A FRAMEWORK FOR FINDING POSSIBLE HISTORIC POLLUTANT SOURCES:
VANCE COUNTY, NC AS A CASE STUDY

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Abstract

Breast cancer is an important health issue in the United States, as the most common cancer and the second leading cause of death among women. Since genetic and lifestyle factors account for only approximately 25-47% of breast cancer cases, environmental pollutants likely explain a significant portion of breast cancer incidence. The Nicholas School of the Environment and the Comprehensive Cancer Center at Duke University are collaborating on a project looking at environmental causes of possible breast cancer clusters in six counties in North Carolina: Caswell, Durham, Granville, Orange, Person, and Vance. There is a need for identification of possible pollutant sources in the counties, along with construction of a systematic way to find relevant facilities.

This paper briefly examines the connection between the environment and breast cancer and aims to construct an organized framework for finding possible pollutant sources with the resources available in national and state databases. Vance County is selected as a case study due to preliminary research indicating its unusually high rate of breast cancer in young women (25-34 years old), and the highest discrepancy between black and white women in fiscal year survival rates. The adaptive process of creating the framework was performed simultaneously with the research for the case study, using peer-reviewed literature, internet research, and meetings with state environmental managers.

The resulting framework consists of five stages designed as an iterative flowchart. Using Vance County as a case study, the successes and difficulties presented in the process are evaluated. National and state databases were used to collect facility and pollutant information that might be connected to the breast cancer cluster. The disorganization and lack of information located online hindered the search for historic pollutant sources in Vance. It was difficult to find facility information connected with emitted pollutants. Recommendations on improving the process include the importance of establishing clear goals and limitations, the lack of information found in national and state databases, and a need for overall improved database management. Future research may include field sampling and spatial analysis using geographic information systems (GIS).

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Introduction

The Nicholas School of the Environment and the Comprehensive Cancer Center at Duke University are collaborating on a project looking at environmental causes of possible breast cancer clusters in six counties in North Caroline: Caswell, Durham, Granville, Orange, Person, and Vance. Two of the key questions in the project are, "What pollutants may be connected to the breast cancer cluster, and where can we find them?" Finding the answer to this question is a project in itself. The large scale of the umbrella project necessitates an approach that breaks down the analysis into manageable parts. This particular project aims to construct a framework that will aid in finding possible pollutant sources in a single rural county. To make the framework more relevant and useful, a case study involving Vance County will be used to construct and test the framework with real-world challenges and limitations.

The reasoning for attempting such a task is the large impact of breast cancer on public health. Breast cancer is the most common cancer among women, with incidence rates as high as 119.3 per 100,000 women in 2006 (CDC 2006). In North Carolina, however, over a five year period (2003-2007), the breast cancer incidence was 149.6 per 100,000 women (NCSCHS 2010). For Vance County in particular, breast cancer incidence for the same five year period was 127.1 per 100,000 women (NCSCHS 2010). Duke CCC researchers found that Vance County has an unusually high rate of breast cancer in young women (25-34 years old), and the highest discrepancy between black and white women in fiscal year survival rates (Joel Meyer, personal communication). The connection between environmental pollutants and breast cancer is evidenced by the former's carcinogenic properties (Rudel et al. 2007) and the latter's connection to the endocrine system (Russo et al. 2000). Analyzing a breast cancer cluster and its possible environmental connections can provide the opportunity to identify risk factors for certain locations or groups (Laden and Hunter 1998).

In this paper the connection between environmental pollutants and breast cancer is discussed, with some of the recent research and scientific reasoning. An introduction to Vance County is included to familiarize readers with its demographics, industry, and health statistics. The process of constructing the framework while working though finding pollutant sources in the case study is the focus of the paper. The successes, difficulties, and resources encountered will help future research proceed, along with the framework itself.

Breast Cancer

Incidence and Importance

Breast cancer is an important health issue in the United States because it is the most common cancer among women in the United States (Rudel et al. 2006) occurring in every 119.3 per 100,000 women in 2006 (CDC 2006). Among white women, the incidence appears to be decreasing to the current rate, while holding steady at the current rate for black women over the past ten years (Altekruse et al. 2010). It is also the second leading cause of death in women with a mortality of 24.2 per 100,000 women in 2006 (CDC 2006). Breast cancer is uncontrolled growth and/or aberrant apoptosis of abnormal cells located in the breast tissue, as the result of cumulative damage to cellular DNA that promote oncogenes and inactivate tumor suppressor genes (Russo et al. 2000). The DNA damage, with resulting mutations and genomic changes in a dose-dependent fashion, turns normal cells to initiated cells which may then mutate to neoplastic cells (Klaunig and Kamendullis 2004) which may occur with only two genetic "hits" or mutations necessary for the onset of carcinogenesis (Balmain 2003). The three-step initiation, promotion, and progression process (Appendix 1, Figure 1) may take years to develop (Miller and Sharpe 1998). Additionally, the long maturation period of breast tissue provides many opportunities for genetic damage that provide the basis for neoplastic growth. The female breast undergoes many changes during prenatal development, early childhood, puberty, pregnancy, and menopause where DNA mutations occur and hormonal activity is high (Gray et al. 2008). Specifically, during puberty and pregnancy, ductal expansion and lactation differentiation are times of increased cell proliferation, while returning to the pre-pregnancy state increases cell apoptosis (Bissell et al. 2002). The whole process is regulated by the endocrine system via its influence on cell proliferation and differentiation (Russo et al. 2000).

Known risk factors for breast cancer include early menarche, lack of pregnancy or lactation, hormone replacement therapy, higher socioeconomic status, and postmenopausal obesity (Coyle 2004). Inherited genetic mutations of tumor suppressor genes also increase risk for breast cancer development. However, less than 10% of all female breast cancer cases are due to these heritable genetic mutations such as *BRCA1* and *BRCA2* (Campeau et al. 2008). An epidemiological study of twin cohorts in northern Europe examined the influence of hereditary factors on the causation of cancer based on the comparison of cancer risk between monozygotic twins and dizygotic twins. Lichtenstein et al. 2000 found that inherited genetic factors play a less important role in carcinogenesis than environmental factors for most cancers, except for colorectal, prostate, and breast cancer. These cancers showed a statistically significant of heritable factors. However, their study determined that heritable factors only accounted for approximately 27% of their breast cancer cases, while environmental factors, both shared and non-shared between twins, were estimated to account for 73%. In the United States, some estimate that genetic and lifestyle risk factors combined explain 25-47% of breast cancer cases (Coyle 2004) while other estimates are higher at 45-55% (Laden and Hunter 1998). Therefore, while genetic factors account for some breast cancer incidence, the rest of the cases necessitate further research into the carcinogenesis process, biological mechanisms, and complex cellular processes.

Evidence for the Environmental Influences and Breast Cancer

The concern for environmental influences in breast carcinogenesis is raised by several key observations, including geographic differences in breast cancer incidence. The United States has a four to seven fold higher incidence than Asia (Davis et al. 1998). Also, when immigrants move from lower-risk countries to higher-risk countries, their breast cancer risk changes to mirror the risk of the destination country (Brody and Rudel 2003). The increase is also evident in subsequent generations. Pollutants are thought to play a major part in the environmental causation of breast cancer. The rise of breast cancer cases in the United States is correlated with the proliferation of chemicals increased since World War II (Gray 2008) though in more recent years this may be due to better detection methods. Specifically, large increases of breast cancer incidence in the 1970s and 1980s are thought to be the direct result of the Breast Cancer Detection Demonstration Project and the rise of mammography technology (Lacey Jr. et al. 2002). Additionally, the more recent decrease in incidence may be linked to saturation in screening mammography (Jemal et al. 2007). As the number of women undergoing screening stabilizes, the incidence rates fall due to a smaller pool of previously undiagnosed cases.

Based on the mechanisms described below, environmental pollutants have carcinogenic potential. Furthermore, epidemiologically, the National Toxicology Program has identified 42 chemicals associated with increased incidence of breast cancer, while other research studies have identified as many as 160 chemicals (Brody and Rudel 2003). A study by Rudel et al. in 2007 identified 216 chemicals associated with at least one study showed increased mammary gland tumors in five databases: the International Agency for Research on Cancer (IARC)

Monograph summaries, the U.S. National Toxicology Program (NTP) Technical Reports, the NTP 11th Report on Carcinogens, the Carcinogenicity Potency Database, and the Chemical Carcinogenesis Research Information System (CCRIS). The chemicals were then separated into 11 use and source categories, with the most chemicals being pharmaceuticals, unclassified, and industrial chemicals (Appendix 1, Figure 2). This is a small percentage of the reported 84,000 chemicals listed on the Toxic Control Substances Act (TSCA) chemical inventory list (US EPA 2010), of which 3,000 are produced more than 1 million pounds per year, and have not been tested, for the most part, for carcinogenicity (Rudel et al. 2007).

Some environmental pollutants also have estrogenic potential and are endocrine disruptors. Endocrine-disrupting compounds are defined as "exogenous agents that change endocrine function and cause adverse effects at the level of the organism, its progeny, and/or subpopulations of organisms" (Birnbaum and Fenton 2003). An endocrine disruptor can mimic or block a hormone, or promote or inhibit production and transport of hormones (Coyle 2004). Studies focus on chemicals that are estrogenic because they are key hormones in breast carcinogenesis and may even be required for it to occur (Brody and Rudel 2003). Environmental pollutants that have estrogenic potential include organochlorine pesticides, phthalate esters, alkylphenols, and phenolic compounds like bisphenol-A (Miller and Sharpe 1998). Metabolites of these compounds may also have direct and indirect genotoxic effects (Yager 2000). Additionally, environmental chemicals that affect the production and metabolism of endogenous hormones may be more important than receptor-mediated endocrine disruptors (Sharpe and Irvine 2004).

It is difficult to prove with certainty that exposure to hormones is directly related to breast cancer development, especially epidemiologically, for several reasons (Miller and Sharpe 1998). First, undetectable small changes in hormone levels may have severe effects on the sensitive endocrine system. Second, hormone levels vary widely between individuals and in particular tissues. Furthermore, patterns of hormone increases may be more important than actual levels. Third, epidemiological studies looking for concrete associations between exposure and cancer development need long follow-up periods because of the long-latency period associated with cancer (see Timing of Exposure section), which is often not possible, or involving too many variables, leading to an inability to draw concrete conclusions. It is then even harder to prove a connection between environmental pollutants and their weakly estrogenic properties to breast cancer.

Mechanisms

Direct DNA Damage

Reactive oxygen species (ROS) play a part in many chronic diseases which include cancer (Klaunig and Kamendullis 2004). Reactive oxygen species are produced when oxygen is not completely reduced to water and then forms free oxygen radicals. Many biological processes, such as oxidative metabolism and immune system defense mechanisms, can produce ROS. Antioxidants are used to minimize damage, but when an imbalance between ROS and antioxidants occur, oxidative stress results. Oxidative stress can lead to direct DNA damage and mutations of oncogenes (Kang 2002). Persistent DNA damage leads to replication errors and genomic instability which are present in carcinogenesis (Klaunig and Kamendullis 2004). For breast cancer, in particular, oxidative stress end products are found to be increased in breast cancer patients than nonpatients. Malondialdehyde, an end product of peroxidative degradation of polyunsaturated fatty acids, has been found at increased levels in the serum of breast cancer patients, along with higher levels of DNA adducts in normal breast tissue than noncancer patients (Kang 2002). Thus is it plausible that environmental agents that cause oxidative stress could contribute to breast cancer.

Endocrine Disruptors

New theories point to hormonal influences in carcinogenesis, especially in reproductive tissues. The endocrine system is highly sensitive and regulates many biological and cellular processes in the human body. Estrogen is a key hormone in promoting normal tissue growth and differentiation. However, it plays a role in neoplastic growth, evidenced by presence of an estrogen receptor, ERα, in a majority of breast cancers (Russo et al. 2000). Elevated estrogen levels in gestating mothers have been associated with an increase in breast cancer in the resulting offspring (Birnbaum and Fenton 2003). There are three mechanisms that are thought to explain estrogen's role in carcinogenesis. First, receptor-mediated hormonal activity is related to cellular proliferation. As mentioned previously, increased cellular proliferation provides more opportunities for genomic DNA damage and replication errors. Second, metabolic activation of estrogen mediated by cytochrome P450 causes increased mutation rates. The quinone metabolites, in particular, can form DNA adducts and oxidative damage to lipids and DNA (Yager 2000). Third, estrogen may interfere with the DNA repair mechanism, which results in accumulation of DNA lesions that precede neoplastic growth (Russo et al. 2000). Although the relationship between estrogen and carcinogenesis needs further research and clarification, the present evidence indicates there may be a causal link. Increased estrogen levels may be due to endogenous sources, but also exogenous exposures in the environment, leading to increased speculation about the role of the environment, especially endocrine disruptors, in carcinogenesis.

Timing of Exposure

A main component of the complications of studying associations between environmental pollutants and cancer is that timing of exposure to genotoxic and mutagenic agents is critical in its onset. As mentioned previously, the progression of cells from normal to cancerous can take many years. Therefore, the initial event causing DNA damage and mutation may occur very early on. In environmental carcinogenesis, the exposure to exogenous agents during infancy or childhood may be the most important. In developing fetuses, cell differentiation and division and the lack of a complete blood-brain barrier contribute to a high susceptibility to carcinogens (Birnbaum and Fenton 2003). During prenatal exposure, imprinting of breast cells may make them more sensitive to future exposures (Davis et al. 1998). It is especially true in exposure to endocrine-disrupting chemicals (Miller and Sharpe 1998). In addition, it has been shown than multiple estrogenic chemicals may cause a greater effect than each individual chemical, even when each is below threshold (Brody and Rudel 2003). Another consideration is that exposure to environmental chemicals is hard to analyze and quantify per individual, due to availability of emissions data and detection methods. Being able to accurately predict or measure individual exposure is a key difficulty of epidemiological studies.

It is also worth noting that there is a disconnect between research indicating significant influence of non-genetic risk factors and insufficient data regarding the role of environmental pollutants in breast carcinogenesis. The analysis of the twin cohorts by Lichtenstein et al. 2000 very clearly indicates that hereditary cancers are the minority of cancer incidence. However, they also define their environmental factors as anything non-genetic including lifestyle factors such as obesity and smoking, or medical treatments like hormone replacement therapy, which are known risk factors for breast cancer (Coyle 2004). Distinguishing the plausibility of influence of environmental pollutants on breast cancer is based on circumstantial evidence that includes differences in geographic incidence and observed rise of breast cancer in the United States occurring with the increase in environmental pollutant exposure (Laden and Hunter 1998), the carcinogenic potential of environmental pollutants, and the connection of changes in the endocrine system to breast cancer. The presence of an estrogen receptor in many breast tumors, as well as animal studies showing endocrine-disrupting effects of environmental chemicals (Brody and Rudel 2003) indicates that there is an influence of exposure to estrogenic chemicals and increase health risks, including cancer. The complex maturation process of the breast, as well as the integral role of the endocrine system, makes it very plausible for there to be links between carcinogenic and estrogenic environmental pollutants and breast cancer. There is a need for research on the association of environmental pollution and breast cancer, as it continues to be the most common cancer and second leading cause of death in women. An analysis into potential geographic clusters of breast cancer cases, such as the collaboration between the Nicholas School and the Comprehensive Cancer Center at Duke, provides an opportunity to probe the relationship causal relationship between the environment and breast cancer.

Vance County

The study site is Vance County in North Carolina. It is located on the North Carolina-Virginia border and its neighboring counties are Granville, Warren, and Franklin Counties (Appendix 2, Figure 1). Kerr Lake is a major water source and recreational area located in the county. Vance encompasses a land area of 253.52 square miles with a density of 169.1 persons per square mile. The county population is estimated to be 43,056 in 2009 (US Census Bureau 2010). Its county seat is the city of Henderson, with a population of 16,095 in 2000 (US Census Bureau 2000).

Demographics

Vance County population has a racial makeup that is 48.8% white, 49.5% black, 0.3% American Indian/Alaska Native, 0.6% Asian, and 0.8% other. 68.1% of the population has graduated from high school, compared to 78.1% in North Carolina, and 80.4% in the United States (US Census Bureau 2010). The majority of the population is between 25 to 54 years of age, with the largest age group being between 35 and 44 years of age (Appendix 2, Figure 2). 25.7% of the county's population is estimated to live below the poverty line and the median household income is $34,093 (US Census Bureau 2009). The unemployment percentage was 8.9% in Vance County, compared to 6.2% in North Carolina and 5.8% nationwide in 2008 (BLS 2010).

Industry

Historically, the biggest employers in Vance County have been tobacco and textile facilities, especially Harriet and Henderson Yarn, but many of those facilities have closed in the past decade. Currently, the biggest manufacturing employers are Saint Gobain Containers, Pacific-Coast Feather Company, and P&G Pet Care. Construction companies are also top employers. However, the largest current employers in the county are not manufacturers, but rather are in education, civil service, and retail (Vance County EDC 2009).

Health Profile and Trends

According to a nationwide county health study performed by the University of Wisconsin Population Health Institute (UWPHI), Vance County is among the lowest (i.e. worst) ranked out of the 100 counties in North Carolina for mortality and morbidity (UWPHI 2010). It is 93rd in mortality (defined as premature death, years of potential life lost before age 75) and 88th in morbidity. The North Carolina Department of Health and Human Services has also detailed trends over the past 15 years that depict higher infant mortality rates, age-adjusted total cancer rates, and prevalence of obesity in children ages 5 to 11 in Vance County compared to state averages (NCDHHS 2009).

Additionally, Vance County is ranked 7th[1] out of 100 North Carolina counties in highest annual cancer incidence rates for the period of 2002-2006 (NCI 2010). However, when comparing the rate of incidence of breast cancer of the state to Vance County, we find that Vance County's numbers are lower. In North Carolina, the incidence is 149.6 per 100,000 women in 2003-2007 while Vance County's breast cancer incidence in was 127.1 per 100,000 women (NCSCHS 2010). Also, while the number of *new* cases in the state has remained constant over the last decade, the number of new cases in Vance has decreased slightly in recent years (NCDHHS 2009). Although the county's numbers are favorable when compared to

[1] There is confusion between the mortality and morbidity county ranking and the annual cancer incidence county ranking. In the former, a higher ranking means lower mortality/morbidity rates, which is good. However, in the latter, a higher ranking corresponds to higher cancer incidence rates, which is unfavorable.

the state, its incidence rate is still higher than the nationwide average, 119.3 per 100,000 women in 2006 (CDC 2006). Preliminary analysis done by the Comprehensive Cancer Center indicates presence of a potential breast cancer cluster among black women adds to the need to examine the possible environmental influences on the county's breast cancer incidence in an organized way.

Methods

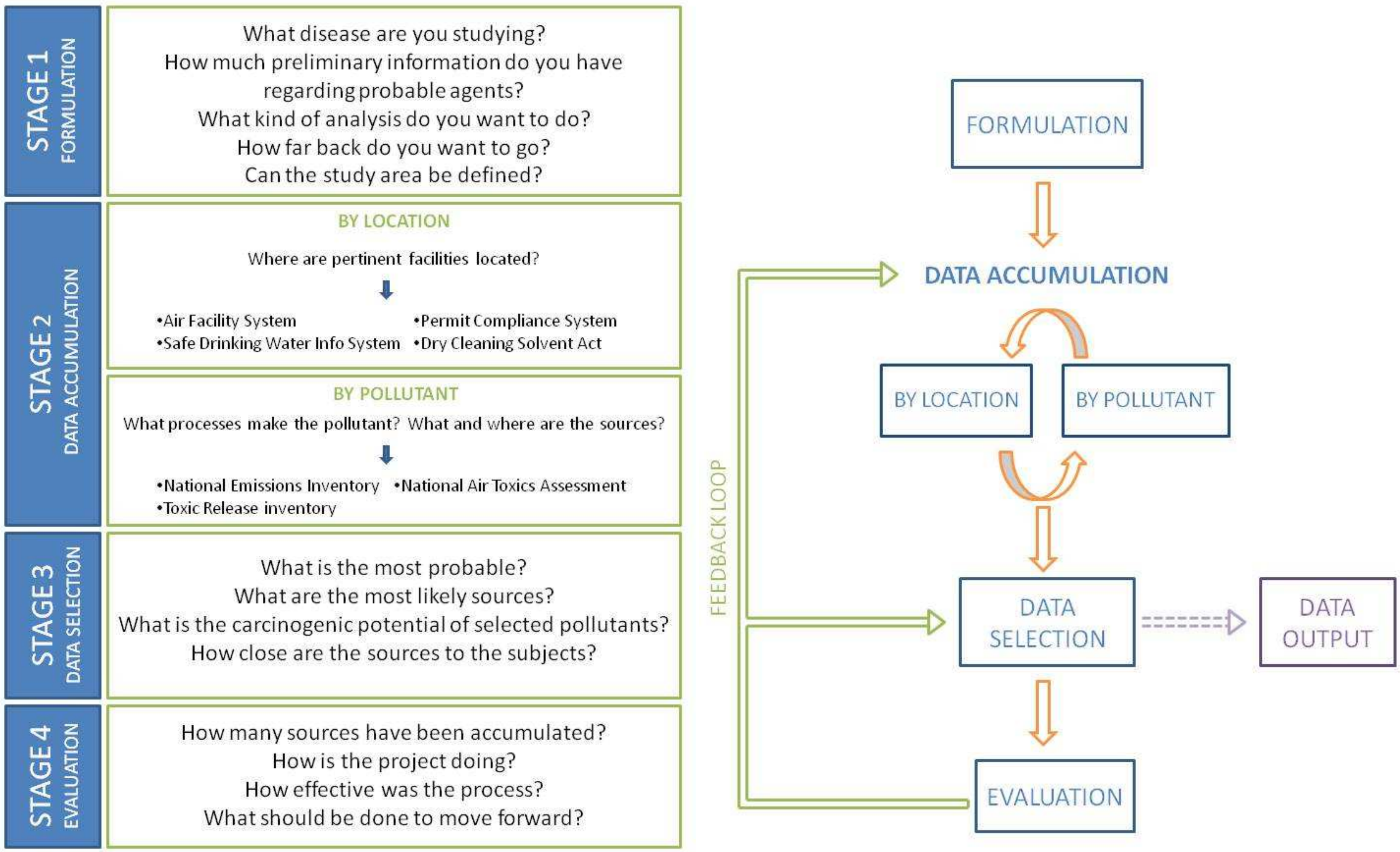
Generally, the project involved extensive internet research and literature review. More detailed methods are detailed in the framework section. Narrowing the focus to breast cancer and Vance County enabled the project to be completed in a shorter time frame than the umbrella project by the Nicholas School and Comprehensive Cancer Center. The project was performed as a multi-step process, starting with literature review. Finding literature regarding the relationship between environmental pollutants and breast cancer is a key step in finding pollutant sources. However, this approach is limited by what linkages have been identified, and there may be some that have not yet been identified. The scientific literature provides a basis for linking exposure to environmental pollutants and breast cancer, and which pollutants may be better candidates for further research. Government databases were accessed via the websites of the Environmental Protection Agency (EPA) and North Carolina Department of Environmental and Natural Resources (NCDENR). These databases provided information to sites that may potentially be pollutant sources. In addition to reading peer-reviewed literature and internet research, visits with state environmental managers and the permit room at the North Carolina Department of Natural Resources' Solid Waste Department provided additional information on the extent of records kept by the state. The permit room will be a source for more specific data as the project moves forward. Communication with state officials via email and interviews provided information about various databases and their capabilities and progress. Databases were then separated into categories so that the framework could be constructed as a multi-stage process with a logical progression. The entire process is documented for future research for identification of difficulties, resources, and tips.

Framework

Framework introduction

This framework is the product of an adaptive process. The initial idea behind it helped form the skeleton, while the bulk of the content was added through the process of the case study in Vance County, North Carolina. The framework was created alongside the case study to test its efficacy in organizing the process of finding pollutant sources. It is intended to help guide similar research by setting a structure and finding relevant information sources on environmental pollutants. Its main strength lies in using a real research question to evaluate its effectiveness and document the extent of available information on historical and current pollutant sources. First, the graphic and its organization will be discussed. Each of the stages is described. The second section details the relationship of the framework to the breast cancer case study in Vance County. The results from the study, web links to online databases, and other resources are collected in Appendix 3.

Framework graphic



Organization

The framework is organized into four stages: formulation, data accumulation, data selection, and evaluation. A fifth stage, data output, is included in the framework but is not covered as it is outside the scope of this paper. The flow graphic above illustrates the cyclical process of the framework. The evaluation of the process enables feedback to lead to changes in the data accumulation and selection stages. Iterative revision of the process will enable the final data output to be more streamlined and informed, resulting in a better product.

The first stage, **formulation**, prompts the user to define the research question and preliminarily narrow the search for potential sources. The questions range from geographical to conceptual. These questions address setup, the selected disease, and the current status and goals of the study. Users may want to think of other questions that are more specific to their particular study. A well-defined research purpose sets up the framework to be more successful, as goals and limitations are discussed early in the process. All the questions need not be answered, but as more questions are answered the goals of the project will be better defined. A list of formulation questions is located in Appendix 3 and is intended to help the user define their research question and establish goals.

Data accumulation is the second step and starts with two approaches. Both approaches require the state and county to be specified. First, the location approach concentrates on using addresses or to find sources. This may be used best if the location is particularly important, or if the geographical boundary is a primary criterion. Users taking the location approach must specify a state. Then, depending on how much information is known, county or zip code is entered into various EPA and state databases. Most databases are only able to offer pollution information on a county basis, whereas others will then provide addresses of the resulting facilities. Many of the databases used for the location approach may be found on the EPA's new Envirofacts website, which is a source of information on pollutants searchable by geographic location.

The second approach to data collection is the pollutant approach, which starts with a select group of relevant pollutants or processes. The selected chemical is inputted into the database which either shows the amount emitted in the county or the facilities in the county that emit that pollutant. The relevant national databases here are the National Air Toxics Assessment (NATA) and the Toxic Release Inventory (TRI). A list of relevant databases from the EPA and state of North Carolina, their descriptions, and the type of information included is available in Appendix 3. They are a good source of information at the beginning stages of data collection. However, it is important to note the limitations of the information included in the databases. Facilities that are required to report those particular agencies meet certain requirements such as minimum facility size or emission levels and only provide preliminary information.

Although there are two initial approaches, they are not completely separate, as indicated by the cycling arrows. Starting with the location approach leads to pollutants found in the area and the locations of their facilities. With the pollutant approach, having pollutants in mind directs the search and leads to locations. Also, as previously mentioned, specifying the county and state are necessary for both approaches. Spatial data on pollutant sources will be an important part of further research and analysis.

The third stage, **data selection**, is dependent many factors, which will be unique to each case. Sources may be selected based on location, connection of the pollutant to the disease, and availability of data. For example, researchers may want to choose facilities that are located within a certain radius of the patients, with documented emissions that are likely to reach subjects' homes. Or, researchers might choose facilities that emit certain pollutants of interest. Lastly, they may have to eliminate sources due to lack of information on emissions, date of operation, or

Although this paper does not cover the fourth stage, **data output**, the framework aims to make it possible to use the selected data to do other analyses. Formatting the selected data would be an important precursor to using it in subsequent analyses, such as a hotspot database, possible field sampling locations, and geographic information systems (GIS). An interactive Microsoft Access database may be a way to record a hotspot database searchable by industry, pollutant, or address. Field sampling locations can also be determined from the selected data. GIS offers a way to see the selected sources spatially, which can be used to determine patterns or significance to patients. Mapping the potential sources requires the addresses in a specific format for geocoding purposes. The resulting spatial map may include a layer with points detailing where certain pollutants are produced or where particular industry is located. Data output is an important stage, with the formatting leading to more advanced analysis for the entire project.

Evaluation is the final stage and is an analysis of the success of the process and constructive thinking of ways in which it can be improved. The answers to the questions posed here provide feedback for the data accumulation and selection stages and the process reiterates if necessary.

Vance County as a Case Study

The Nicholas School of the Environment and Duke Comprehensive Cancer Center's project in Vance County, North Carolina, provides an opportunity to develop and use the framework in a real situation. The main objective of this case study is to structure and apply the framework, document the overall process, and evaluate its effectiveness. Therefore, the case study is not wholly independent from the framework, but rather a tool in its creation. We discuss the process of finding pollutant sources for Vance County and the databases and problems encountered during the study.

Formulation

The formulation questions were formed after the project commenced as a response to some of the problems we encountered during the process. Organizing them into groups based on the set up, the selected disease, and the study's status and goals helped break down and address some of the key issue. In our case, the umbrella project provided some of the answers to the questions. Our focus is on breast cancer in Vance County, North Carolina. Our main research question is to determine what pollutant sources in the county might be connected to the breast cancer cluster by setting up an organized framework to follow. Other questions were determined as the process continued, and we established our own time constraints separate from the larger project. Since we did not know how far back in time the records online would cover, we decided that we would try to look back as far as there were records online. As some of the databases were new or published online with the most recent results first, the upper limit seemed to be in the late 1980's. In our characterization of breast cancer, its long latency period and connection to carcinogens directed the pollutant search. Also, there were no specific pollutants connected to these particular cases, so we used the literature as a starting point for target pollutants. Finally, we thought it probable that future research would include sampling and GIS maps, making addresses and pollutant information high priority for the results of the data selection process.

Data Accumulation

The process for gathering the data started with a focus on historical environmental events, based on the long latency period of breast cancer. Historical industry in the area included tobacco processing and textiles. Internet searches were conducted for notable environmental events, such as a big spill or contamination that might cause adverse environmental conditions. Newspaper archives and historical records were not extensive online, which made searching for historical event data difficult. No large-scale environmental events were found. Next, we looked at Brownfield, Superfund, and Inactive Hazardous Waste Site databases and moved on to more specific databases like the Air Facility Systems (AFS) which monitors air pollution from stationary sources, and the Dry-cleaning Solvent Act (DSCA) which details dry cleaners around the state that have contaminated their surrounding area. We added databases that focused on toxics, including the Toxic Release Inventory (TRI) and the National Air Toxics Assessments (NATA). The full list of database websites and descriptions is located in Appendix 3.

Generally, most of the data located in these databases list the current facilities and current emissions. The records on what facilities were in the county or what their emissions were in the past are hard to locate. Many times this information has not be put online or just do not exist. We inquired after the records in the Solid Waste department of the North Carolina Department of Environmental and Natural Resources (NCDENR) to see if they could be easily analyzed for relevant details. However, records kept at the permit room are unorganized and are filed back to 2001. Visits to the permit room require knowledge of specific facilities of interest. Each permit is extensive, but not easily translated to cursory browsing. Very few records have been digitized and can be looked at on the permit room's computer. The documents dated earlier than 2001 are unfiled and located in boxes in storage. Permission to view the permit room was acquired through contact with Mark Poindexter, head of the Solid Waste branch, and Carmen Johnson, the permit room steward. Appointments, which can be made very easily, are necessary. The permit room should be saved for the last stage of research, with a list of specific facilities in which researchers are interested.

Due to the lack of historical data, we dropped the timeline approach and created the location/pollutant approach. The extra benefit of doing so was that organizing each database into the location or pollutant approach helped organize the type of information found in each one and would allow us to better use the online resources. For the location approach, we used Vance County as our initial location in order to gather as many relevant sources as possible for data selection. We surmised that after a beginning list of facilities was found, we might be able to use more specific location in the data selection process. We entered this location into the databases that were organized by geographic location and gathered the results into an excel spreadsheet. For the pollutant approach, we did not have a list of specified pollutants of interest. To create a preliminary list of pollutants, we created a list of 14 chemicals from Rudel et al. 2007 by selecting, out of 216 identified breast cancer carcinogens, chemicals marked as "high production volume" and "air pollutant." The other categories in the paper are "in consumer products," "food additive," and "occupationally exposed," which do not fit the scope of this project. We searched for them in the NATA database which tracks hazardous air pollutants (HAPs) and produces a list of modeled emissions found in the county from the National Emissions Inventory (NEI). Only three out of the 14 pollutants was found in the 2002 NATA: ethylene oxide, nitrobenzene, and *o*-toluidine. Each of the 14 pollutants was also entered into the TRI database under Vance County, but none were found. Although we were unable to find facility and emissions information for these 14 carcinogens, it might be due to the general nature of the list and its focus on air pollutants. A list of 13 chemicals used in textile manufacturing (Appendix 3, Table A3-11), a widespread historical industry in Vance, was culled from the International Agency for Research on Cancer (IARC) Monograph on flame retardants and other textile chemicals. They were not found in the TRI or NATA databases. These textile chemicals may not be one of the 650 chemicals that TRI tracks. Also, it is unlikely they are categorized as air pollutants, which may explain their absence in the NATA database. Other projects with specified pollutants in mind may find the pollutant approach more successful.

Data selection

Our data selection process was difficult for several reasons. For many of the databases, there were no records for Vance County which excluded some databases like the Superfund and DSCA records. For others, there were multiple reasons why we could not determine whether the facility was relevant. When starting with location, sometimes no pollutant information would be attached. Or, if there was pollutant information attached, we were unable to narrow down the location from the county level to a finer scale, due to lack of information about the patients. Generally, we were unable to make a satisfactory selection of possible facility pollutant sources . However, we were able to find a TRI database interface that organized results by year, and listed facilities and their emissions. The data was also available in Excel and Access format for analysis. We have included the Vance County carcinogen release results from the first four years available, 1987-1990, and also the latest year, 2008, for comparison in Appendix 3 (Tables A3-6 to A3-10). In 1989 there was a significant release of methylene chloride from Saint Gobain Containers, Inc (Appendix 3, Table A3-8). Methylene chloride is one of the 14 breast cancer carcinogens selected from Rudel et al. 2007. Although this is a preliminary result, it indicates that the process might be successful if the right information is available for analysis. The data selection stage requires the most time and information in order to make decisions about which facilities are more likely than others to be connected to the breast cancer cluster. Unfortunately, the information was not widely available at this time, but may be available in the future.

Evaluation

Evaluation of the process of finding pollutant sources in Vance County is found in the next section, along with evaluation of the entire process and framework.

Evaluation

Although we were unable to select pollutant sources to the scale we envisioned, the process of creating this framework still yielded insights for future projects and frameworks. Looking back on the process, results, and case study allows for a distinct opportunity to address data deficiencies and suggestions for future improvements. Addressing problems now will aid future attempts at finding environmental pollutants connected to health issues.

It was not our aim to construct the framework independently from the case study, as we used Vance County and breast cancer to create the framework and test its efficacy. Therefore, we did not follow it strictly for the project and cannot evaluate it from that standpoint. However, there are still key points to be made about the process of making the framework. Our evaluation of creating and following a framework starts with a key point in stage one: formulation. The questions we posted in stage one for laying out the research project were the result of the difficulties we faced in approaching the project initially. Seeing only the big picture in the very beginning made the project seem unmanageable and difficult to move forward. The benefit of having more well-defined research questions, tasks, and goals at the beginning is a better overall process. In addition, it is necessary to point out that the adaptive process of making the framework alongside the case study precluded the intended cyclic nature of the framework. We were constantly changing elements in response to problems in process instead of going through the whole process and cycling back. Perhaps some researchers may also want to use the framework as a skeleton and adapt it constantly instead of completing a cycle and feeding

While starting with internet searches of historical environmental events did not yield concrete results, we decided to use the internet-based databases as a primary research tool. We were unable to search effectively through the paper permits because of the lack of organization at the North Carolina Department of Environmental and Natural Resources' Solid Waste permit room, which reinforced the idea of the internet as a viable tool. Many of the EPA's databases are now online, with search tools that aid in our research. However, the EPA is still in the process of digitizing their records prior to 2000 (though the TRI database has records online back to 1989) while adding current records to their online databases. Since we are using the internet as our primary search tool, our dependency figures heavily in the data accumulation and selection stages as we are limited to what we can find online. For example, we were able to find a database of dry cleaners and data of the extent of their solvent contamination in the surrounding areas from the state's Dry-cleaning Solvent Cleanup Act (DSCA). However, the DSCA has only studied a fraction of the thousands of dry cleaners in the state that have opened and closed over the years. There is a possibility that an extensive solvent contamination from a long-closed dry cleaner might be causing environmental health problems and no record of its existence found online.

The data accumulation stage is split into two options: location and pollutants. In this way we hope the process is clearer because we are able to define the type of starting information users might have and illustrate how to use it. Another way we debated organizing data sources is by mode of exposure: via air, water, or soil. This approach turned out to be too specific for an extensive search. However, it may be useful for users who may already know a lot of information about their disease's etiology and want to categorize their known pollutant sources in the data selection stage.

As the process moved forward we eliminated a lot of databases because their pollutant emissions did not seem to match a more widespread exposure to the patients. For example, a search into traditional crops and pesticide use in Vance County concluded with the recommendation from the Vance County Agriculture Extension specialist Paul McKenzie that only farmers and their workers would have substantial exposure to the pesticides. We had no background information to link the women to farms and pesticides. Patient privacy is a valid concern and must be considered in our environmental health research. However, the lack of information on the patients' occupations, habits, and residences prohibits more thorough research into what may be causing these particular cases of breast cancer. Perhaps, with proper consideration, an anonymous survey with questions about those key aspects of the patients' lives might be collected and used generally to direct selection. The scale of location is an important consideration. If specifying down to the parcel is unavailable, the neighborhood or region of the county would still be helpful as it is a smaller scale than the county. Another key piece of information to gather is how long the patient has lived in the target county. As cancer takes years to develop, it would be helpful to know whether the patient has spent a substantial amount of time in the county. Anonymous surveys would be able to help answer those questions and protect patient privacy.

The databases we relied on for information for pollutant sources also caused difficulties in the case study. First, there was a lack of information included in database results, mainly pollutant information attached to facility lists. Generally, the databases are formulated for a specific purpose and therefore only include information relevant to that purpose. For example, the NATA database is a model formulated to give you the amount of each pollutant in the county in that particular year. Its aim is not to account for who has emitted what in the county. Other databases, like the TRI, segregate each facility's individual report so that it is more difficult to compare facilities in the types of pollutants they emit. Another database, the Inactive Hazardous Waste Sites list, is primarily a list of locations, not a repository of pollutant information. There would be no information on what kind of pollutants might be leaking from the site, which would be important in determining whether that site might possible affect the health of its neighbors. However, we were able to find one TRI website that provides facility data and pollutant data in a yearly database that can be formatted in either Microsoft Excel or Access. Each facility's name, address, and reported pollutant emissions are located in the same file, which makes it very convenient for our type of analysis. Being able to connect facilities to their locations and emissions is a key part in determining their effect on the surrounding population.

Further missing useful information is the facility's date of operation. Many facilities are labeled inactive or closed, but we had no way of finding out when they were in operation. When looking at historical sites, information on when these facilities were in use would be very important to establishing timelines. Although it would be difficult to eliminate a facility based on its date of operation, it would still be helpful to determine probability of being connected to our disease of interest. Including the date of operation in future database management would be a source of simple yet relevant data.

Secondly, there is a general need for practical online database management. For example, there are two different websites used to access the TRI database and each produces different results (Appendix 3, List of Databases). There are three improvements necessary for efficient use and subsequent analysis of the information in the databases. First, reformat the websites leading to each database to be simpler, clearer, and easy to find is a key priority in environmental health research. Second, connect related databases in a user-friendly interface. Third, clearly state the information found in each database and make Microsoft Excel or Access versions available for researchers to easily organize and use the data.

Future research

With the improvements suggested in the evaluation section, research into the connection between environmental pollutants and health outcomes will be easier to analyze. Patient surveys, pollutant information, connected databases, and database management will improve the data accumulation and selection stages. Continuing with the results from the pollutant source search, GIS maps and field sampling will provide further insights into the connection between environmental pollutants and the breast cancer cluster in each of the six counties in North Carolina.

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APPENDIX 1: Breast Cancer

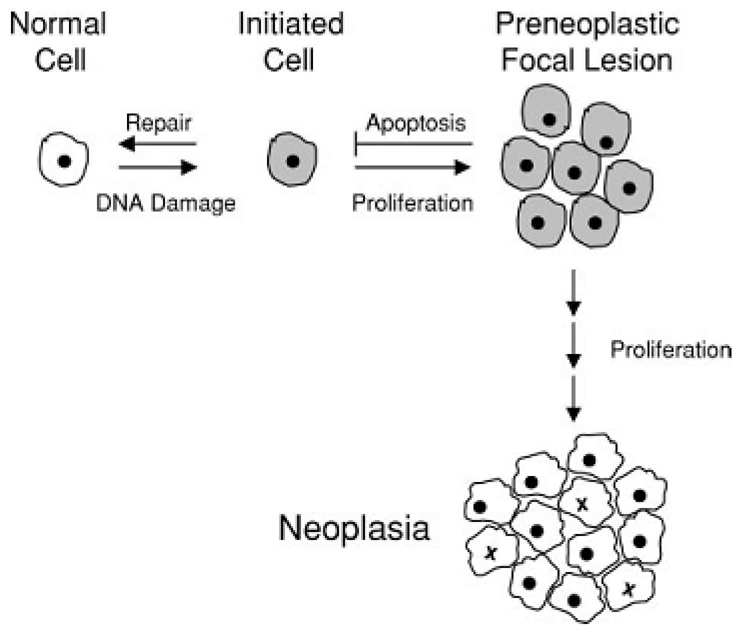

Figure 1. The initiation, promotion, and progression of a normal cell to a neoplasia in Klaunig and Kamendullis 2004.

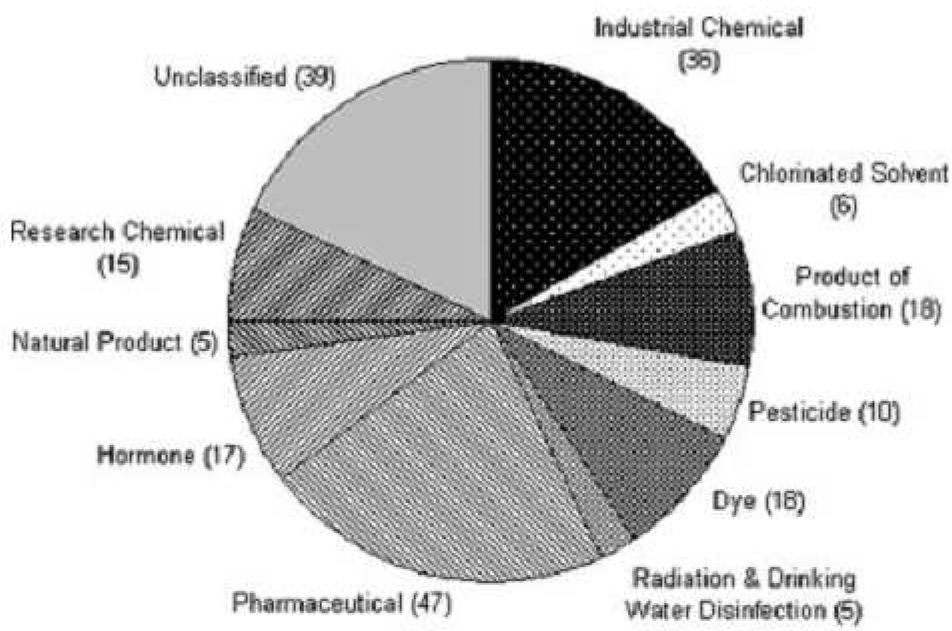

Figure 2. Chemical use and source breakdown of the 216 mammary gland carcinogens in Rudel et al. 2007.

APPENDIX 2: Vance County

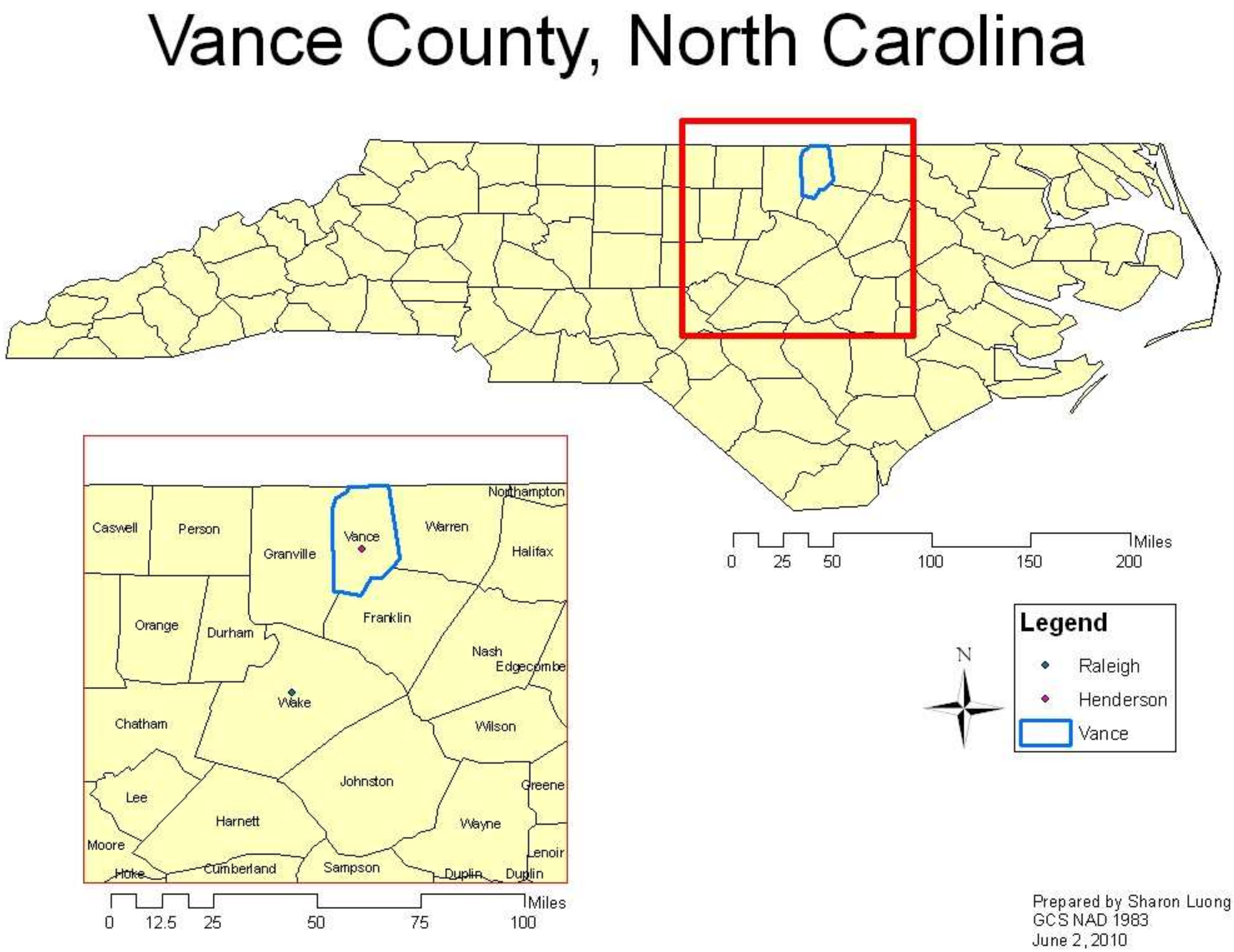

Figure 1. Location of Vance County in North Carolina.

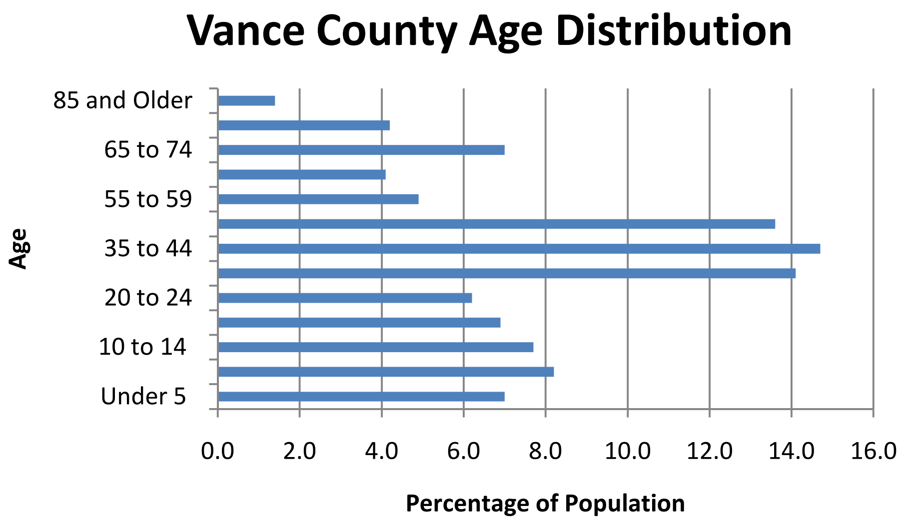

Figure 2. Vance County Age Distribution. Data from US Census Bureau 2000.

APPENDIX 3: The Framework and Case Study

FORMULATION QUESTIONS

THE STUDY SETUP
What kind of analysis do you want to do with the results? Survey, laboratory sampling, or fact-gathering?
Ideally, how far back in time do you want to go? Why?
Can the study area be defined? Is it defined by political or environmental boundaries? How will this affect the analysis?
What is the time frame in which the study is to be completed?

THE DISEASE
What disease are you studying? Why did you select it?
What kind of disease is it? Infectious, chronic, or long-latency?
What is the disease's connection to the study area?
What is the extent of the evidence that environmental pollution is a causative agent?

THE STUDY STATUS
How much preliminary information do you have regarding probable pollutant agents?
Are there plans for physical sampling? Patient surveys?
What is the extent of knowledge about industrial processes in the area? How familiar are you with the study area?
Does the state have records you can access?
Are there other groups working on similar projects?

THE STUDY GOALS
What is the ideal end product of the study? GIS map, list of possible sources, report?
What would you like to communicate to your audience?
What would best aid the project as a whole?
How in-depth would you like the end result? Down to the pollutant, the address, the mode of exposure?

Database Addresses and Descriptions

Air Facility System (AFS)
http://www.epa.gov/enviro/html/airs/airs_query.html
AFS contains reports from stationary sources of air pollution regulated by the EPA, state, and local agencies. Search by location, pollutant, or both. Output is individual reports.

Brownfields
Main Site: www.ncbrownfields.org
Active project inventory
http://portal.ncdenr.org/web/wm/bf/projectinventory
Brownfield sites are underutilized properties with environmental contamination. Developers enter into agreements with the state to clean up the contamination and prepare the site for redevelopment. This database lists sites that are active in the program, eligible for a Brownfield agreement and in a stage of data-collecting.

Dry-cleaning Solvents Cleanup Act (DSCA)
http://portal.ncdenr.org/web/wm/dsca
The DSCA provides funds for remediation of contaminated dry-cleaning sites in North Carolina. Their inventory (under Remediation) lists sites that have applied for entry into the program, and therefore does not include all past and present dry-cleaning facilities. The inventory is listed by county and includes the name of the site, the address, and the status of the remediation. It also lists the Project Manager of the site.

Inactive Hazardous Sites
http://portal.ncdenr.org/web/wm/sf/ihshome
The North Carolina Division of Waste manages maintains a database of sites they have with historical and present hazardous substances and pollutant contamination. They are responsible for assessment and remediation. There are different

National Air Toxics Assessments
Main site: http://www.epa.gov/ttn/atw/natamain/index.html
1996: http://www.epa.gov/ttn/atw/nata/tablemis.html
1999: http://www.epa.gov/ttn/atw/nata1999/tables.html
2002: http://www.epa.gov/ttn/atw/nata2002/tables.html#table1
NATA compiles a list of emissions and modeled ambient concentrations of 180 hazardous air pollutants (HAPs) in 2002, with more limited data is available for 1996 and 1999. Each database tracks hazardous air pollutants (HAPs) and produces a list by county of the HAPs. It is not recommended to compare assessment years as the methodologies for each year are improved extensively. A search by state and county is available, as well as searching by a specific pollutant across the United States. This might be a good place to start for a list of possible pollutants in selected counties. It does not identify sources or their locations.

National Emissions Inventory (NEI)
http://www.epa.gov/ttn/chief/eiinformation.html
The NEI contains information about sources of criteria air pollutants and their precursors, and hazardous air pollutants. This includes point, nonpoint, and mobile sources. The emissions data is collected by local and state agencies, and is available in large zipped files for data analysis. NEI is updated every three years.

Toxic Release Inventory (TRI)
Envirofacts: http://www.epa.gov/enviro/facts/tri/search.html
Basic Data Format: http://www.epa.gov/tri/tridata/current_data/index.html
The TRI database tracks 650 toxic chemicals and chemical groups from industrial and other facilities through disposal, recycling, and other releases. TRI accessed from Envirofacts gives facility information, with individual reports. Generally only the most recent year is available. The Basic Data Format TRI page is organized by year (1987-2008) and state. The raw data format must be converted via comma-delimited text files to Microsoft Excel or Microsoft Access. The instructions for the data format conversion are included.

Superfund
North Carolina: http://www.epa.gov/region4/waste/npl/index.htm#NC
Superfund sites are abandoned locations with hazardous waste contamination that is detrimental to wildlife, ecosystems, and people. The Superfund database is organized by facility name, and includes online reports and contact information for the site manager.

Although we did not address water-based databases, here are a few websites that may be of interest.

Drinking Water Watch, North Carolina
https://www.pwss.enr.state.nc.us/DWW/

Safe Drinking Water Information System
http://www.epa.gov/enviro/html/sdwis/sdwis_query.html

Private Drinking Water Wells Information
http://www.epa.gov/safewater/privatewells/index2.html

Table A3-1. Vance County Inactive Hazardous Sites

Name	Address	City
Bowmann Body Shop (Fred's)	St Andrews Church Rd	Henderson
Burkart Carolina	1730 Dabney Dr	Henderson
Closed City of Henderson Landfill	NC 39 & St Andrews Church Rd	Henderson
Coffey, Sara property	339 W Young Ave	Henderson
Henderson Coal Gas Plant		Henderson
Lauren's Glass/Ball-Incon Glass Pack	US 1 South	Henderson
Moore's Company	US 1 Business & SR 1001	Henderson
Novak, Gene	1259 Oak Ridge Ave	Henderson
Perry Builders - Mobile tract	Nicholas St & Skenes Ave	Henderson
Perry Builders - Raleigh Rd	2846 Raleigh Rd	Henderson
Spur Station #1286	404 N Garnett St	Henderson
Tungsten Queen Mine/Atlas Mine	SR 1348	Townsville

Table A3-2. NC Brownfields Program Vance County Sites

Name	Address	City	Status
Burkhart Carolina	1703 Dabney Dr.	Henderson	Finalized

Table A3-3. Dry Cleaning Solvent and Cleanup Act 2008 Vance County Sites

Vance	None

Table A3-4. Carcinogens from Rudel et al. 2007 located in Vance County NATA.

Chemical Name	CAS Number	HPV Chemical	Air pollutant	NATA 1996	NATA 2002
1,2-Dibromoethane	106-93-4	·	·		
1,2-Dichloroethane	107-06-2	·	·		
1,3-Butadiene	106-99-0	·	·	·	
1,4-Dioxane	123-91-1	·	·		
Acrylamide	79-06-1	·	·		
Benzene	71-43-2	·	·	·	
Carbon tetrachloride	56-23-5	·	·	·	
Ethlylene oxide	72-21-8	·	·	·	·
Isoprene	78-79-5	·	·		
Methylene chloride	75-09-2	·	·	·	
Nitrobenzene	98-95-3	·	·		·
Nitromethane	75-52-5	·	·		
o-Toluidine	95-53-4	·	·		·
Vinylidene chloride	75-35-4	·	·		

*NATA 1999 data missing due to incompatible data format.

Table A3-5. Landfills in Vance County.

Name	Type	Activity	Status	Permit	Address	City
VANCE COUNTY CDLF	CD	LF	InactiveClosed	9101-CDLF-1998	NC HWY 39	HENDERSON
VANCE COUNTY LANDFILL	MSW	LF	InactiveClosed	9101-MSWLF-1974	NC HWY 39	HENDERSON
WASTE INDUSTRIES-VANCE COUNTY	MSW	Trans	Active	9102T-TRANSFER-1997	3453 NC Highway 39 N.	Henderson
HENDERSON CITY OF	CD	LF	InactiveClosed	91A-DEMO-	HWY 39 N.	HENDERSON
JACK HUGHES DEMO LANDFILL	CD	LF	InactiveClosed	91B-DEMO-	ALPHA STREET	HENDERSON
King & Son Septic Tank Service	Septage	Hauler	Active	NCS-00003	1550 St. Andrews Church Road	Henderson
Bailey Company	Septage	Hauler	Active	NCS-00285	P.O. Box 2162	Henderson
K T Moore Septic Tank Service	Septage	Hauler	Active	NCS-00758	712 North Chavis Road	Kittrell
Steele Creek Marina	Septage	Hauler	Active	NCS-01055	P.O. Box 430	Townsville

CD: Construction and Demolition
MSW: Municipal Solid Waste
LF: Landfill

Table A3-6. 1987 TRI Carcinogen releases, Vance County

Facility Name	Street Address	ZIP	Latitude	Longitude	Chemical	CAS #/ Compound ID	Total Releases (lbs)
PERRY BUILDERS OUTLET INC.	RALEIGH RD.	27536	36.282	-78.406	CHROMIUM	007440473	1450
PERRY BUILDERS OUTLET INC.	RALEIGH RD.	27536	36.282	-78.406	ARSENIC	007440382	1450
KENNAMETAL INC	139 WAREHOUSE RD	27537	36.289	-78.405	COBALT	007440484	500
PERRY BUILDERS OUTLET INC.	CEDAR ST.	27536	36.311	-78.403	ARSENIC	007440382	1450
PERRY BUILDERS OUTLET INC.	CEDAR ST.	27536	36.311	-78.403	CHROMIUM	007440473	1450
EASTERN MINERALS INC	170 EASTERN MINERALS RD	27536	36.271	-78.404	COBALT	007440484	250

Table A3-7. 1988 TRI Carcinogen releases, Vance County

Facility Name	Street Address	ZIP	Latitude	Longitude	Chemical	CAS #/ Compound ID	Total Releases (lbs)
KENNAMETAL INC	139 WAREHOUSE RD	27537	36.289	-78.405	COBALT	007440484	500
EASTERN MINERALS INC	170 EASTERN MINERALS RD	27536	36.271	-78.404	COBALT	007440484	250

Table A3-8. 1989 TRI Carcinogen releases, Vance County

Facility Name	Street Address	ZIP	Latitude	Longitude	Chemical	CAS #/ Compound ID	Total Releases (lbs)
SAINT-GOBAIN CONTAINERS INC	620 FACET RD	27537	36.2849	-78.39309	PCBs	001336363	22365
SAINT-GOBAIN CONTAINERS INC	620 FACET RD	27537	36.2849	-78.39309	METHYLENE CHLORIDE	000075092	22572
KENNAMETAL INC	139 WAREHOUSE RD	27537	36.2892	-78.40493	COBALT	007440484	500
PUROLATOR PRODUCTS CO	US NO 1 BYPASS S	27536	36.3124	-78.37893	FORMALDEHYDE	000050000	250
EASTERN MINERALS INC	170 EASTERN MINERALS RD	27536	36.2711	-78.40371	COBALT COMPOUNDS	N096	250

Table A3-9. 1990 TRI Carcinogen releases, Vance County

Facility Name	Street Address	ZIP	Latitude	Longitude	Chemical	CAS #/ Compound ID	Total Releases (lbs)
KENNAMETAL INC	139 WAREHOUSE RD	27537	36.2892	-78.40493	COBALT	007440484	500

Table A3-10. 2008 TRI Carcinogen releases, Vance County

Facility Name	Street Address	ZIP	Latitude	Longitude	Chemical	CAS #/ Compound ID	Total Releases (lbs)
KENNAMETAL INC	139 WAREHOUSE RD	27537	36.2892	-78.40493	COBALT	007440484	8.5

Table A3-11. Chemicals used in textile manufacturing.

Chemical name	CAS #	Use
Chlorendic acid	115-28-6	Flame retardant precursor
Chlorinated paraffins		Flame retardant
Decabromodiphenyl oxide	1163-19-5	Flame retardant
Dimethyl hydrogen phosphite	868-85-9	Flame retardant
Tetrakis(hydroxymethyl)	124-64-1	Flame retardant precursor
Phosphonium salts		Catalyst
Tris(2-chloroethyl) phosphate	115-96-8	Flame retardant
Para-chloro-ortho-toluidine	95-69-2	Dye precursor
Disperse blue 1		Dye
Disperse yellow 3		Dye
Vat yellow 4		Dye
5-nitro-ortho-toluidine	99-55-8	Dye
Nitrilitracetic acid	139-13-9	Chelating agent