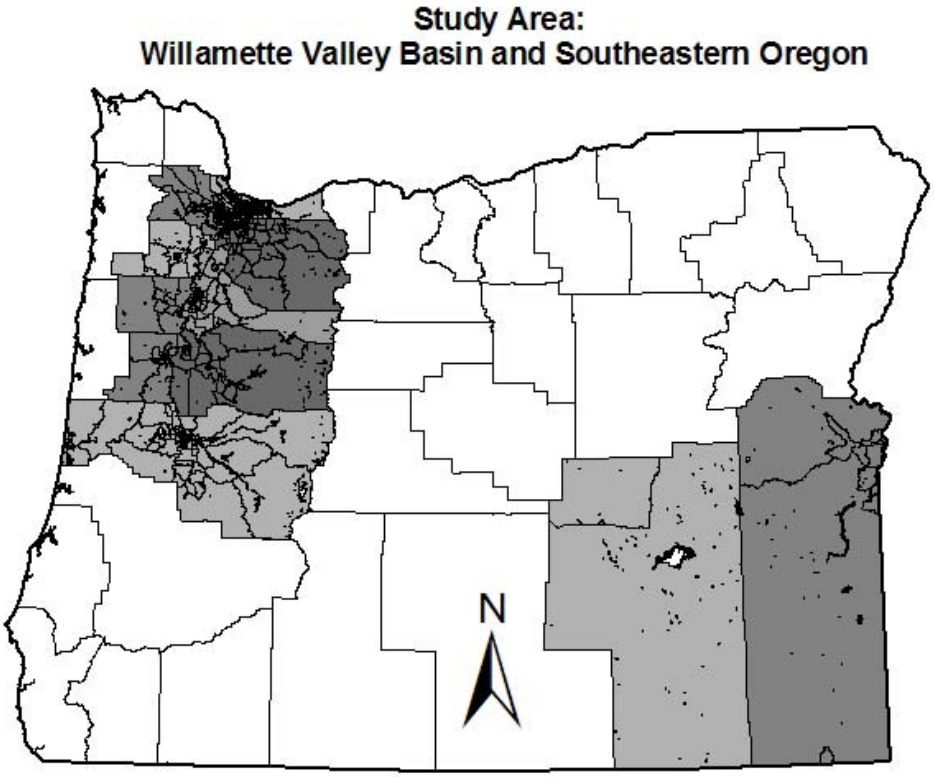


Figure 3. Geographical Regions of Study

Data Collection

This study used information from four data sets. Arsenic concentrations in groundwater were obtained from the USGS National Water Information System (NWIS), Water Quality Samples database which is comprised of thousands of data points collected nationwide. Data points have unique geographic identifiers that when imported into the GIS will place them into the corresponding census tract. The database with water quality samples for Oregon was publicly available online (USGS, 2005). Water quality data collected by USGS are not collected for public health purposes. Meaning, sample sites are not selected to monitor potential human exposure. Arsenic concentration data have been aggregated into quintiles at the census tract level for use in analysis.

The second data set consisted of data points of community drinking water systems with reported arsenic concentrations serving residents located in the identified

census tracts. These data were available through the Oregon Department of Human Services (DHS) Drinking Water Program (DWP) (Oregon DHS, 2006). DHS's Drinking Water Program administers and enforces drinking water quality standards for public water systems in the State of Oregon. The program also collects data reporting the location of the water systems, the type of water system, the number of residents using the system, the rate of compliance on reporting violations and the types of violations if observed or reported (Oregon DHS, 2006).

Initial data cleanup of the arsenic concentration data was required to eliminate unnecessary data categories and data points located outside of the study area. The arsenic concentration data from both the USGS database and the DHS Drinking Water Program were put into the GIS, using longitude and latitude coordinates, to determine the census tract in which they were located. Data from the two sets were then combined. An aggregated arsenic concentration value was calculated for each census tract by combining the concentration values from the two data sets. For analytical purposes the arsenic data will be separated into five quintiles based upon concentration levels (Table 2). The arsenic concentration divisions of the quintiles match those of a similar study conducted in New Mexico monitoring cancer incidence and drinking water arsenic levels (Flowers, 2005).

Table 2. Census Tract and Arsenic Concentration Quintiles

Census Tract Groups by Arsenic Concentration	**Aggregate Arsenic Concentration Levels**
Quintile 1	0 to 0.9 µg/L (ppb)
Quintile 2	1 to 10 µg/L (ppb)
Quintile 3	10.1 to 30 µg/L (ppb)
Quintile 4	30.1 to 50 µg/L (ppb)
Quintile 5	≥50.1 µg/L (ppb)

The third data set consisted of population and demographic data that were Census 2000. Data are publicly available at the census tract level through the U.S.

Census Bureau website (US Census Bureau, 2006). Data were downloaded by age and gender for the study from the US Census Bureau's *American FactFinder* website. Spreadsheets of population data requested contained total population counts for all age intervals and gender groups for each census tract in the study area counties. The age intervals included in the study (Table 3) had to be extracted individually and in some cases combined.

Table 3. Age and Gender Population Breakdown for Data Analysis

Age intervals for Male and Female Populations
40 to 49
50 to 59
60 to 69
70 to 79
80+

The fourth data set consisted of cancer data from the 210 census tracts included in the study area. Cancer data were obtained from the Oregon State Cancer Registry (OSCaR). OSCaR began collecting morbidity and mortality cancer data in 1996. The data set is complete through 2002, making seven years worth of data available for analysis. The study was first approved by OSCaR's advisory board and subsequently approved by Oregon State University's Institutional Review Board for the Protection of Human Subjects. After both approvals were granted, research analysts at OSCaR assisted in organizing the cancer counts for seven years of data into the appropriate census tract quintile (Table 2). Cancer counts by site (bladder, liver, lung, and kidney) were acquired by seeking permission through the appropriate channels at the state registry (OSCaR, 2004). The OSCaR advisory board approved the study and then released cancer counts by census tract groups dependent upon arsenic concentrations.

OSCaR provided the researcher with cancer counts for the four internal cancer types that were investigated. Cancer counts were given in age and gender specific groups based upon the designated arsenic concentration quintile which they fit. The

registry reported that a certain percent of cases are missing from the records provided do to the geocodability (Table 4) of the addresses given in the original records provided to the registry at time of diagnosis. In this study the majority of missing cases were attributable to rural cancer cases that were not able to be geocoded to place of residency due to an insufficient address type such as *Rural Route* or *P.O. Box*.

Data collection and preparation for this study (Figure 4) involved many steps and was time intensive. All data sets used for analysis required a varying amount of manipulation.

Table 4. OSCaR Percent of Cancer Cases with Geocoding Match by County

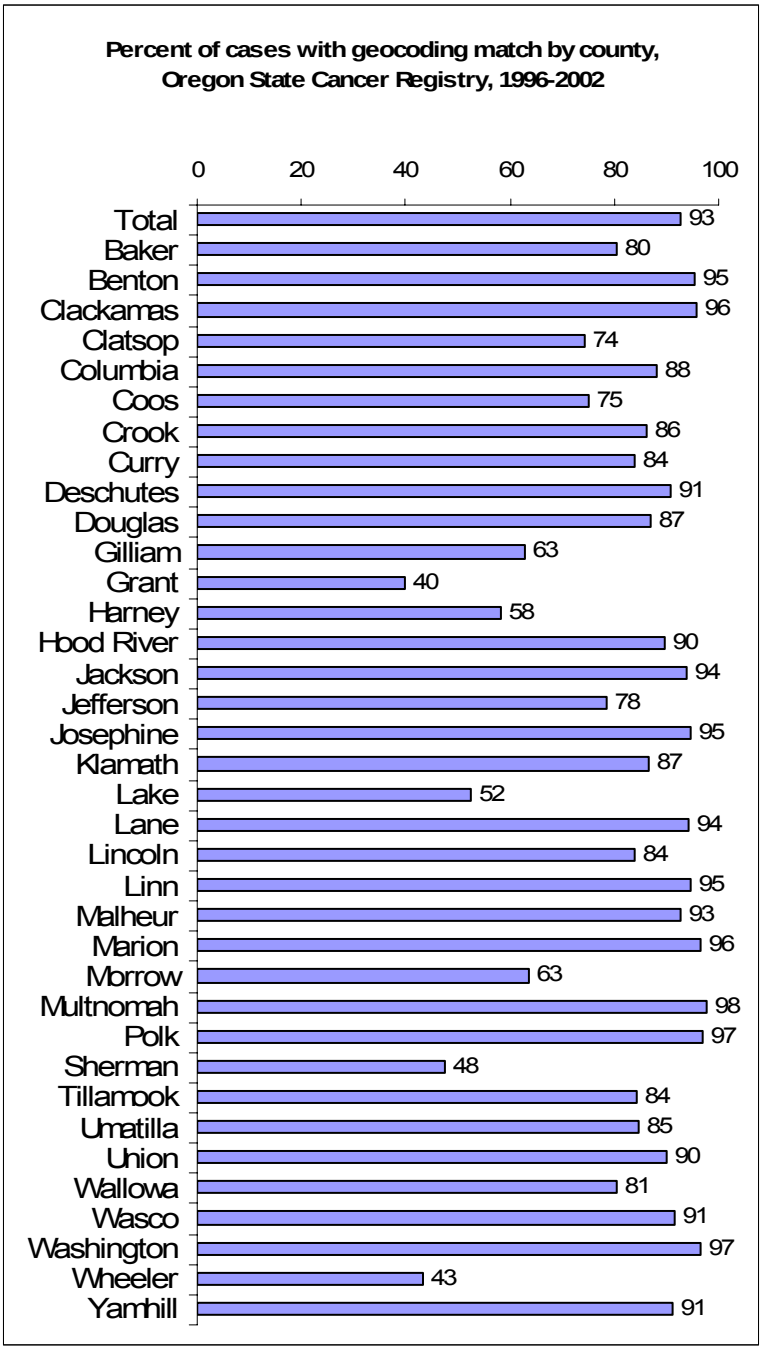
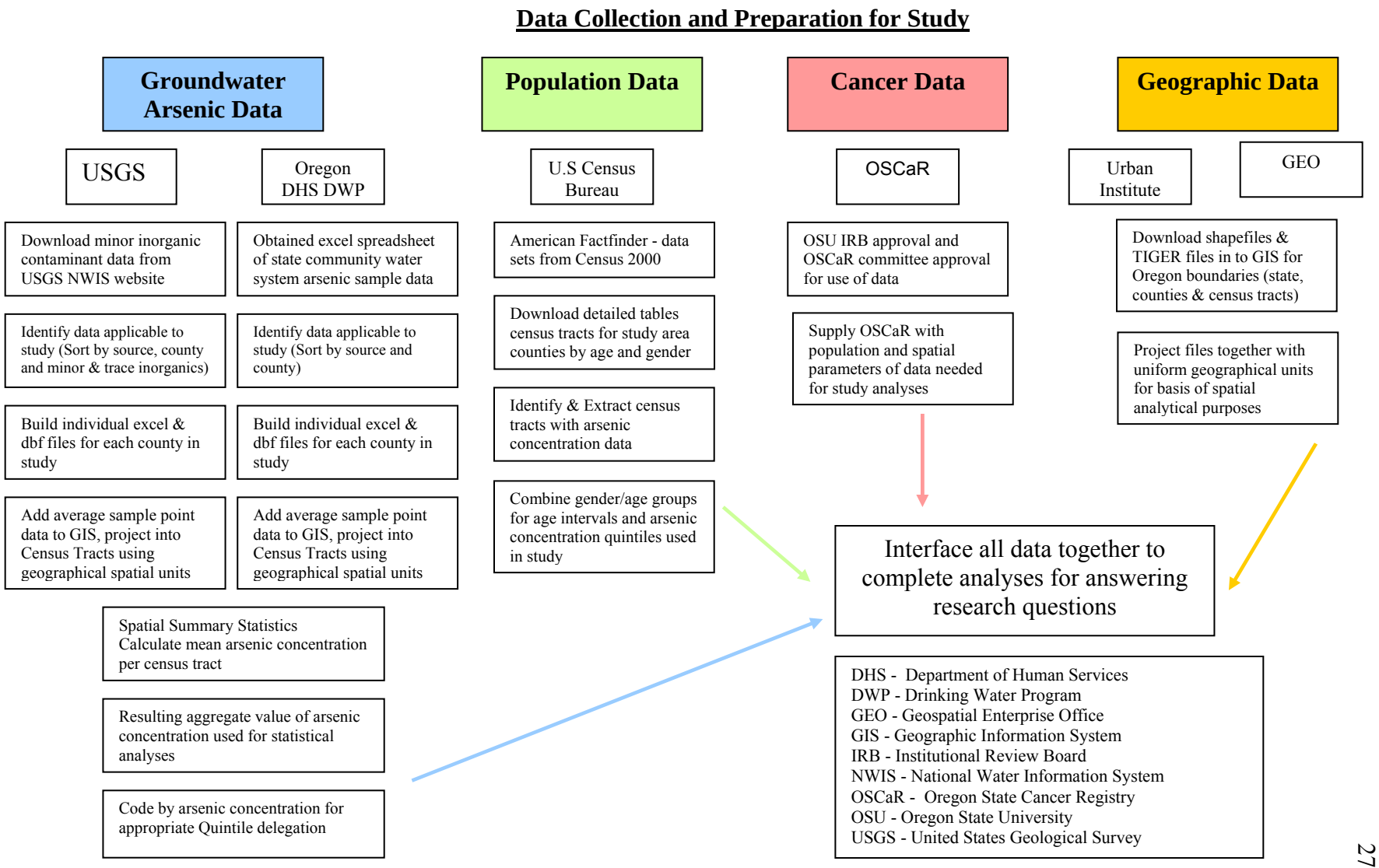


Figure 4. Flowchart of Data Collection and Preparation for Analysis



Data Analysis

Table 5 contains descriptions of the variables, their definitions, scale of measurement and how they were measured for the study.

Table 5. Definition and Measurement of Variables

VARIABLE	DESCRIPTION	SCALE OF MEASUREMENT	MEASUREMENT
Age-Gender Specific Incidence Rates for Oregon	State rates for bladder, liver, lung & kidney cancer cases	Continuous	Age-Gender rate per 100,000 for State of Oregon
Expected cancer cases	Cancer cases expected for specific age-gender populations for census tract quintiles	Continuous	Cancer counts calculated from State incidence rates and census tract populations per arsenic concentration quintile
Observed cancer cases	Actual cancer case counts for specific age-gender populations for census tract quintiles	Continuous	Cancer counts from OSCaR per arsenic concentration quintile
Arsenic Concentrations Quintile 1	Arsenic Concentrations (0 - 0.9ppb)	Ordinal & Discrete	Census tract mean arsenic values ranging from 0 to 0.9ppb
Arsenic Concentrations Quintile 2	Arsenic Concentrations (1 - 10ppb)	Ordinal & Discrete	Census tract mean arsenic values ranging from 1 to 10ppb
Arsenic Concentrations Quintile 3	Arsenic Concentrations (10.1 - 30ppb)	Ordinal & Discrete	Census tract mean arsenic values ranging from 10.1 to 30ppb
Arsenic Concentrations Quintile 4	Arsenic Concentrations (30.1 - 50ppb)	Ordinal & Discrete	Census tract mean arsenic values ranging from 30.1 to 50ppb
Arsenic Concentrations Quintile 5	Arsenic Concentration (≥50.1ppb)	Ordinal & Discrete	Census tract mean arsenic values ≥50.1ppb
Age-Gender population for census tracts of arsenic quintiles	Population counts for census tracts within counties of study area from the 2000 U.S. Census	Continuous	Male Population (40-49, 50-59, 60-69, 70-79, 80+) Female Population (40-49, 50-59, 60-69, 70-79, 80+)

Statistical Analysis

Chi-square calculations for gender groups for each cancer type were used to compare the observed cancer cases to the expected cancer case count for the five census tract groups (Table 2). Expected case counts for bladder, liver, lung and kidney cancers were calculated from the age-gender specific incidence rate for the state of Oregon. Age-specific incidence rates were calculated by dividing the number of cases with a specific cancer type in each age group by the number of person-years of observation in that group.

Poisson regression was used to attempt to determine if significant differences of observed cancer occurrence exist within the three categories; age, gender, and census tract quintile groups. The highest ranked value in each category was used as the reference groups (Table 6). This test was also employed to identify possible effects between the cancer count and the corresponding arsenic concentration within census tracts to identify the strength of association between the two variables.

Risk ratios with confidence limits were calculated among each category, controlling for the other two variables to provide further statistical support risk differences among categories.

Statistical analyses were conducted using Microsoft Excel 2003 (Microsoft Corporation; Redmond, WA USA) and SAS 9.1 for Windows (SAS Institute, Inc.; Cary, NC USA) software.

Table 6. Categorical Levels for Statistical Analysis

Category	**Values**
Age	***1 - 40-49 (reference group)***
	2 - 50-59
	3 - 60-69
	4 - 70-79
	5 - 80+
Sex	1 - male
	2 - female (reference group)
Census Tract Quintile	***1 - quintile 1 (0-0.9 ppb)***
	(reference group)
	2 - quintile 2 (1-10 ppb)
	3 - quintile 3 (10.1-30ppb)
	4 - quintile 4 (30.1-50 ppb)
	5 - quintile 5 (≥50.1ppb)

Spatial Analyses

Geo-spatial analytical methods were used to spatially illustrate relationships between arsenic groundwater concentrations and census tracts within the study area. Data from USGS, OR DWP, US Census Bureau were converted to a geodatabase, which provided a spatial representation of the data by linking attributes such as arsenic concentrations and geographic units to geographic coordinates.

Visual distributions of variables are displayed in maps generated from a GIS. ArcGIS 9.1 (ESRI, Redlands, CA USA). GIS was used to store, manipulate and analyze information on arsenic concentrations, community water system and population density at the census tract level.

RESULTS

The results of this study are presented in three sections. The first section presents descriptive information about groundwater arsenic concentrations. The second section describes the results that respond to the first research question. The third section combines results from both the second and third research questions.

Groundwater Arsenic Concentrations in Study Area

Table 7 shows the number of arsenic concentration points averaged from both the USGS and the Oregon Drinking Water Program (ORDWP) data sets. There were a total of 1,312 arsenic concentration data points averaged among the census tracts included in the study; 367 points (27.9%) came from the USGS data set and 945 (72.1%) came from the ORDWP data set. Important differences that exist between the data regarding arsenic collection methods of each agency are: (1) the USGS acquires water data without a public health agenda to investigate the occurrence, quantity, quality, distribution waters that constitute the Nation's water resources and (2) the ORDWP collects data from public drinking water systems to enforce drinking water standards in Oregon. Figures 5 and 6 display the locations of the point data collected by each agency, USGS and ORDWP.

Table 7. Arsenic Concentration Point Data Counts

Counties	USGS	ORDWP	Total
Benton	16	37	53
Clackamas	31	183	214
Lane	39	184	223
Linn	29	102	131
Harney	25	24	49
Malheur	7	23	30
Marion	28	180	208
Multnomah	16	72	88
Polk	41	23	64
Washington	100	53	153
Yamhill	35	64	99
Total	**367**	**945**	**1,312**

Figure 5. Map of USGS Arsenic Data Points

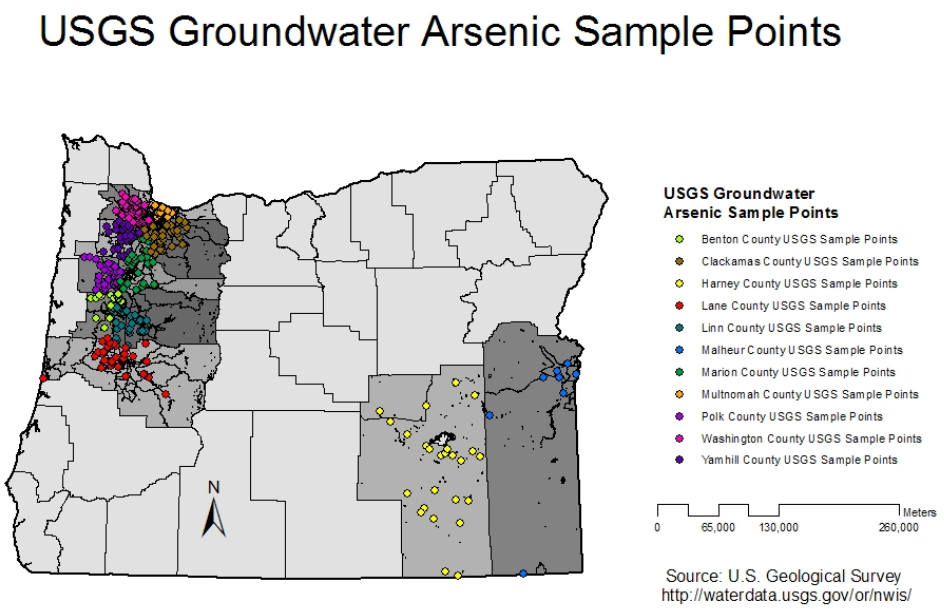


Figure 6. Map of Oregon Drinking Water Program Arsenic Data Points

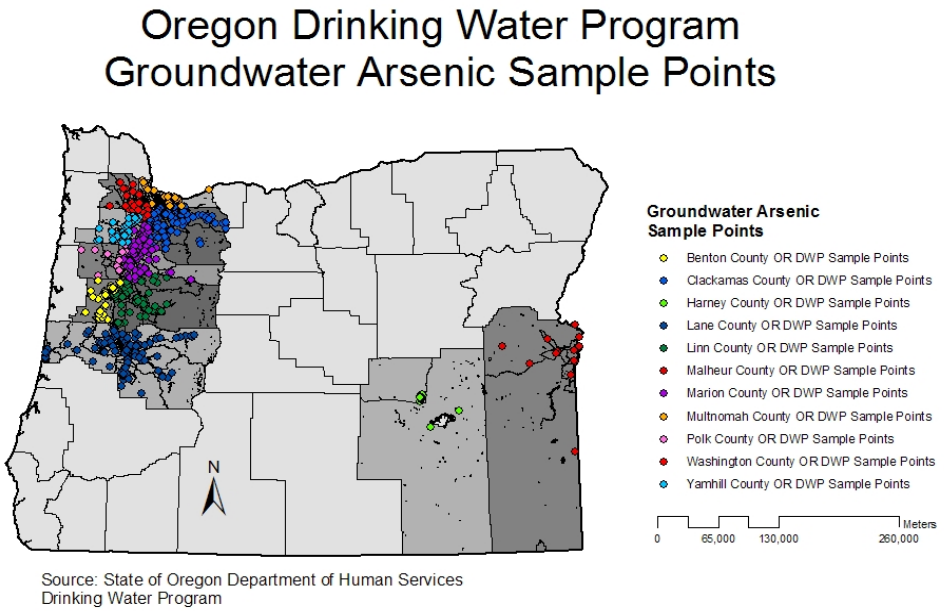


Table 8 shows the percentages of census tracts per county with arsenic concentration data. A total of 210 census tracts in the study area were found to have arsenic concentration data. The percentage of census tracts per county included in the study ranged from 18% (31/170) in Multnomah County to 100% (2/2) in Harney County. Census tracts typically without arsenic data, excluding them from this study, were located in the urban centers of county, such as the Portland Metropolitan Area in Multnomah County, Salem in Marion County and the Eugene Area in Lane County.

Table 8. Census Tract Distributions with Arsenic Data per County

Counties	Census Tracts per County	Census Tracts with Arsenic Data (n=210)	% of Census Tracts with Arsenic Data
Benton	21	8	38%
Clackamas	62	36	58%
Lane	79	36	46%
Linn	23	16	70%
Harney	2	2	100%
Malheur	9	7	78%
Marion	52	29	56%
Multnomah	170	31	18%
Polk	12	7	58%
Washington	81	30	37%
Yamhill	14	8	57%

Shown in Table 9 are the range of the aggregate values of arsenic found within each county and the quintile in which the data were further analyzed. Aggregate arsenic values used in the analyses were calculated in two steps; (1) calculation of the average arsenic value from each data set individually (USGS and Oregon Drinking Water Program) per census tract; and, (2) calculation of the mean from the two averaged values per census tract. The majority of the averaged data points were placed into either Quintile 1 (0-0.9 ppb) or Quintile 2 (1-10.0 ppb). The current maximum contaminant level (MCL) for arsenic in drinking water is 10μg/L (ppb). Figures 7 and 8 are choropleth maps illustrating the spatial patterns of the aggregate arsenic concentrations found per census tract.

Table 9. Census Tract by County and Arsenic Concentration Quintile

Counties	**Quintile 1** (0-0.9 ppb)	**Quintile 2** (1-10.0 ppb)	**Quintile 3** (10.1-30 ppb)	**Quintile 4** (30.1-50 ppb)	**Quintile 5** (≥50.1 ppb)
Benton	6	2			
Clackamas	20	16			
Lane	13	15	4	3	1
Linn	3	13			
Harney		1			1
Malheur		1	4	1	1
Marion	13	16			
Multnomah	11	19			1
Polk	4	3			
Washington	13	9	6	2	
Yamhill	3	5			

Figure 7. Map of Willamette Valley Aggregate Arsenic Concentrations by Quintile

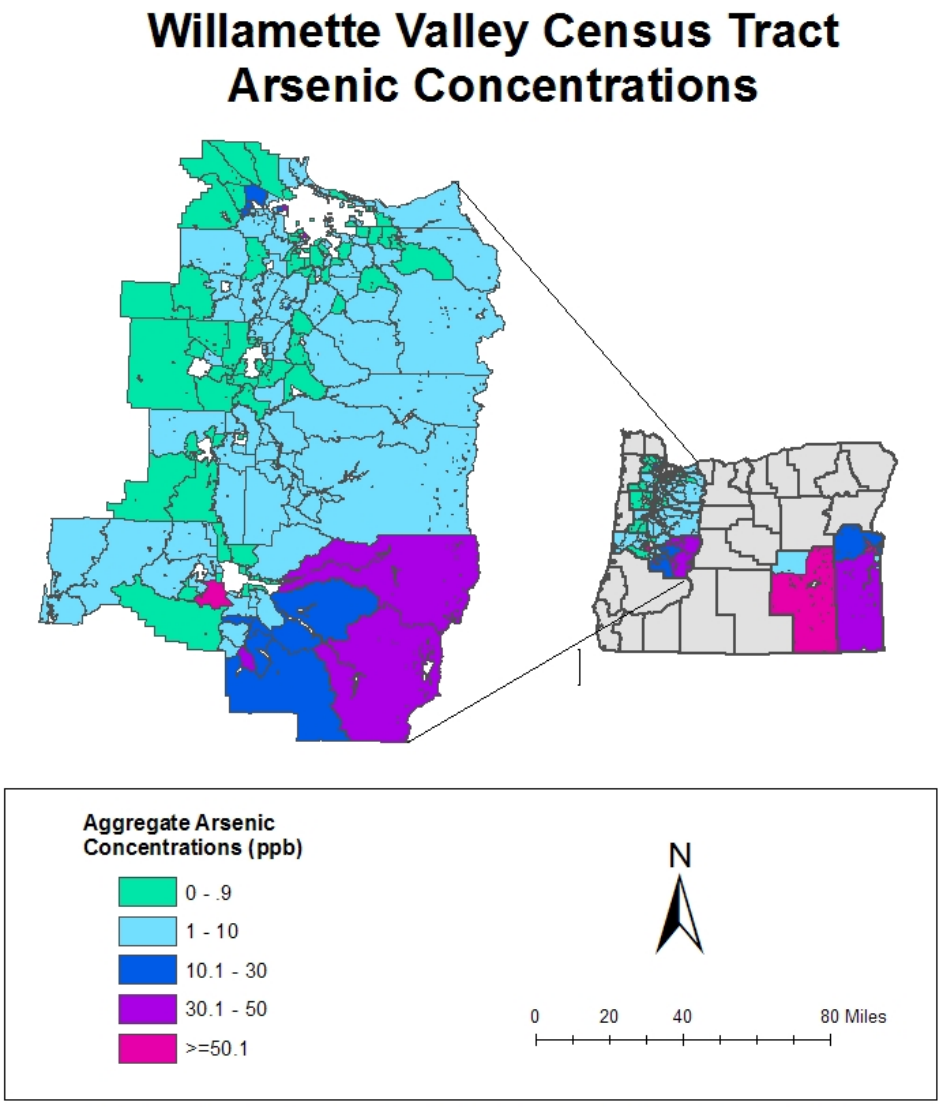
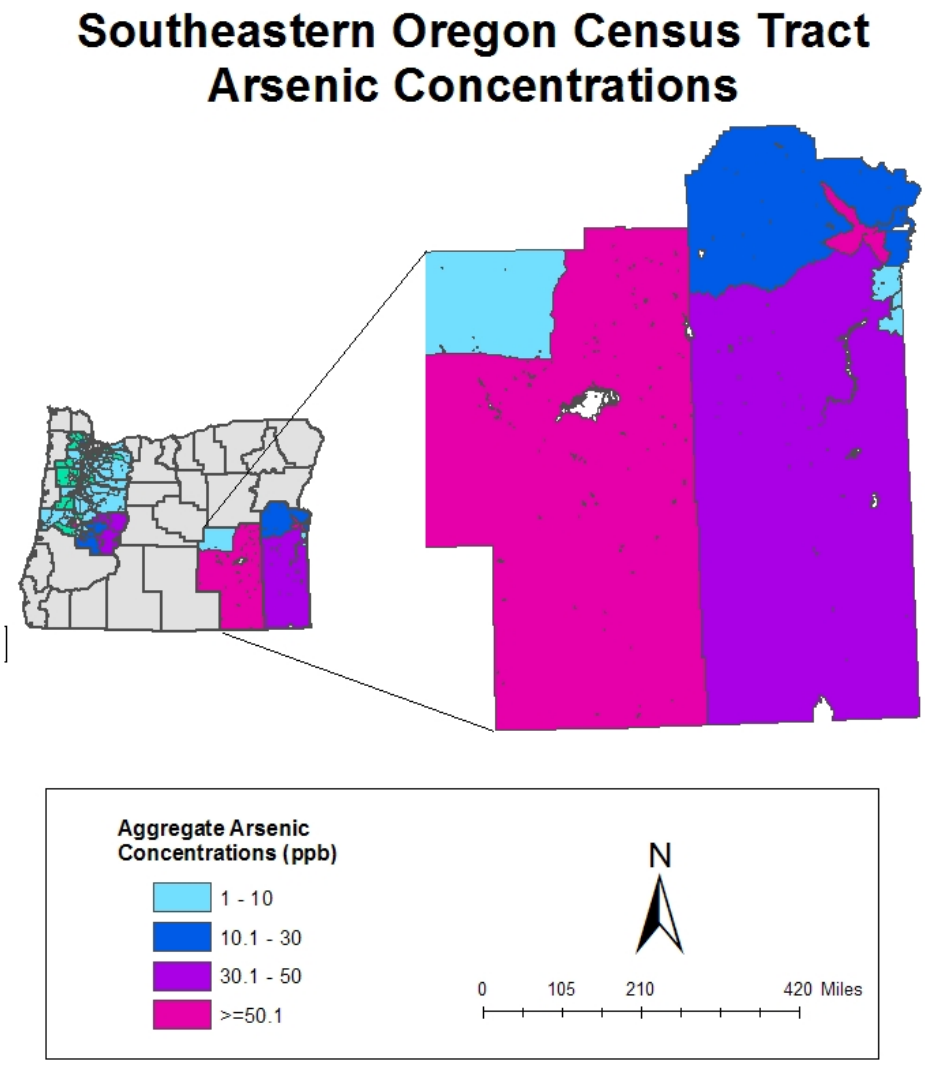


Figure 8. Map of Southeastern Oregon Aggregate Arsenic Concentrations by Quintile



Depicted in Table 10 is the range of averaged arsenic concentration values from each data set per county. The values of arsenic per county ranged from 0µg/L (ppb) found in both USGS and OR DWP data, to 411µg/L (ppb) found in the OR DWP data set, and 1,006µg/L (ppb) found in USGS data set. To obtain aggregate arsenic concentration data, arsenic concentration values were averaged for each data set, and final aggregated values of each census tract were computed. The aggregate of these values ranged from 0 ppb to 333 ppb. Lane County had the highest averaged concentrations of arsenic reported in the Willamette Valley region and Harney had the highest for the southeastern region. The values shown in Table 10 demonstrate that averages of the data set do not show the true range of arsenic concentration values that are found within the entire study area.

Table 10. Summary of Arsenic Concentrations Points per County

Counties	**USGS** Arsenic Concentration Range of points **(ppb)**	**OR DWP** Arsenic Concentration Range of points **(ppb)**	**Aggregate** Arsenic Concentration Range (average of all points) **(ppb)**
Benton	0 - 6	0 - 3	0 - 1.4
Clackamas	0 -6	0 - 40	0 - 3
Harney	0 - 50	0 - 411	2 - 79
Lane	0 - 1,006	0 - 170	0 - 240
Linn	0 - 12	0 - 39	0 - 6
Malheur	6 - 180	0 - 55	5 - 58
Marion	0 - 17	0 - 34	0 - 17
Multnomah	0 - 2	0 - 333	0 - 333
Polk	0 - 7	0	0 - 2
Washington	0 - 65	0 - 22	0 - 47
Yamhill	0 - 44	0 - 23	0 - 8

Research Question 1

The first research question sought to determine the spatial relationships between groundwater arsenic concentrations and age-specific cancer incidence rates within the two study areas in Oregon. Various steps were required to gather and organize the data to answer the research questions (See Figure 4 in Chapter 3). Population data preparation consisted of the following steps: (1) downloading of demographic files from Census 2000 website (U.S. Census Bureau, 2006); (2) identification of census tracts with arsenic concentration data; (3) tabulation of study age-sex intervals from identified census tracts; and, (4) categorization into appropriate arsenic concentration quintile for analyses. The averaging of arsenic concentrations as explained in the previous section was done to categorize the census tracts into quintiles.

Table 11 describes the person-year or population breakdown by quintile, age and sex. The population counts in Table 11 are combined totals from all census tracts included in each corresponding quintile group. Also, shown below in Figure 5 is the age-specific population distribution among the arsenic concentration quintiles analyzed for the study. Demonstrated in both Table 11 and Figure 5 is that 90.3 percent of the study population resides in Quintile 1 and Quintile 2. Meaning, the majority of the study population analyzed were in census tract with arsenic concentrations below the current MCL of 10μg/L (ppb). The remaining three quintiles which have arsenic levels above the MCL contain 9.7 percent of the study population.

Table 11. Person-years Used in Calculations from Census 2000 per Quintile

Age-Sex Group n = Person-Years	**Quintile 1**	**Quintile 2**	**Quintile 3**	**Quintile 4**	**Quintile 5**
Male 40-49	n = 34,811	n = 40,808	n = 5,280	n = 2,026	n = 1,262
Male 50-59	n = 26,070	n = 31,998	n = 3,493	n = 1,586	n = 1,015
Male 60-69	n = 13,981	n =17,938	n = 2,042	n = 1,006	n = 646
Male 70-79	n = 10,221	n = 12,781	n = 1,460	n = 800	n = 427
Male 80+	n = 5,291	n = 5,854	n = 775	n = 370	n = 158
Female 40-49	n = 35,141	n = 41,792	n = 4,523	n = 2,052	n = 1,290
Female 50-59	n = 25,803	n = 31,878	n = 3,379	n = 1,632	n = 1,009
Female 60-69	n = 14,962	n = 18,959	n = 2,068	n = 1,091	n = 646
Female 70-79	n = 13,422	n = 15,272	n = 1,767	n = 924	n = 457
Female 80+	n = 9,657	n = 9,450	n = 1,183	n = 480	n = 243
Totals	n = 189,359	n = 226,730	n = 25,970	n = 11,967	n = 7,153
Percent of Study Population	41.1%	49.2%	5.6%	2.6%	1.5%

Figure 9. Age-specific Population by Arsenic Concentration Quintile

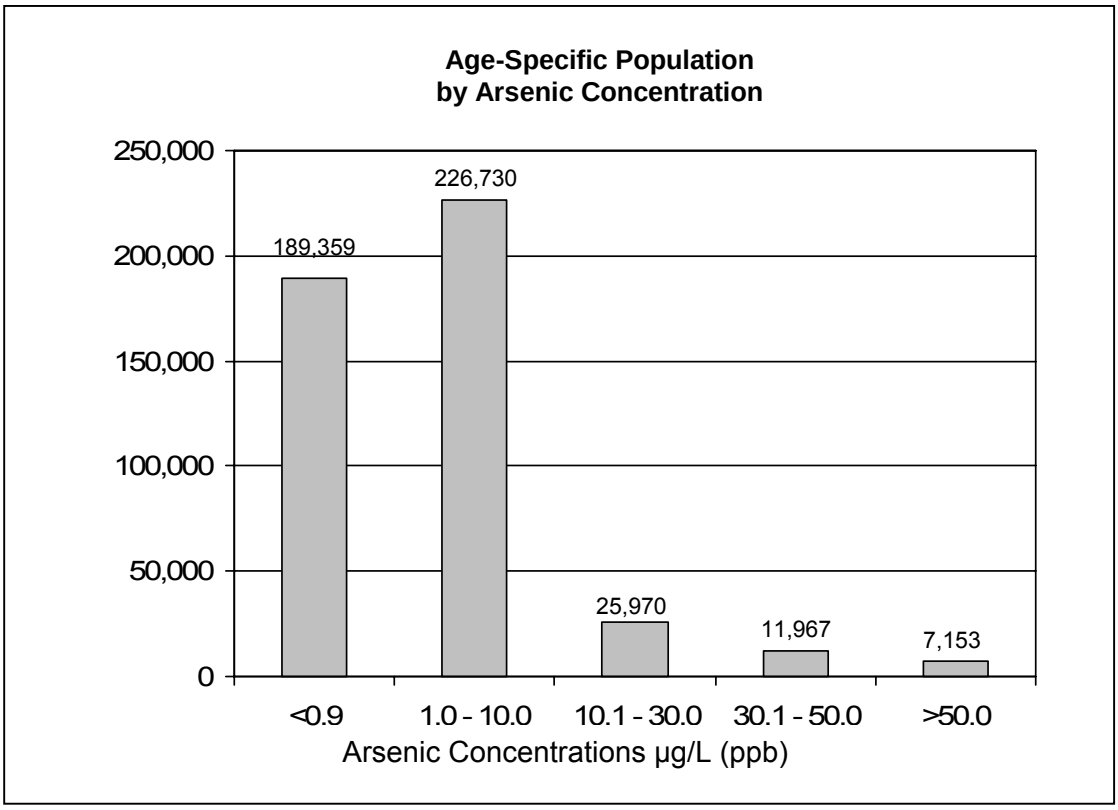
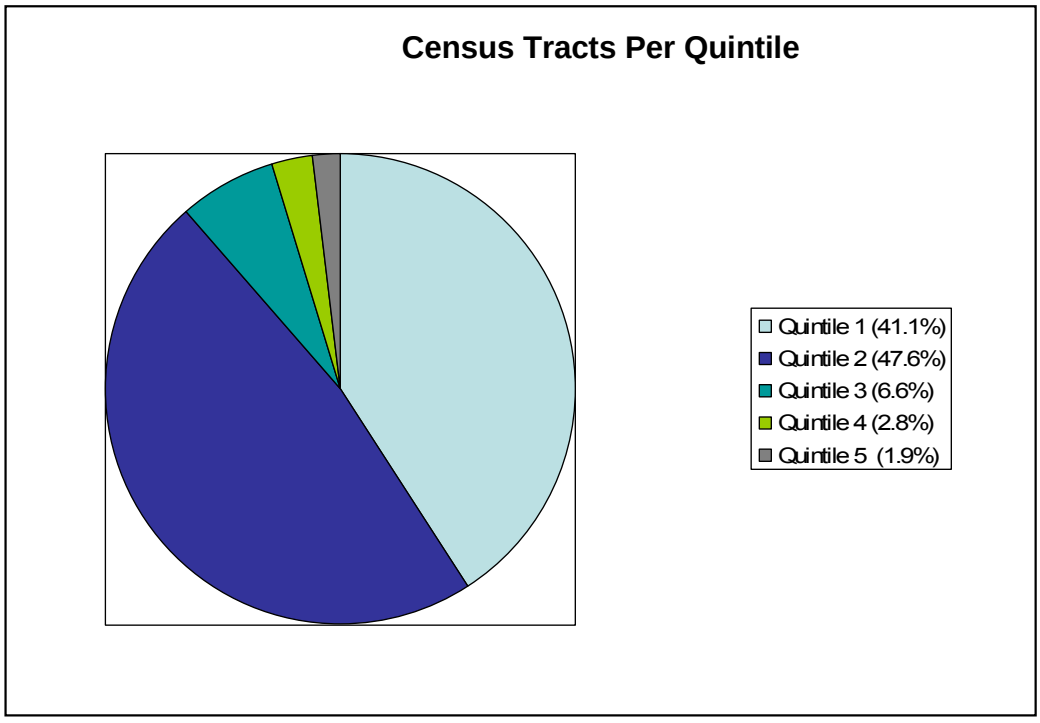


Figure 10 is the breakdown of census tracts per arsenic concentration quintile used for the statistical analyses. For the percentage values below, the number of census tracts of a quintile were divided by the total number of census tracts (n=210) included of the study area. Of the arsenic quintiles used for the analyses of this study Quintiles 1 and 2 (88.7% of census tracts) are below the MCL of 10 µg/L(ppb) and Quintiles 3, 4, and 5 (11.3% of census tracts) have concentrations above the MCL.

- Quintile 1: 41.1% (86/210)
- Quintile 2: 47.6% (100/210)
- Quintile 3: 6.6% (14/210)
- Quintile 4: 2.8% (6/210)
- Quintile 5: 1.9% (4/210)

Figure 10. Census Tracts per Quintile



Research Questions 2 and 3

The second research question investigated if overall age-specific cancer incidence rates are higher within census tracts that have higher concentrations of arsenic when compared to overall state cancer rates. The third research question examined if age-specific incidence rates of specific cancers (e.g. bladder, kidney, liver, and lung cancers) are higher within census tracts with arsenic concentrations in groundwater at or above 10µg/L.

Tables 12 reports Chi-square calculations for age and sex-specific differences of the observed and expected cancer counts per quintile group for bladder, kidney, liver, lung and the four cancer types combined. Expected cancer counts for each cancer type were calculated from the state age and sex-specific incidence rates. The Chi-square analysis per arsenic concentration census tract quintile included all age intervals for each sex. The degrees of freedom (df) for each Chi-square value calculated from 5 x 2 tables are 4 ((Columns-1)*(Rows-1)). Columns are the observed and expected cancer counts, and rows are the five age intervals per sex.

Overall, there were two Chi-square calculations per census tract quintile resulting in a total of 50 Chi-square calculations testing for significant differences of cancer incidence based upon arsenic concentration. There were no significant findings when all cancer types were combined, testing for significance between observed and expected cancer counts for sex groups per quintile. The Chi-square values among all the individual cancer types also had non-significant Chi-square values suggesting arsenic concentration did not contribute to differences between the observed and expected cancer counts within the study area.

Table 12. Chi-square Values for Age & Sex-specific Incidence Rates: Differences between Observed & Expected Cancer Counts

Cancer Type:	Bladder		Kidney		Liver		Lung		Overall	
		df = 4		df = 4		df = 4		df = 4		df = 4
Sex & Quintile (all age intervals)	**Chi-square**	**P value**	**Chi-square**	**P value**	**Chi-square**	**P value**	**Chi-square**	**P value**	**Chi-square**	**P value**
Male Quintile 1	0.21	0.99	0.44	0.98	0.61	0.96	1.35	0.85	0.32	0.98
Male Quintile 2	0.85	0.93	0.03	0.99	0.80	0.94	0.06	0.99	0.63	0.95
Male Quintile 3	6.22	0.18	0.57	0.96	0.17	0.99	0.63	0.96	0.13	0.99
Male Quintile 4	0.41	0.98	0.23	0.99	0.12	0.99	0.01	1	0.03	0.99
Male Quintile 5	0.13	0.99	1.20	0.87	0.82	0.94	0.09	0.99	0.01	1
Female Quintile 1	0.17	0.99	0.02	1	0.02	0.99	0.11	0.99	0.25	0.99
Female Quintile 2	0.08	0.99	0.48	0.97	2.06	0.72	0.99	0.91	0.97	0.91
Female Quintile 3	1.08	0.89	0.00	1	0.76	0.94	0.90	0.92	1.17	0.88
Female Quintile 4	0.37	0.98	0.00	1	0.21	0.99	0.65	0.95	1.36	0.85
Female Quintile 5	0.12	0.99	0.55	0.96	0.11	0.99	0.45	0.98	0.18	0.99

Shown in Table 13 are the observed and expected cancer counts used in the "Overall' Chi-square statistical analysis. The observed cancer counts are the numbers supplied from OSCaR that were able to be geocoded. This is important to note because as indicated from Table 4 (in Chapter 3) not all cases were geocodable, meaning an unknown number of missing cases were unavailable for the analyses of this study. Also highlighted in Table 13 is the process in which expected cancer counts within each quintile were calculated for the combined cancer group. The calculations were based upon the overall state age-specific incidence rates by using the following equation;

Expected Cancer Count = (Person-years (age-specific per quintile))*(State Age-specific incidence rate)/100,000.

Table 13. Combined (Bladder, Kidney, Liver, Lung) Cancer Incidence: Expected v. Observed Counts for Census Tract Quintiles

Age-Sex Group	Age-Specific Incidence Rate (Cases/Pop * 100,000)	Expected v. Observed **Quintile 1**		Expected v. Observed **Quintile 2**		Expected v. Observed **Quintile 3**		Expected v. Observed **Quintile 4**		Expected v. Observed **Quintile 5**	
Male 40-49	44.3	15.4	15	18.1	26	2.3	3	0.9	2	0.6	1
Male 50-59	157.3	41	42	50.3	48	5.5	8	2.5	3	1.6	2
Male 60-69	438.6	61.3	62	78.7	92	9.0	9	4.4	5	2.8	2
Male 70-79	775.4	79.3	87	99.1	95	11.3	11	6.2	6	3.3	3
Male 80+	873.3	46.2	46	51.1	50	6.8	6	3.2	2	1.4	2
Female 40-49	23.8	8.4	7	9.9	9	1.1	1	0.5	0	0.3	0
Female 50-59	100.5	25.9	28	32.0	31	3.4	3	1.6	1	1.0	2
Female 60-69	274.9	41.1	40	52.1	58	5.7	7	3.0	3	1.8	2
Female 70-79	426.8	57.3	56	65.2	71	7.5	3	3.9	2	2.0	2
Female 80+	370.5	35.8	31	35.0	39	4.4	3	1.8	1	0.9	1

State age-specific populations, cancer counts and incidence rates for the combined and individual cancers analyzed in this study are found in Table 14. The population counts are from Census 2000, cancer counts are cases reported to OSCaR in the year 2000, and incidence rates were calculated from the two data sets. The resulting age-specific incidence rates are the figures referenced to calculate the expected cancer case values for quintile groups used in the Chi-square analyses. For every type of cancer and the combined cancer group, a pattern of higher incidence for older age groups for both sex groups was noted. The increasing cancer incidence found for the aging population is an expected trend.

Table 14. Age-specific Population Cancer Counts and Cancer Incidence Rates for the State of Oregon

		Bladder		Kidney		Liver		Lung		Combined	
	Census 2000 Population	Cancer Count	Age Specific IR	Cancer Count	Age-Specific IR	Cancer Count	Age-Specific IR	Cancer Count	Age-Specific IR	Cancer Count	Age-Specific IR
Male 40-49	268,833	34	12.6	10.0	10.0	16	6.0	42	15.6	119	44.3
Male 50-59	202,786	87	42.9	24.2	24.2	20	9.9	163	80.4	319	157.3
Male 60-69	117,411	131	111.6	35.8	35.8	21	17.9	321	273.0	515	438.6
Male 70-79	88,857	186	209.3	56.3	56.3	17	19.1	436	490.7	689	775.4
Male 80+	44,427	107	240.8	60.8	60.8	12	27.0	242	544.7	388	873.3
Female 40-49	273,305	7	2.6	4.4	4.4	1	0.4	45	16.5	65	23.8
Female 50-59	206,062	21	10.2	13.6	13.6	8	3.9	150	72.8	207	100.5
Female 60-69	126,583	38	30.0	18.2	18.2	5	3.9	282	222.8	348	274.9
Female 70-79	112,930	53	46.9	39.0	39.0	7	6.2	378	334.7	482	426.8
Female 80+	79,349	54	68.1	26.5	26.5	6	7.6	213	268.4	294	370.5

The effects of arsenic concentration, sex, and age on incidence rates were examined using a Poisson regression model. Risk ratios were calculated using the arsenic concentration quintiles (0-0.9ppb, 1-10ppb, 10.1-30ppb, 30.1-50ppb and ≥50.1ppb), two sex categories, and five age categories (40-49, 50-59, 60-69, 70-79, 80+). Risk ratios indicate whether the variable being analyzed has an increased, decreased or no additional risk when compared to a reference group of the category, controlling for other variables. Risk ratio values below one indicate a protective or decreased risk, risk ratio values above one indicate an increased risk of a group and risk ratios values equaling one have neither associated with an increased or decreased risk. Ninety-five percent confidence intervals (CIs) around these rates were obtained based on Poisson distributions (appropriate for rare events).

Goodness of fit of the Poisson regression model was examined by deviance statistics (Table 15). The values showed no statistically significant deviations, indicating an adequate fit of the model. Non-significance is confirmed because the deviance values are 'smaller' than the critical region defined by the chi-square distribution (alpha = 0.05).

Table 15. Goodness of Fit Assessment of Poisson Regression Model

Goodness of Fit Assessment					
	Bladder	**Kidney**	**Liver**	**Lung**	**Combined**
Degrees of Freedom (df)	40	40	40	40	40
Chi-square Critical Value (alpha =0.05)	55.76	55.76	55.76	55.76	55.76
Deviance Value	39.98	28.28	28.39	29.08	22.54

After controlling for sex and age, Table 16 shows for all cancer types combined that the higher quintile groups had slightly elevated risk ratios, using Quintile 1 as the reference group. This was found for all quintiles except for Quintile 3 that indicated a slightly decreased or protective risk. All risk ratio values were non-significant with confidence intervals containing the null value (risk ratio of 1).

The individual analysis of each cancer type (Table 16) subsequently revealed the same non-significant results indicating that higher arsenic concentrations did not increase the incidence rate of the four cancers (bladder, kidney, liver and lung) after

adjusting for age and sex. However, increased values of risk were found in all cancer types: bladder cancer (Quintiles 2, 3, and 4); kidney cancer (Quintiles 2, and 5); liver cancer (Quintiles 2, 3, 4, and 5); and lung cancer (Quintiles 2 and 5). In the individual analysis of cancer types, the confidence intervals also included the null value, supporting the non-significance of the results.

Table 16. Risk Ratios and CIs Controlled for Arsenic Concentration

	Combined					
	Risk Ratio	95% CI	P value			
Quintile 5 (≥50.1 ppb)	1.07	0.66 1.75	0.76			
Quintile 4 (30.1-50 ppb)	1.12	0.59 1.33	0.56			
Quintile 3 (10.1-30 ppb)	0.94	0.71 1.25	0.68			
Quintile 2 (1-10 ppb)	1.05	0.92 1.19	0.47			
Quintile 1 (0-0.9ppb) *Reference Group*	1.0	N/A	N/A			
	Bladder				**Kidney**	
	Risk Ratio	95% CI	P value	Risk Ratio	95% CI	P value
Quintile 5 (≥50.1 ppb)	0.88	0.28 2.79	0.84	2.06	0.31 5.19	0.75
Quintile 4 (30.1-50 ppb)	1.31	0.63 2.71	0.46	0.72	0.17 2.96	0.65
Quintile 3 (10.1-30 ppb)	1.45	0.87 2.41	0.15	0.69	0.25 1.93	0.48
Quintile 2 (1-10 ppb)	1.08	0.82 1.43	0.56	1.02	0.67 1.53	0.94
Quintile 1 (0-0.9ppb) *Reference Group*	1.0	N/A	N/A	1.0	N/A	N/A
	Liver			**Lung**		
	Risk Ratio	95% CI	P value	Risk Ratio	95% CI	P value
Quintile 5 (≥50.1 ppb)	2.38	0.31 18.46	0.40	1.04	0.57 1.91	0.88
Quintile 4 (30.1-50 ppb)	1.38	0.18 10.75	0.75	0.85	0.51 1.41	0.52
Quintile 3 (10.1-30 ppb)	1.28	0.28 5.8	0.74	0.81	0.56 1.18	0.28
Quintile 2 (1-10 ppb)	1.28	0.6 2.74	0.51	1.03	0.88 1.21	0.71
Quintile 1 (0-0.9ppb) *Reference Group*	1.0	N/A	N/A	1.0	N/A	N/A

Overall, the results of research questions 2 and 3, based on quintile groups indicated that higher arsenic concentrations were not significantly associated with the incidence rates of the cancer types analyzed. It is important to note increased risks were not expected for Quintile 1 and 2 because arsenic values included in these quintiles are at or below the regulated maximum contaminant level (MCL) of 10µg/L.

Regarding the controlled variables results are described to give further understanding are as follows. Additional analyses were done to further investigate the data used in this research. Regression analysis was used to test for differences between male and female and for age intervals

We found an increase of risk for males in the study population after adjusting for arsenic concentration and age (Table 17). Risk ratios differed significantly based on sex for combined cancer types and the individual cancer types, with males showing varying amounts of increased risk when compared to women. Bladder and kidney cancers showed the largest increase of risk at 4.65 and 6.05, respectively.

Table 17. Risk Ratios and CIs Controlled for Sex

	Combined					
	Risk Ratio	95% CI	P value			
Male	1.87	1.65 2.12	<0.0001			
Female *Reference Group*	1.0	N/A	N/A			
	Bladder				**Kidney**	
	Risk Ratio	95% CI	P value	Risk Ratio	95% CI	P value
Male	4.65	3.38 6.4	<0.0001	1.78	1.19 2.66	0.004
Female *Reference Group*	1.0	N/A	N/A	1.0	N/A	N/A
	Liver				**Lung**	
	Risk Ratio	95% CI	P value	Risk Ratio	95% CI	P value
Male	6.04	2.32 15.74	0.0002	1.372	1.18 1.59	<0.0001
Female *Reference Group*	1.0	N/A	N/A	1.0	N/A	N/A

With respect to age, after adjusting for arsenic concentration and sex, age groups older than 40-49 had significantly increased risk ratios when all cancer types were combined. As shown in Tables 18 the overall cancer incidence in the eldest age group 80+ may have 15.49 times higher incidence rate ($p = <.0001$) than the reference age group of 40-49. Among the calculations for individual cancer types also reported in Table 18 a similar pattern exists with significant increases in incidence rates among the older populations. As found with the Chi-square values (Table 12) this is an expected trend among the population. There are few exceptions to this trend, it was found for liver cancer (Table 18), that the increased incidence rates were only significant in the 70-79 age interval with a 2.81 increase ($p = 0.033$) when compared to the reference group (40-49).

Table 18. Risk Ratios and CIs Controlled for Age

	Combined					
	Risk Ratio	95% CI	P value			
80 +	15.49	11.65 20.62	<0.0001			
70 -79	15.92	12.18 20.81	<0.0001			
60 - 69	10.15	7.73 13.32	<0.0001			
50 - 59	3.45	2.59 4.61	<0.0001			
40 - 49 *Reference Group*	1.0	N/A	N/A			
	Bladder				**Kidney**	
	Risk Ratio	95% CI	P value	Risk Ratio	95% CI	P value
80 +	15.10	8.73 26.10	<0.0001	10.28	4.57 23.11	<0.0001
70 -79	13.63	8.15 22.76	<0.0001	8.06	3.75 17.37	<0.0001
60 - 69	7.15	4.20 12.18	<0.0001	5.92	2.74 12.81	<0.0001
50 - 59	2.63	1.49 4.64	0.0008	4.09	1.93 8.67	0.0002
40 - 49 *Reference Group*	1.0	N/A	N/A	1.0	N/A	N/A
	Liver				**Lung**	
	Risk Ratio	95% CI	P value	Risk Ratio	95% CI	P value
80 +	2.06	0.55 7.66	0.276	21.61	14.39 32.44	<0.0001
70 -79	2.81	1.08 7.28	0.033	23.79	16.16 35.01	<0.0001
60 - 69	0.77	0.21 2.86	0.703	15.86	10.74 23.42	<0.0001
50 - 59	1.31	0.52 3.30	0.565	4.41	2.93 6.67	<0.0001
40 - 49 *Reference Group*	1.0	N/A	N/A	1.0	N/A	N/A

DISCUSSION

The purpose of this study was to determine if there is a spatial relationship between groundwater arsenic concentrations and cancer incidences within two geographical regions of Oregon.

Geographic Distribution of Arsenic and Exposure Estimates

Maps of the regions depicting arsenic concentration levels in groundwater show that arsenic is widely distributed but concentration levels can vary greatly between census tracts located in close proximity. The distribution of arsenic in the region may be affected by geological formations that are known to be associated with higher arsenic levels such as the Fisher and Eugene formations located in the southern part of the Willamette Basin (Hinkle et al., 1999). In addition, Harney and Malheur counties in the southeastern region of Oregon display a clustering of higher arsenic concentrations which also may be related to the geologic composition of the area.

The range of arsenic concentrations within each county and in some cases census tracts varied greatly. For example, Lane County had an upper limit arsenic concentration of 1,006 ppb (μg/L), but after aggregating all groundwater data points the highest concentration used in the analysis for the county was 239 ppb. This latter aggregated concentration is considerably lower and demonstrates an obvious limitation to accurately estimating arsenic concentrations in groundwater, and for estimating human exposure. The study combined U.S. Geological Survey (USGS) data and Oregon Drinking Water Program (DWP) public water system data to provide a more complete picture of groundwater arsenic in Oregon that may be used for domestic water supplies. It is acknowledged, however, that there are differences in methodologies in collection practices, different organizational motives for data collection and differences in laboratory analytical reporting for the two data sets. For example, the USGS does not collect water quality samples for the purpose of understanding human exposure to contaminants, but rather to monitor for groundwater characteristics. In contrast, the Oregon DWP collects community water system data to enforce public health regulations.

The arsenic concentration values used as the surrogate exposure level for the local populations are aggregates of all arsenic samples collected in each corresponding census tract. This approach of integrating two independent sources of water quality data has not been done before in Oregon and may not accurately define the exposure risk of sub-populations. The assumption of arsenic ingestion was based upon the presence of arsenic sampled from the groundwater, but well-water consumption data were not collected. However, nearly 50% of residents in Oregon residents use have drinking water supplies solely from groundwater sources, and nearly one quarter of state's population relies on private well water for domestic water use (DEQ, 2007; Hutson et al., 2004). It is, therefore, important to have a better understanding of the arsenic concentrations in water potentially used for drinking. In addition, it is not known what percent of this population tests or treats their water supply for arsenic.

Surrogate exposure levels are not the optimal measurement for analysis but when used with a GIS, may give a better understanding of associations between environmental contaminants and disease rates. Data collected from existing databases were not collected for the purpose of identifying causal relationships between arsenic concentrations and cancer rates. It is more desirable to either take direct measurements or estimates of contaminants in the drinking water and then validate exposure levels of the contaminant (Nuckols et al. 2004). In the absence of this the use of GIS can provide the technology to estimate contaminant source proximity when the contaminant cannot be directly measured. An objective of this study was to utilize secondary data sets for the contribution to the Environmental Public Health Tracking (EPHT) network, which by definition does not support direct exposure measurement of the contaminant for the study population.

Relationships between Arsenic Concentrations and Cancer Incidence

The majority of census tracts (88.7%) and study population (90.3%) fall into Quintiles 1 and 2, which have arsenic concentrations below the MCL of 10µg/L. An increase of cancer incidence was not expected in these quintiles. In contrast, Quintiles 3, 4, and 5 account for 11.3% of the census tracts. In these Quintiles, 9.7% of the study population lives in areas that have arsenic concentrations above the MCL. Although

cancer incidence rates might be expected to increase with increasing groundwater arsenic concentrations in Quintiles 3, 4 and 5, the results in this study show otherwise.

Using the arsenic Quintile 1 (0 - 0.9 μg/L) as a reference point, this study found that arsenic concentration levels in groundwater do not impact the incidence rates of bladder, kidney, liver or lung cancer in populations over the age of 40 in regions with arsenic concentrations above 1 μg/L. These findings are contradictory to the majority of epidemiologic studies conducted globally that report correlations between arsenic exposure and numerous adverse health outcomes (Basu et al., 2001; Mandal & Suzuki, 2001; NRC, 2001; PSR, 2005; Rahman et al., 2001; Zierold et al., 2004). For example, the results from the study by Morales et al. (2004) suggested that arsenic concentrations at or above 50 μg/L are associated with a substantial increase of risk for bladder, liver and lung cancers. However, Steinmaus et al. (2003) did not find an increased cancer risk for their study conducted in the western United States with chronic exposures of groundwater arsenic nearing 100 μg/L.

Long-term chronic exposure to arsenic is known to initiate carcinogenic and non-carcinogenic health outcomes in humans. The USEPA recently reduced the maximum contaminant level (MCL) of arsenic permissible in public water supplies from 50 μg/L to 10 μg/L. This new MCL was established after rigorous assessments of the epidemiologic studies that suggested a significant correlation between the onset of adverse health effects and arsenic ingestion from drinking water. The World Health Organization and the USEPA both classify inorganic arsenic as a human carcinogen (ASTDR, 2000; Morales et al., 2000). The epidemiologic studies reviewed by the NRC (2001) for setting the allowable contaminant level in drinking water of the United States supports this claim and concluded that at chronic exposure levels of 10 μg/L, cancer incidence may be about 1 in 300 (Mead, 2005).

It is believed that the dose-response relationship of arsenic ingestion may be closely related to other factors of an individual's overall health status, and that other factors may mask any increased cancer rates associated with increased concentrations of arsenic. The study did not control for other characteristics that may act synergistically to cause adverse health effects with arsenic exposure such as smoking, nutritional status or ultraviolet light (Basu et al., 2001; Rahman et al., 2001;

Steinmaus, et al., 2003). In addition, the issue of the prolonged latency periods associated with the onset of chronic diseases such as cancer may also contribute to the challenges of discovering conclusive associations between a single environmental hazard and a diagnosis. It is also possible that the limitations of the statistical methods used contributed to these results.

The results showed significant increases in cancer rates for population age intervals over the age of 50 for both sexes, which is to be expected. Males were also found to have an increased risk of cancer. These results do not necessarily show that these populations had higher rates of cancer due to increased concentrations of arsenic in groundwater, but may be explained by a combination of other factors that lead to the development of cancer, such as dose amount, chronic or acute exposure, the frequency of exposure of arsenic, genetics, age and health status or other unknown risk factors (ASTDR, 1998; NRC, 2001; PSR, 2005).

One of the objectives of this study was to determine if there are spatial relationships between arsenic concentrations in the Willamette Valley Basin and Southeast Oregon and incidence rates of four types of cancer. Calculations comparing observed and expected cancer counts of arsenic concentrations of census tract quintiles were not found to be significant. One reason for this may be that the methodology of aggregating groundwater concentrations was not at all accurate in estimating exposure, which then contributed to an inaccurate assessment of related health effects among the study population. The use of more sophisticated contaminant dispersion models and more in-depth analysis of high arsenic concentration areas may have disclosed a better depiction of existing spatial patterns with regards to arsenic exposure and health outcomes (Brody et al., 2004; Cromley and McLafferty, 2002; Nuckols et al., 2004).

Geocoding of Cancer Cases

The populations in the study areas are unevenly distributed. The southeastern region of the state is referred to as frontier land, implying low population per square mile. Census tract boundaries are defined by population and the tracts of the southeastern region are notably larger and have the majority of high arsenic concentration census tracts included in the study (Figure 8, Results). This population

disparity is evident in the age-specific population breakdown by quintile in Table 11 and Figure 9 (Results) that shows Quintiles 3, 4 and 5 combined contributing 9.7% (n=45,090) of the overall study population.

The lifestyle differences existing between urban and rural populations and their overall health status may be related to the hazards affecting them which are influenced by such things as local industry and environmental features. In addition, many regions of the U.S. are prone to migration, and most chronic diseases have long latency periods. The region is mostly rural and many people lack access to health care services more readily available in more populated urban areas of the state. Rural populations do not seek medical attention as often as their urban counterparts and are less likely to receive recommended preventive services. These factors may influence the rate of disease reporting of the region (Agency for Healthcare Research and Quality [AHRQ], 2004), and thus, the cancer cases reported to the Cancer Registry. For example, populations in rural regions may postpone healthcare visits which may delay a medical diagnosis of a health condition much later than their urban counterparts. Such differences can skew research results when analyzing age-specific incidence, for instance if the onset of a chronic disease was several years before diagnosis and the subsequent reporting to a data collection registry.

The western region of Oregon, and more specifically, the Willamette Valley Basin, represents the population center of the state, giving it more influence on state cancer incidence rates. Census tract land areas are significantly smaller in the urban areas, and these smaller geographic units are better for defining spatial relationships. It is, however, the rural populations whose water supplies are not regulated by the SDWA that were of particular interest for this study. Linking environmental hazard data geographically is a noted challenge of the EPHT network (McGeehin, 2004). The use of dispersion and transport models with a GIS to estimate exposure levels of contaminants were used in several studies (Bellander, et al., 2001; Nyberg et al., 2001; Reif et al., 2003) and are found to be superior to point data for conducting exposure assessments. Therefore, the geographic unit of analysis specified for the study may not be discriminating enough to find the epidemiologic effects occurring in rural regions.

Geocoding the place of residence of individuals with specific health outcomes are crucial for including all reported cases in spatial analytical methods and GIS applications. Table 4 (Results) indicated that fewer percent of cancer cases located in the more rural counties of the state were geocodable by OSCaR and therefore not included in the calculations of incidence rates. Of the eleven counties included in this study, ten of the counties had a greater than 90 percent of cancer cases geocoded. Harney County is the exception, with only 58 percent of cases being geocodable. This exclusion of cases may significantly reduce the ability to study the interactions of rural populations with the environmental hazards that affect them.

Missing cases are more likely to be in rural census tracts due to the P.O. Box and Rural Route addresses, where private drinking water wells are most common and drinking water regulations are not enforced, therefore, underestimating the number of cancer cases used in the study analyses. This may lead to an underestimation of the number of cases missing from the study introduces an unknown amount of error into the methods used to analyze the effect arsenic exposure may have on the cancer incidence rates. Other researchers have noted problems when studies lack complete data and the importance of high quality data. For example, the hazard-exposure-outcome model discussed by Cromley and McLafferty (2002) reinforces the concept that achieving a reliable spatial representation of the existing risk depends on the accuracy of the data input into the model.

Contributions to EPHT Network and Future Studies

An important objective of the study was to contribute to the CDC's development of the Environmental Public Health Tracking (EPHT) network by exploring the compatibility of existing secondary data sets for linking arsenic groundwater concentrations and cancer incidence. Under ideal conditions, compatibility of data standards and vocabularies for each data set would be verified. However, quality assurance of the data was not validated, but rather, implied through the standards of each agency's collection and reporting methods. The compatibility of data sets is essential for the success of the EPHT network. Historically, the collection of environmental and health data have been divided among various agencies with

limited interactions, making data linkage a major challenge (IOM, 2004). This has also been noted by McGeehin et al. (2004), who emphasized the importance of standardizing hazard, exposure and health effect data to confidently find associations of causation between environmental factors and health risks.

This study did incur challenges of data compatibility and required extensive data preparation activities (See Figure 4 in Materials and Methods). For example, the population data acquired from the US Census Bureau required the downloading of individual census tract files per county. From these files it was necessary to sort out the needed census tracts and combine their age groups into the age intervals assessed in this study. Another time intensive data preparation exercise was the aggregation of the arsenic concentration data sets. Preparation of these data involved numerous steps, including determining from which census tract a measurement was sampled, building data base files for each county compatible with the GIS, and projection of all files into the GIS.

Another objective of this study was to serve as an exploratory tool for identifying a regional public health concern that can be followed up with comprehensive analytical studies of the region. These follow-up studies would be recommended for regions of the state that were found to have arsenic concentration at or above the current MCL regulated by the SDWA. Rural regions of the state that rely on private groundwater wells not regulated by the federal standard would also be appropriate. In addition, this study showed that rural census tracts and counties are missing a greater number of cases than the urban or more populated areas of the state. This exclusion of cases may significantly reduce the ability to study the interactions of rural populations with the environmental hazards that affect them.

Future studies would benefit from the collection of individual survey data collecting individual exposure history and health status for case-control or cohort study designs. Additional geographic layers such as hydrologic units, geological features, soil types, land use would also allow comprehensive modeling of environmental interactions. Similar methods have been used in studies conducted worldwide and in other regions of the United States. The location and contaminant levels of individual drinking water wells in Bangladesh, the northeast U.S., New

Jersey and New Mexico were imported to approximate the populations affected by arsenic exposure (Ayotte et al., 2003; Cohen et al., 1999; Flowers, 2005; Hassan et al., 2003). Miller et al. (2005) successfully utilized hydrologic units in a GIS analysis to delineate wellhead protection areas around public supply wells.

The study results should not be generalized beyond the defined study area. Even for the eleven counties included in the analysis, population demographics were not uniform and natural environments greatly varied. This may indicate some unknown differences between the local attitudes and awareness of existing environmental contaminants. Also, the statistical and spatial analytical problems inherent to substituting individual-level data with aggregate data may not identify the actual risk to individuals.

CONCLUSIONS AND RECOMMENDATIONS

Maps of the regions depicting arsenic concentration levels in groundwater show that arsenic is widely distributed but concentration levels can vary greatly between census tracts located in close proximity. The distribution of arsenic in the region may be affected by geological formations that are known to be associated with higher arsenic levels. In addition, Harney and Malheur counties in the southeastern region of Oregon display a clustering of higher arsenic concentrations which also may be related to the geologic composition of the area. However, this study suggests that groundwater arsenic levels above the federal MCL in selected areas of Oregon are not significantly correlated with increasing rates of internal cancers (e.g. bladder, kidney, liver, lung).

A spatial study of groundwater arsenic and associated health outcomes had not been done previously in Oregon. This study relied on secondary data collected by various government agencies to establish relationships of arsenic exposure and health outcomes among the study population. It has been recognized that several aspects of data collection, reporting and geographic linkage are in need of standardization for building better compatibility between data sets collected by different government and private agencies. The availability of complete health, environment and geographic data are essential for the success of EPHT for identifying hazards, monitoring distribution, and analyzing health trends.

This study did incur challenges of data compatibility and required extensive data preparation activities of several of the data sets. One such data manipulation was the integration of two independent sources of water quality data and may not have accurately defined the exposure risk of sub-populations in regions of Oregon analyzed in this study. Additionally, the data collected from the existing databases were not collected for the purpose of identifying causal relationships between arsenic concentrations and cancer rates.

The use of geographic information systems (GIS) for environmental epidemiology has great potential. The spatial characteristics of data must be considered to produce meaningful research results with a GIS. The scale of

geographic units chosen should effectively demonstrate proximity of an environmental hazard to better estimate personal exposure levels of the study population. This study used aggregated arsenic values for census tracts which may have over estimated the population exposed to arsenic. Also illustrated, by this study, are the range of arsenic concentrations that may be naturally occurring in groundwater sources in Oregon.

The majority of census tracts (88.7%) and study population (90.3%) fall into Quintiles 1 and 2, which have arsenic concentrations below the MCL of 10μg/L. It would not be expected to see an increase of cancer incidence in these quintiles. In contrast, Quintiles 3, 4, and 5 account for 11.3% of the census tracts. In these Quintiles, 9.7% of the study population lives in areas that have arsenic concentrations above the MCL. Although cancer incidence rates might be expected to increase with increasing groundwater arsenic concentrations in Quintiles 3, 4 and 5, the results of this study show otherwise.

Using the arsenic Quintile 1 (0 - 0.9 μg/L) as a reference point, this study found that arsenic concentration levels in groundwater do not impact the incidence rates of bladder, kidney, liver or lung cancer in populations over the age of 40 in regions with arsenic concentrations above 1 μg/L. These findings are contradictory to the majority of epidemiologic studies conducted globally that report correlations between arsenic exposure and numerous adverse health outcomes. Overall, the results of this study showed that higher arsenic concentrations did not increase the incidence rate of the four cancers (bladder, kidney, liver and lung) after adjusting for age and sex. The results of the study also suggested significant increases in cancer rates for population age intervals over the age of 50 for both sexes, which is to be expected. Other results of interest were that males were found to have an increased risk of the cancer types analyzed.

Geocoding cancer data requires significant effort but provides the level of resolution needed for geo-spatial data linkages. The method of incorporating age-specific incidence rate of cancer types among census tract quintiles used in this study may not have been refined enough to statistically show correlations of arsenic exposure and health outcome. Also, having a certain percent of cancer cases missing

from the analyses may partially explain the non-significant results associated with the high arsenic concentration of rural census tracts.

A lower proportion of cancer cases located in the more rural counties of the state were geocodable by OSCaR and, therefore, not included in the calculations of incidence rates. Of the eleven counties included in this study, ten of the counties had a greater than 90 percent of cancer cases geocoded. Harney County is the exception, with only 58 percent of cases being geocodable. This exclusion of cases may significantly reduce the ability to study the interactions of rural populations with the environmental hazards that affect them.

Missing cases are more likely to be in rural census tracts due to the P.O. Box and Rural Route addresses, where private drinking water wells are most common and drinking water regulations are not enforced, therefore, underestimating the number of cancer cases used in the study analyses. Not knowing the number of cases missing from the study introduces an unknown amount of error into the methods used to analyze the effect arsenic exposure may have on the cancer incidence rates.

It is recommended that advanced geographic analyses techniques be used in the future for assessing arsenic concentrations of the study area. The use of a finer geographic resolution with additional geographical layers for modeling environmental dispersion of arsenic into drinking water sources would improve contaminant proximity to study populations. Adding detailed geographic layers such as hydrologic units, geological features, soil types, and land use would also allow comprehensive modeling of environmental interactions. As an alternative to assessing exposure levels with a surrogate exposure method it is recommended that sophisticated contaminant dispersion models be used, allowing a more in-depth analysis of high arsenic concentration areas. Surrogate exposure methods may introduce analytical limitations and inaccuracies. Dispersion models offer an improved of estimation of exposure concentrations of arsenic in drinking water. This would benefit analytical methods used to find correlations between arsenic ingestion and increased health risks in the study regions. The number of census tracts identified by this study to have arsenic concentration samples at or above the current MCL warrant further investigations at a refined geographic scale that may reduce the number of limitations affecting the

spatial-analytical methods. The use of advanced analytical methods may disclose a better depiction of existing spatial patterns with regards to arsenic exposure and health outcomes.

In addition, due to the exploratory nature of this study, a number of follow-up studies with varying designs are recommended. Future studies would benefit from the collection of individual survey data of individual exposure history and health status for case-control or cohort study designs. For example, to help investigate local knowledge and attitudes towards arsenic the recruitment of study participants to assess uses of water contaminated with arsenic and exposure verification with the use of bio-monitoring techniques. Further studies utilizing secondary data sets would rely on the researcher having an understanding of the study population to aid with the logical linking of data sets to define environment, hazard and health data relationships. Of special research interest are the rural populations reliant on groundwater sources for domestic use not regulated by the Safe Drinking Water Act.

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