

**THE HYGIENE HYPOTHESIS AND CHILDHOOD ASTHMA IN
ORANGE COUNTY, NORTH CAROLINA**

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ABSTRACT

**ASHLEY R. WARD: The Hygiene Hypothesis and Childhood Asthma in Orange County, North Carolina
(Under the direction of Dr. M. Meade)**

This thesis examines childhood asthma in Orange County, North Carolina and its relationship to the Hygiene Hypothesis. The Hygiene Hypothesis challenges traditionally held views on hygiene and asserts that decreased exposures to microbes during an infant's first year of life results in the poor development of the immune system. According to this hypothesis, the lack of development in the immune system is at least partially responsible for the increasing number of autoimmune disorders, asthma being one of them. In addition to the cross-sectional analysis, spatial analysis is used to determine spatial patterning or clustering of childhood asthma cases in the county. A cross-sectional study was conducted including 427 households (1000 children). First and fourth grade households were surveyed via the Orange County School System. Geographic information was voluntarily collected on each household that participated. The results of the survey demonstrate that the primary factors impacting childhood asthma in Orange County are genetics, premature birth, daycare attendance, and urban/suburban living.

Spatial analysis reveals areas of high prevalence in the county but clusters of questionable significance.

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I. Introduction

Background

Over two thousand years ago, Hippocrates recognized asthma as an illness determined by external conditions, and coined the term “asthma” after the Greek word for “panting.” In the 12th century, Maimonides suggested that sufferers from asthma should relocate to a better climate, and in 1660, Konrad Schneider, a German physician, proposed that the cause of asthma is exposure to irritants¹. These determinations are being echoed centuries later as modern scientists attempt to explain the doubling of the rate of asthma in the world’s most developed nations². Due to the rapidity of the change, genetics is not considered to be a factor³. Researchers have discovered that immigrants from nations that have lower asthma rates suffer from asthma at the higher rates of western nations once they have relocated to these areas.⁴ Public health officials are searching for answers, and are exploring the possibility that the solutions lay not solely within the genetics of the human

¹ Goldstein, Inge F., and Goldstein, Martin. How Much Risk? A Guide to Understanding Environmental Health Hazards. New York: Oxford University Press, 2002.

² Ibid. page 263.

³ Smyth, Rosalind. “Asthma: A Major Pediatric Health Issue.” Respiratory Research. 3.1 (2002): S3-S7.

⁴ Goldstein. page 263.

body, but within the air that is breathed and in the environment in which the body lives.

The World Health Organization (WHO) has specifically targeted childhood asthma as a widespread, international public health problem.⁵ With the causes of the shift in worldwide asthma rates still unknown, organizations such as the WHO are focusing on prevention methods that consist largely of controlling, or improving the exposure to commonly known risk factors. The definition of asthma is also becoming more clearly defined as a hyperresponsive, inflammatory disease. This allows for more productive treatment. It is believed that better intervention and treatment earlier in life decreases the severity in adulthood.⁶ To begin an understanding of childhood asthma, it is crucial to understand the function and development of the organ most affected by the disease: the lungs.

According to Dunitz's Textbook of Pediatric Asthma, during development in the first trimester of pregnancy, the fetus's airways in the lungs are formed, and by the sixteenth week of gestation, the branches called bronchi are complete (see Figure 1). At about the twenty-second week of gestation, the bronchioles and alveoli in the lungs are developed sufficiently

⁵ Dunitz, Martin. Textbook of Pediatric Asthma: An International Perspective. London: Martin Dunitz, Ltd, 2001.

⁶ Ibid.

to allow for gas exchange-the primary function of the respiratory system. This growth continues throughout birth, and until the age of eight to ten, children are continually developing the number of alveoli. Alveoli are clusters of tiny air sacs at the end of the bronchioles that provide the means by which oxygen is transferred into the blood through capillaries surrounding the sacs. During these same stages of development, the body creates a chest wall that's purpose is not only to protect the lungs, but to serve as a pump that encourages gas into and out of the lungs. During gestation, the chest wall is not developed sufficiently to operate in this manner due to the configuration of the rib cage, the placement of the diaphragm during the fetal life, and the lack of development of the chest wall muscles due to long periods of rapid-eye-movement sleep in which chest muscle activity is significantly lower.⁷ It is these three developmental components that can greatly impact the tendency to develop respiratory failures in infants and children with asthma, as well as lead to abnormal lung function at maturity.⁸ For example, the placement of the diaphragm is significant in that a more horizontal placement causes the rib cage to pull inward during respiration, rather than elevating the rib cage as is normally the case, and causing the diaphragm to be more prone to fatigue. The development of the chest wall

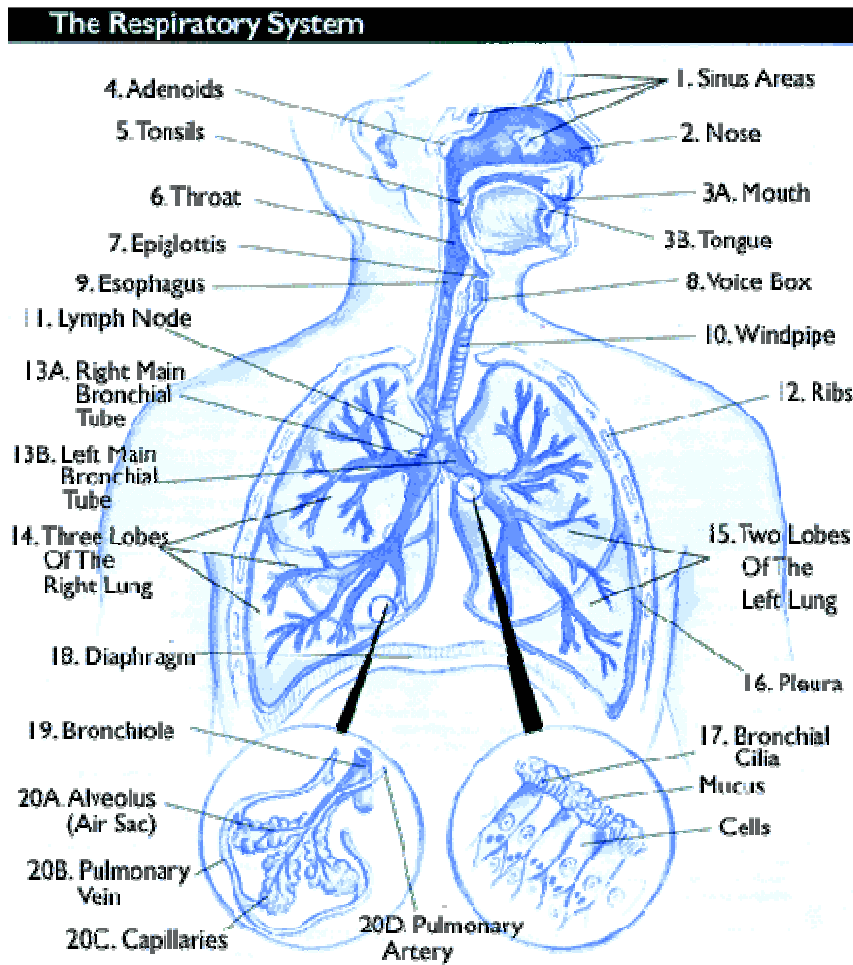
⁷ Ibid.

⁸ Ibid.

muscles are equally significant in that at birth, the chest wall is very compliant, but will later develop more resistance. Should this not develop properly, the ability to pump is greatly reduced.⁹ While much of the concentration on asthma occurs after birth, it is apparent that for infants and young children with asthma, the early development of the lungs is crucial to their ability to adequately counteract the effects of the disease, and reduce the morbidity of asthma. It is also clear that due to these abnormalities in

⁹ Ibid.

asthmatic children, exposures increase both the severity and the persistence



of asthma.

Figure 1: Diagram of Respiratory System

An asthma attack occurs when the bronchiole tubes become inflamed allowing a reduced amount of oxygen to reach the alveoli and enter the blood stream. The lack of oxygen in the bloodstream causes the body to burn up the oxygen currently in the cells, and creates a greater demand for oxygen. Asthma attacks can occur at any time and at any frequency depending upon

the asthmatic, his or her environment, his or her allergies, or many other factors. The symptoms of an attack often include wheezing, tightness in the chest cavity, and difficulty exhaling. There is a possibility of death during an asthma attack; however, with the development and use of treatments and medications, the likelihood of death is greatly reduced. It is also important to note that while children can “outgrow” asthma, abnormal lung function continues throughout the asthmatics life, with a twenty percent chance of reoccurrence in adulthood.¹⁰

The Problem

Childhood asthma has become the number one reason for hospitalization of children in many parts of the United States, and the second most common reason (following pneumonia) in others. According to the Allergy and Asthma Foundation (www.aafa.org), it is estimated that 14 million school days are missed every year due to asthma, and as much at \$18.7 billion annually are spent on asthma. Traditionally, high asthma rates occurred primarily in poor, urban areas. This is no longer the case. Asthma rates, especially childhood asthma rates, have doubled in the world’s most

¹⁰ Breyse, Patrick, et al. “The Relationship Between Housing and Health: Children at Risk.” Environmental Health Perspectives. 112.15 (2004): 1583-1588.

developed regions¹¹, and the geographic distribution of the disease is not that of traditional observation. North Carolina has not been spared as childhood asthma rates have been estimated to be as high as 27% in certain areas, and incur a cost of about \$100 million per year.¹²

The effects of an asthma attack do not only impact the patient and days missed from school. These figures do not take into consideration the equal amount of workdays missed by parents and caregivers of children who suffer from asthma. In addition, there are costs related to health care providers and Medicaid programs to treat attacks and provide medication for prevention. It is also estimated by the Allergy and Asthma Foundation of America that in the United States there are more than seventeen million people suffering from asthma; therefore, these costs are expected to rise. Of these seventeen million people, five million are children under fourteen years of age.¹³

It is with great interest that the world's public health officials and physicians struggle to determine the causes of this disease. At one time, many associated asthma with areas of pollution, overcrowding, and unsanitary housing environments. However, there is a new approach that

¹¹ Goldstein, Inge F., and Goldstein, Martin. How Much Risk? A Guide to Understanding Environmental Health Hazards. New York: Oxford University Press, 2002.

¹² DHHS Asthma Study First of its Kind: Results Reveal Extent of Prevalence. North Carolina Department of Health and Human Services: 21 March 2001.

¹³ Bryant-Stevens, Tyra, and Li, Yuelin. "Community Asthma Education Program for Parents of Urban Asthmatic Children." Journal of the National Medical Association. 96.7 (2004): 954-960.

focuses not on these locations, but on the possibility that too little exposure to insults doesn't create a smaller chance of developing childhood asthma, but a greater one. In the following studies, there are several researchers who are asserting that too much hygiene may be unhealthy in that the body's decreased exposure to these insults results in an increased response from the immune system. This new approach has been called the "hygiene hypothesis."

At its core, the Hygiene Hypothesis states that changes in both the indoor and outdoor environments due to increases in hygiene practices has decreased the microbial exposure to infants during their first year of life¹⁴. It is this lack of exposure that has meant the inadequate development of the immune system, and an inflammatory response later in life when confronted with certain allergens. This theory is somewhat controversial in that it challenges currently held views on hygiene practices, and calls for a close examination of the impact that cultural and social behaviors have on the environment, and consequently on health.

¹⁴ ¹⁴ Strachan, David P. "Hay Fever, Hygiene, and Household Size." British Medical Journal 299 (1989): 1259-1260.

Statement of Purpose

This thesis examines childhood asthma in Orange County, North Carolina and its relationship to the Hygiene Hypothesis.¹⁵ Through the examination of current trends in childhood asthma in Orange County, North Carolina, the association, if any, between childhood asthma and the Hygiene Hypothesis can be investigated. Although the traditional approach is accurate in considering asthma in urban areas, researchers have noted that indicators present in the urban environment are not equally present in the suburban environment where childhood asthma has also been increasing¹⁶. Even more puzzling is the lack of prevalence in childhood asthma in farming environments¹⁷. It is because of this inconsistency that researchers have been examining the link between the western lifestyle and increases in asthma prevalence.

This study collects data via survey from parents of Orange County elementary school students. Specifically, the research questions are: **1)** Can the Hygiene Hypothesis be used to explain childhood asthma prevalence in Orange County, North Carolina? And **2)** how is asthma prevalence affected

¹⁵ Strachan, David P. "Hay Fever, Hygiene, and Household Size." British Medical Journal 299 (1989): 1259-1260.

¹⁶ Smyth, Rosalind. "Asthma: A Major Pediatric Health Issue." Respiratory Research. 3.1 (2002): S3-S7.

¹⁷ Douwes, Jeroen and Pearce, Neil. "Asthma and the Westernization Package." International Journal of Epidemiology. 31 (2002): 1098-1102.

by spatial differences in socio-environmental factors in Orange County? In collecting the data, I hypothesize that: **1)** A correlation between the Hygiene Hypothesis and childhood asthma in Orange County, North Carolina will be determined, and **2)** a distinct spatial variation will be present that corresponds with rural non-farm, middle income areas and the presence of childhood asthma.

Review of Literature

Traditionally, researchers have attributed asthma to factors such as tobacco smoke; pesticide or chemical use within the home; mold, cockroach, or dust mite allergens; and genetics. Geographically, these elements are associated with poor, urban areas. However, increases in asthma have not been only concentrated in these areas, but in rural areas as well. Because of the shift in the areas of asthma prevalence, researchers are examining the differences between poor urban areas and rural areas. The previously held truths about asthma risk factors are still relevant, but it is clear that there are other factors influencing the development of asthma that researchers are aggressively examining.

In 1989, epidemiologist David Strachan suggested that lower family size and higher standards of personal cleanliness led to increases in asthma, an argument that would later evolve into the Hygiene Hypothesis¹⁸. Just over a decade later in 1998, German pediatrician, Erika Von Mutius studied the increasing prevalence of hay fever and allergies in children of East and West Germany.¹⁹ Her findings supported Strachan in that children of West

¹⁸ Strachan, David P. "Hay Fever, Hygiene, and Household Size." British Medical Journal 299 (1989): 1259-1260.

¹⁹ Mutius, Erika von, Weiland, Stephan K., Fritsch, Christian, Duhme, Heinrich, and Keil, Ulrich. "Increasing Prevalence of Hay Fever and Atopy Among Children in Leipzig, East Germany." The Lancet 351 (1998): 862-866.

Germany, an area she described as having progressed to the western lifestyle, exhibited a greater prevalence of atopic disorders, such as eczema and asthma. Throughout the late 1990's and early into the 21st century, researchers continually examined the links between western lifestyle and various autoimmune disorders, asthma being one of them.

The Hygiene Hypothesis asserts that with little or no exposure to allergens, such as pet dander or hair, farm animals, and various endotoxins, the immune system of an infant develops inadequately. The two components of the immune system, T1 and T2 cells, develop based upon "practice" that the immune system receives through exposure to a variety of elements. Without such exposure in early infancy while the infant has its mother's immunity, the immune system develops inadequately. The result is an inflammatory response later in life when the immune system is faced with elements that it has no acquaintance with. One such inflammatory response is asthma. This theory finds itself at opposite ends of the spectrum from traditional theories that examined childhood asthma in poor, urban areas and related it positively to cockroach infestation, and indoor and outdoor air pollution. Instead, the hygiene hypothesis relates exposure to certain allergens during infancy as having a negative relationship with the development of asthma.

Studies of asthma in terms of urban poverty show that exposure to household chemicals and pesticides; and cockroach, dust mite, and mold allergens increase a child's likelihood of developing asthma. In April 2002, Virginia Rauh, Ginger Chew and Robin Garfinkel published the article "Deteriorated Housing Contributes to High Cockroach Allergen Levels in Inner-City Households" in the journal Environmental Health Perspectives. Their work involved 132 Dominican or African American low-income households in Manhattan, New York, and measured the deterioration of the households against the level of allergens measured in the households. They determined that there is a positive relationship between the level of deterioration and the level of allergens, especially cockroach allergens. The purpose was to associate asthma prevalence with socioeconomic status. They assert that the quality of the built environment in low-income housing is in part determined by public policy, and the lack of sufficient household repairs is associated with inadequate city code. Therefore, interventions made to repair the inadequacies can directly affect the prevalence of asthma among poor urban populations.

In 2000, Karen Huss, et al, studied 1041 children ages five to twelve years that had been diagnosed with mild to moderate asthma. Six allergens were identified in the homes of the children, who lived in one of eight North

American cities. Among these allergens were those from cats, dogs, cockroaches, and molds. They also measured for tobacco smoke in the home. They found that the risk factors most significant in sensitization tests were those from cockroach and mold allergens. Cat and dog allergens were not correlated to positive sensitization tests, which they attributed to other, possibly confounding factors.

In her article "Asthma: A Major Pediatric Health Issue," Rosalind Smyth attributes the increase in asthma to a combination of risk factors, some from poor urban settings and others from rural settings. However, one suggestion that she makes applies to both settings. Diet, obesity, exercise patterns, and a decreased intake of antioxidants contribute to higher prevalence of childhood asthma. To examine the wide variety of asthma risk factors, she compared asthma rates in the United Kingdom, New Zealand, Australia, North America, Peru, and Costa Rica with rates from South Korea, Russia, Uzbekistan, Indonesia, and Albania. She discovered that the English-speaking countries had higher prevalence rates, which she attributed to environmental factors associated with Western lifestyles. Among these factors she listed air pollution, genetic factors, and hygiene. For air pollution she discovered that the prevalence differed with type of pollution; for example areas with high pollution occasionally had lower prevalence rates.

For genetics factors, she cited earlier studies that determined that; “studies of migrant populations have shown that people who move from one country to another acquire the same asthma prevalence as the host population.”²⁰ For factors relating to hygiene, she found a positive correlation between hygiene and prevalence; the countries that had the lower standards of hygiene often had the lower prevalence.

Therefore, rather than replacing one set of hypotheses, a secondary hypothesis has emerged that offers explanation for the rural population generally not associated with the same exposures as the poor urban population. Andrew Liu and James Murphy discuss the new hypothesis in “Hygiene Hypothesis: Fact of Fiction?”²¹ According to their research, the severity of asthma is worse in urban areas (when determined by increasing hospital visits), but these risk factors found in urban areas differ from those found in rural areas. This observation raises questions regarding western lifestyle, and its contribution to increasing prevalence in rural areas. Liu addresses this again in his article “Something Old, Something New: Indoor

²⁰ Smyth, Rosalind. “Asthma: A Major Pediatric Health Issue.” Respiratory Research. 3.1 (2002): S3-S7.

²¹ Liu, Andrew H., and Murphy, James. “Hygiene Hypothesis: Fact or Fiction?” Journal of Allergy and Clinical Immunology. (2003): 471-478.

Endotoxin, Allergens, and Asthma.”²² In this article, he compares the effects of endotoxins and indoor allergens on asthmatics to their effects on the development of the immune systems before the development of asthma. Once a child has developed asthma, exposure to endotoxins and indoor allergens can worsen the disease, but should a child be exposed to higher levels of endotoxins and indoor allergens in infancy, the chances of developing asthma decrease.

A. Sherriff, et al, conducted another study that sought to examine the relationship between indoor cleanliness and the development of asthma in children. Their results are outlined in an article entitled, “Hygiene Levels in a Contemporary Population Cohort are Associated with Wheezing and Atopic Eczema in Preschool Infants.”²³ This study examined the associations between hygiene levels within the household, and wheezing and eczema in children under the age of three. One correlation considered was that mothers who kept their infants very clean tended to have an increased use of household cleaning chemicals. This factor was used to determine a “hygiene score.” The parents in the study were asked to respond to questions at the

²² Liu, Andrew H. “Something Old, Something New: Indoor Endotoxin, Allergens, and Asthma.” Paediatric Respiratory Reviews. 5.A (2004): S65-S71.

²³ Sheriff, A., and Golding, J., and ALSPAC Study Team. “Hygiene Levels in a Contemporary Population Cohort are Associated with Wheezing and Atopic Eczema in Preschool Infants.” Archives of Disease in Childhood. (2002) 87: 26-29.

stages of birth to six months, and again between thirty to forty two months. The questions related to awareness of wheezing or rashes that could be eczema. The findings were that symptoms appeared in the thirty to forty two month ranges, showing a connection with early exposure to agents and later development of wheezing and eczema. In addition, those children with a higher hygiene score tended to have higher rates of wheezing and eczema.

Indoor allergens are not the only concern of health officials in examining asthma rates in industrialized nations. "Environmental Hazards to Children's Health in the Modern World"²⁴ is an article that discusses the risks associated with outdoor air pollutants. According to the article, children are at a greater risk of disease due to their increased exposure to environmental agents and their ongoing developmental growth. Though economic growth has been associated with many positive changes in industrialized societies, such as safe drinking water, enough food for the populations, waste disposal, and immunizations, there has also been a transition in the type of diseases children contract. Rather than infectious diseases, children are contracting disease such as asthma and leukemia. Children are at a larger risk of exposure because it has been found that when compared to the percentage of body weight, children eat more food, drink

²⁴ Suk, William A., and Murray, Kerry, and Avakian, Maureen. "Environmental Hazards to Children's Health in the Modern World." Reviews in Mutation Research. (2003) 544: 235-242.

more water, and breathe more air than adults. In addition, as infants, the body's ability to detoxify is reduced and the rapid growth that occurs inside the body in the first stages of life also prohibits the ability to deter certain insults.

S.K. Weiland establishes a relationship between climate and asthma prevalence in his article, "Climate and the Prevalence of Symptoms of Asthma, Allergic Rhinitis, and Atopic Eczema in Children."²⁵ In this study, 3000 children ages thirteen to fourteen were randomly sampled and asked to complete a questionnaire regarding the occurrence of symptoms for asthma, allergic rhino conjunctivitis, and eczema. In total, this study took place in 56 countries involving 463, 801 children. The results showed a positive relationship between the lowest monthly means of temperature and outdoor relative humidity and asthma symptoms. In Europe, locations that had a fifty percent drop in outdoor relative humidity for at least one month per year showed a lower rate of asthma prevalence. According to the written questionnaires, the relative humidity indoors was also positively associated with asthma symptoms. While there were many other variable factors that may play a role in the findings, this was the first study to attempt to relate climate to asthma prevalence.

²⁵ Weiland, S.K., et. al. « Climate and the Prevalence of Symptoms of Asthma, Allergic Rhinitis, and Atopic Eczema in Children. » Occupational Environmental Medicine. (2004) 61: 609-615

Most recently, an article entitled, “Decreased Prevalence of Asthma Among Farm-Reared Children Compared with Those who are rural but Not Farm-Reared”²⁶ appeared in the *Journal of Allergy and Clinical Immunology*. In the article, Alan Adler discussed his study of 4152 school-aged children from kindergarten to twelfth grade in which children who were raised on a farm were compared to those who were not. For asthma, but not with other allergies, he found that children who were raised on a farm were less likely to develop the disease. There were several differences noted between the two lifestyles; among them were family size, exposure to livestock and pets, dampness, molds, and dust, methods of heating and cooking, and dietary habits. A comparison of the two lifestyles has not been widely examined in the United States, and those conducted in Europe, he claims, may not be relevant in the U.S. because of differences in the farming populations and lifestyle between the two continents. Nevertheless, a connection has been assumed that children raised on a farm are less likely to develop asthma. This further supports the hypothesis that early microbial exposure, as would be present in a farming environment, prevents later development of asthma. From this the opposite could also be assumed: lack of exposure in infancy,

²⁶ Adler, Alan. “Decreased Prevalence of Asthma Among Farm-Reared Children Compared with Those Who are Rural but Not Farm-Reared.” *Journal of Allergy and Clinical Immunology*. (2005) 115.1: 67-73.

due to an increase in hygiene for example, increases the likelihood of the development of childhood asthma.

A further examination into the relationship between exposure and immune development surfaced in the literature in 2004. G.A.W. Rook, et al provides an overview of relevant work regarding this subject, and draw conclusions in accord with the previous articles discussed.²⁷ This group asserts that certain micro-organisms are “old friends” that have evolved throughout the development of mammals. These micro-organisms classified as saprophytic mycobacteria, helminthes, and lactobacilli, are not only harmless to the immune system, but provide an important function in the regulation and development of T-cells.²⁸ This reduction in development is noted specifically in this article as depleted in patients with both asthma and Crohn’s disease.²⁹ However, the conclusion reached here questions the emphasis of T-cell underdevelopment, and places more emphasis on the lack of “old friends” that drive t-cell maturation. Going a step further, the conclusions place less value on the role of harmful infections, and insist that the organisms from human evolutionary history are those that are

²⁷ Rook, G.A.W., Adams, V., Hunt, J., Palmer, R., Martinelli, R., Brunet, L. Rosa. “Mycobacteria and Other Environmental Organisms as Immunomodulators for Immunoregulatory Disorders.” Springer Seminars in Immunopathology. (2004) 25: 237-255.

²⁸ Ibid. 242-246.

²⁹ Ibid.

important.³⁰ This assertion was followed by support in various other articles that also emphasized the role of particular exposure, not any microbial exposure.^{31 32 33}

Theoretical Framework

The concepts that guide this research are deep-rooted in ecological studies and in modern, innovative theories. The triangle of disease ecology contributes an ecological approach to health and the recent literature supports the theory of the hygiene hypothesis. In examining the state of health, medical geographers have engaged in a holistic approach to health that focuses on the interaction between population and the environment. Celebrated theorist Rene Dubos presented the idea that "complete freedom from disease and from struggle is almost incompatible with the process of living."³⁴ In doing so, he underscored the continuing, progressive relationship between health and environment and the evolving process of disease that occurs as populations shape and change their environment. As

³⁰ Ibid. 251.

³¹ Bjorksten, Bengt. "Effects of Intestinal Microflora and the Environment on the Development of Asthma and Allergies." Springer Seminars in Immunopathology. (2004) 25: 257-270.

³² Weinstock, Joel V., Summers, Robert W., Elliott, David E. "Role of Helminths in Regulating Mucosal Inflammation." Springer Seminars in Immunopathology. (2005) 27: 249-271.

³³ Zaccone, P., Fehervari, Z., Phillips, J.M., Dunne, D.W., Cooke, A. "Parasitic Worms and Inflammatory Disease." Parasite Immunology. (2006) 28: 515-523.

³⁴ Dubos, Rene'. Mirage of Health: Utopias, Progress, and Biological Change. New York: Harper & Brothers, 1959.

environments change, new struggles emerge. From the time of Snow's 1854 map of cholera in London to the present day work of controversial microbiologist, Paul Ewald, (whose philosophies are provocative and on the edge of research regarding the new evolution of disease³⁵), the concept of humanity's role in shaping disease ecologies has become foundational to the study of health, both in the awareness of its challenges and in the search for treatment. It is the consequence of such wisdom that is the basis for all that follows.

(1) The primary framework that informs this project is the Triangle of Human Ecology. This framework, introduced by Melinda Meade^{36 37}, seeks to situate human health within the perspective of: a) its surrounding environment, physical, social and mental; b) cultural and social human behavior; and c) the interaction of biological susceptibility of population. It determines that human health is the interaction between all aspects of the environment and that human behavior is a component that should be considered along with the physical environment and the biological

³⁵ Ewald, Paul. Plague Time: The New Germ Theory of Disease. Knopf Publishing Group: 2002.

³⁶ Meade, Melinda S. "Medical Geography as Human Ecology: The Dimension of Population Movement." The Geographic Review. 67 (1977): 379-393.

³⁷ Meade, Melinda S. and Earickson, Robert J. Medical Geography. 2nd ed. The Guilford Press, 2005.

composition of the population. The importance of this perspective is crucial in understanding disease and in establishing frameworks for prevention.

This is especially applicable to the Hygiene Hypothesis and its relationship to childhood asthma. The three vertices of the triangle represent the traditional elements of population, environment, and behavior.

Population represents the aspects of childhood asthma that are due to hereditary elements, environment represents those aspects due to indoor and outdoor environment, and behavior represents those aspects that are due to cultural and social human behavior. What the triangle demonstrates is the interaction between all three which comprise the total, in this case, the existence of childhood asthma. This view is counter to a narrow focus on simple heredity or genetics. Demonstrated below is how childhood asthma can be positioned within the triangle:

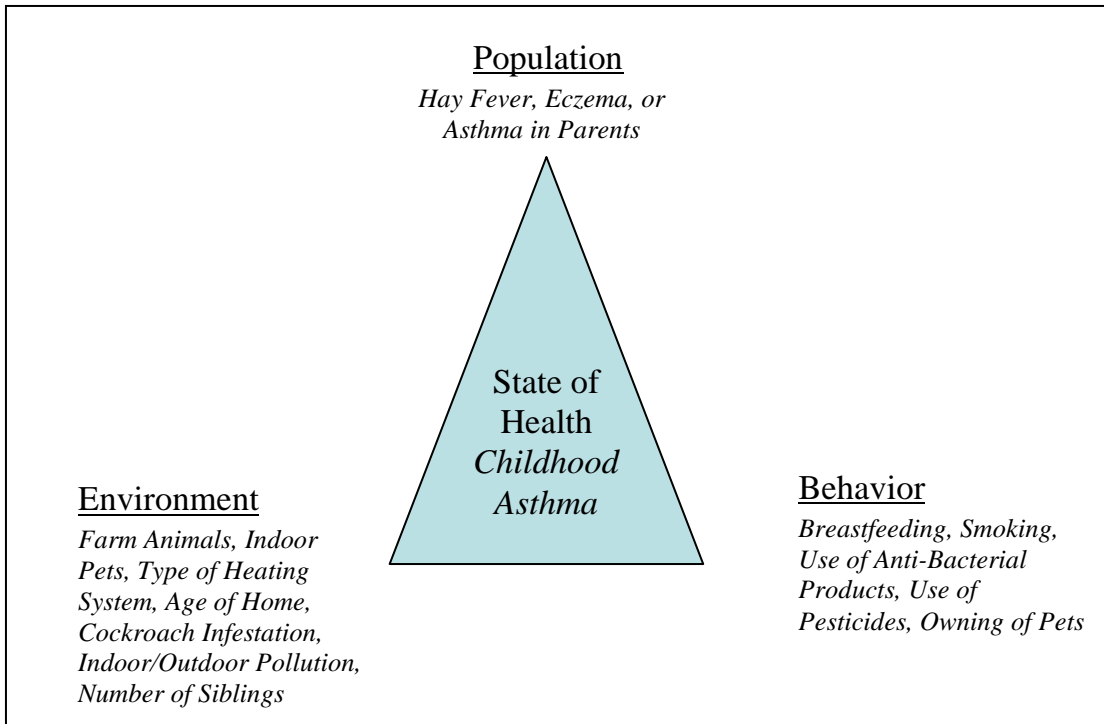


Figure 2: Triangle of Disease Ecology³⁸

³⁸ Meade, Melinda

II. Research Questions and Methodology

1) Can the Hygiene Hypothesis be used to explain childhood asthma prevalence in Orange County, North Carolina?

The purpose of this study is multifaceted. First, I compared the risk factors outlined in the hygiene hypothesis with responses from a survey taken from parents of first and fourth grade elementary school students in Orange County, North Carolina (approximately 1000 students). Based upon the pilot study, these grades were chosen in order to consider the largest number of children, including siblings, while also considering accuracy in reporting activity during a child's first year of life. Participants were asked to complete only one survey per residence, decreasing the likelihood of obtaining data multiple times from the same source.

The cities of Hillsborough and Chapel Hill are located inside of Orange County. However, for the intent of this study, Orange County consists of the county area outside the city of Chapel Hill, and includes the town of Hillsborough (see Figure 3).

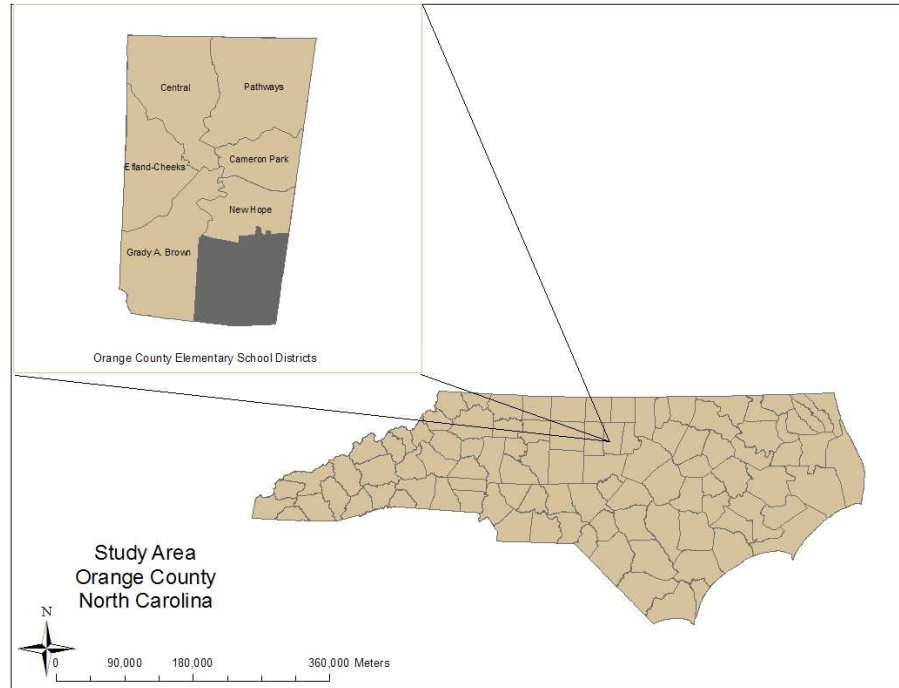


Figure 3: Study Area (Source: UNC GIS Library)

As part of the survey, parents were asked to answer questions about the following: the age of their home, the age and gender of each child living in the home, the presence of respiratory health conditions in each of the children, if so, the age of diagnosis, the infant feeding method of each child (breastfed or formula fed), the presence of pets or farm animals in the first year of life of each child, presence of tobacco smoke in the home, the use of pesticides inside the home, the use of commercially-labeled anti-bacterial products in the home (such as soaps or baby wipes), and the family history of respiratory disease. In addition, parents were asked to discuss the treatment routine of any child diagnosed with asthma, and their thoughts on the causes

of the asthma. The survey was conducted as part of an Orange County health initiative, and was distributed and collected through the school nurses.

Parents received a cover letter from their school's nurse encouraging them to participate, along with the survey (see Appendix 1). The survey was completed and returned to the nurse in a provided envelope to ensure privacy. Additionally, county nurses will participate in a focus group to discuss the outcome of the survey, and how the results compare to their experience with asthma in the county.

To analyze the data, Chi Square analysis was performed as well as multi-variate Logistic Regression using SAS software. The purpose of this analysis was to determine the observed frequency of the elements that compose the Hygiene Hypothesis with the probability of their occurring. In addition, the analysis enabled consideration of differences between group and individual variation.

Description of Study Area

According to the Orange County Economic Development Commission, the median income of families living in Orange County in 2000, excluding the town of Chapel Hill was \$46,794. The median purchase price for a home in this area during this same time period was \$221,734 with 53.8% of homes owned, 39.6% rented, and 6.6% vacant. Unemployment was 3.1%, which is

low compared to the 6.9% North Carolina unemployment rate. The median age was 30.4 years. Therefore, Orange County as defined above typically consists of suburban, middle class households, of whom more than half own their home.

Description of School Districts

There are seven elementary school districts in the Orange County School System: New Hope Elementary, Pathways Elementary, Central Elementary, Grady Brown Elementary, Efland-Cheeks Elementary, Hillsborough Elementary, and Cameron Park Elementary. All of these are districted schools with the exception of Hillsborough Elementary, which is a volunteer-based, year-round school. Therefore, the district map below does not indicate a set district for Hillsborough Elementary:

(Figure 4)

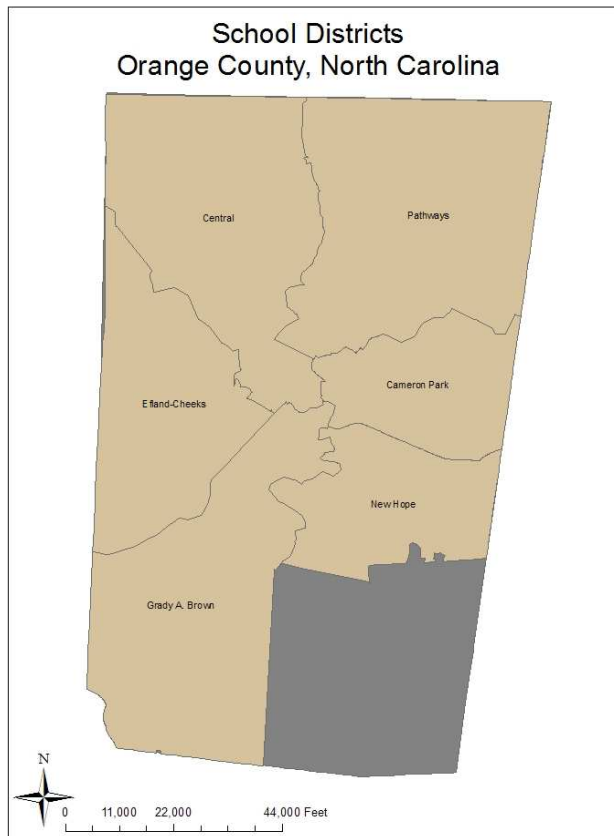


Figure 4: Orange County School Districts (Source: Orange County School System)

In addition, the composition of each school is as follows:

Table 1: School District Statistics (Source: Orange County School System)

Note: Population given in actual numbers.

School District	Am Indian	Asia	Black	Hispanic	Multi	White	Percent Minority
Cameron Park Elementary	2	2	89	30	9	363	26.67
Central Elementary	2	1	124	41	13	135	57.28
Efland-Cheeks Elementary	5	1	116	68	14	252	44.74
Grady Brown Elementary	3	9	58	56	16	368	27.84
Hillsborough Elementary	1	1	43	4	13	324	16.06
New Hope Elementary	3	15	62	105	20	346	37.21
Pathways Elementary	0	2	59	14	16	343	20.97

School District	Percent of Population Participating in the Free Lunch Program
Cameron Park Elementary	30.30
Central Elementary	61.20
Efland-Cheeks Elementary	46.20
Grady Brown Elementary	30.60
Hillsborough Elementary	14.00
New Hope Elementary	33.30
Pathways Elementary	23.40

2) How is asthma prevalence affected by spatial differences in environmental factors in Orange County?

A second objective is to examine the spatial distribution of asthma in Orange County. To accomplish this objective, participants were asked to provide current street addresses, as well as information on their location during a child’s first year of life. Using GIS, this data was geocoded and compared to census data and data obtained through the survey. This analysis served two purposes. First, it allowed for examination of spatial differences in current asthma prevalence as reported by parents. Second, it allowed for analysis of areas of risk based upon the reported data. In addition, spatial cluster analysis was performed using the SaTScan software package. Participation in this step was optional to parents, and used only for spatial analysis; the privacy of participants will be assured through methods intended to respect the confidentiality of survey participants. Surveys will be

secured in storage throughout the period of analysis and completion, and GIS data was presented in such a way to protect the identity of participants.

The SaTScan software package uses the spatial scan statistic³⁹ to determine if spatial clustering of asthma cases occurs in the county. While the software package is capable of determining clusters over both space and time, for the purposes of this study, only spatial analysis occurs. SaTScan uses either a Poisson based model, or a Bernoulli model. For this study the Bernoulli model was chosen because the outcome is a binary event (with asthma or without asthma). Those that self-reported having asthma are considered cases, and controls are those that do not have the disease. The households in the sample are considered the total population, rather than using the actual population as reported in the U.S. Census.

During the process of analysis, the software uses circular scan windows of variable sizes to scan for cases within the study area. According to Emch and Ali, this is an important feature because the sizes of clusters are generally not known before analysis occurs.⁴⁰ The window is centered over several possible grid points positioned throughout the study area and varies

³⁹ Kulldorff, M. "A Spatial Scan Statistic." Communications in Statistics: Theory and Methods. 26: 1481-1496.

⁴⁰ Emch, Michael, and Ali, Mohammad. "Spatial Cluster Analysis for Etiological Research and Identification of Socio-Environmental Risk Factors." Geographic Information Systems and Health Applications. Comp. Khan, O. and Skinner, R.: Idea Group Publishing: Hershey, Pennsylvania.

in size according to an upper limit.⁴¹ Each circle created through this process is a possible candidate for a cluster. Computing the number of points is not possible because of the continually varying window size, therefore, a likelihood ratio is calculated.⁴² The likelihood ratio for the Bernoulli model is as follows:⁴³

$$L(Z,p,q) = \frac{\binom{n}{m} (1-\binom{n}{m})^{(m-n)}}{\binom{N-n}{M-m} (1-\binom{N-n}{M-m})^{(m-n)-(N-n)}}$$

M=number of controls in the area
m=number of controls in the window

The window that is determined to contain the most likely cluster determines the cluster least likely to have occurred by chance. The p-value is determined through a Monte Carlo simulation test, restricting its number to 999.⁴⁴ The software can scan for high rates only, low rates only or both high and low rates.

⁴¹ Kulldorff, Martin. SaTScan User Guide for version 7.0. August 2006. <http://www.satscan.org/>

⁴² Ibid.

⁴³ Emch and Ali

⁴⁴ Kulldorff, Martin. SaTScan User Guide.

III. Survey Results

Table 2: Survey Response by School District

School District	Total Surveys Distributed	Total Returned	Response Rate	Total Children	Total Children With Asthma	Reported Prevalence
Hillsborough Elementary	127	61	48.03%	125	15	12.00%
Efland Cheeks Elementary	144	52	36.11%	132	21	15.91%
Central Elementary	107	48	44.86%	129	23	17.83%
Cameron Park Elementary	174	70	40.23%	168	24	14.29%
New Hope Elementary	180	75	41.67%	172	29	16.86%
Pathways Elementary	156	58	37.18%	133	24	18.05%
Grady Brown Elementary	181	63	34.81%	141	15	10.64%
Totals	1069	427	39.94%	1000	151	15.10%

427 Households including 1000 children are represented in the responses from the surveys, providing nearly a 40% response rate. From this sample, 151 children are reported by their parents to have asthma, resulting in a 15% reported prevalence rate. Of the components thought to be contributing factors in the development of asthma, the following are the results:

Table 3: Results by Variable

Observed Results				
	Asthmatic	Non Asthmatic	Total	Odds Ratio
Breastfed	93	537	630	0.88
Not Breastfed	61	309	370	
Total	<i>154</i>	<i>846</i>	<i>1000</i>	
Pets in Home	68	394	462	0.96
No Pets in Home	82	456	538	
Total	<i>150</i>	<i>850</i>	<i>1000</i>	
Genetic History	43	42	85	4.05
No Genetic History	69	273	342	
Total	<i>112</i>	<i>315</i>	<i>427</i>	
Cockroaches	22	72	94	0.32
No Cockroaches	162	171	333	
Total	<i>184</i>	<i>243</i>	<i>427</i>	
Smoking	26	57	83	1.37
No Smoking	86	258	344	
Total	<i>112</i>	<i>315</i>	<i>427</i>	
Farm Animals	9	46	55	1.09
No Farm Animals	144	801	945	
Total	<i>153</i>	<i>847</i>	<i>1000</i>	
Antibacterial Product Use	111	534	645	1.73
No Antibacterial Product Use	38	317	355	
Total	<i>149</i>	<i>851</i>	<i>1000</i>	
Day Care Attendance	66	262	328	1.74
No Day Care Attendance	85	587	672	
Total	<i>151</i>	<i>849</i>	<i>1000</i>	
Premature Birth	36	70	106	3.45
No Premature Birth	116	778	894	
Total	<i>152</i>	<i>848</i>	<i>1000</i>	

Initially, a Chi Square Analysis is performed to determine which single variables of those listed above lead to a positive outcome (asthma). The following tables demonstrate the Chi Square calculations and values:

Table 4: Chi Square Calculations

	Asthmatic Breastfed	Non Asthmatic Breastfed	Asthmatic Not Breastfed	Non Asthmatic Not Breastfed
f_o	93	537	61	309
f_e	97.02	532.98	56.98	313.02
$(f_o - f_e)^2 / f_e$	0.166567718	0.030320838	0.283615304	0.051627372
χ^2	0.532131231			

	Asthmatic Pets in Home	Non Asthmatic Pets in Home	Asthmatic No Pets in Home	Non Asthmatic No Pets in Home
f_o	68	394	82	456
f_e	69.3	392.7	80.7	457.3
$(f_o - f_e)^2 / f_e$	0.024386724	0.00430354	0.02094176	0.003695605
χ^2	0.053327628			

	Asthmatic Genetic History	Non Asthmatic Genetic History	Asthmatic No Genetic History	Non Asthmatic No Genetic History
f_o	43	42	69	273
f_e	22.29508197	62.70491803	89.70491803	252.295082
$(f_o - f_e)^2 / f_e$	19.22817019	6.836682737	4.77893119	1.699175529
χ^2	32.54295965			

	Asthmatic Cockroaches in Home	Non Asthmatic Cockroaches in Home	Asthmatic No Cockroaches in Home	Non Asthmatic No Cockroaches in Home
f_o	22	72	162	171
f_e	40.5058548	53.4941452	143.4941452	189.5058548
$(f_o-f_e)^2/f_e$	8.454744717	6.401946617	2.386624635	1.807156102
χ^2	19.05047207			

	Asthmatic Smoking in Home	Non Asthmatic Smoking in Home	Asthmatic No Smoking in Home	Non Asthmatic No Smoking in Home
f_o	26	57	86	258
f_e	21.7704918	61.2295082	90.2295082	253.7704918
$(f_o-f_e)^2/f_e$	0.821696624	0.2921588	0.198258197	0.070491803
χ^2	1.382605424			

	Asthmatic Farm Animal Exposure	Non Asthmatic Farm Animal Exposure	Asthmatic No Farm Animal Exposure	Non Asthmatic No Farm Animal Exposure
f_o	9	46	144	801
f_e	8.415	46.585	144.585	800.415
$(f_o-f_e)^2/f_e$	0.040668449	0.007346249	0.002366947	0.000427559
χ^2	0.050809204			

	Asthmatic Antibacterial Product Use	Non Asthmatic Antibacterial Product Use	Asthmatic No Antibacterial Product Use	Non Asthmatic No Antibacterial Product Use
f_o	111	534	38	317
f_e	96.105	548.895	52.895	302.105
$(f_o-f_e)^2/f_e$	2.308527392	0.404195748	4.19436667	0.734383824
χ^2	7.641473633			

	Asthmatic Day Care Attendance	Non Asthmatic Day Care Attendance	Asthmatic No Day Care Attendance	Non Asthmatic No Day Care Attendance
f_o	66	262	85	587
f_e	49.528	278.472	101.472	570.528
$(f_o-f_e)^2/f_e$	5.478250363	0.974341349	2.673907915	0.475571372
χ^2	9.602071			

	Asthmatic Premature Birth	Non Asthmatic Premature Birth	Asthmatic No Premature Birth	Non Asthmatic No Premature Birth
f_o	36	70	116	778
f_e	16.112	89.888	135.888	758.112
$(f_o-f_e)^2/f_e$	24.54894141	4.400281951	2.910724597	0.521733654
χ^2	32.38168161			

Of the variables, genetic history, premature birth, cockroach infestation, and day care attendance are found to be significant. However, because Chi Square only considers the single variable being tested, the results are not

considered to be robust. In order to examine further, a logistic regression model is used.

The logistic model is used in medical and social science to examine the quantitative relationship between binary variables (the presence or absence of asthma) and other variables.⁴⁵ Of the variables in the survey, the following are used in the actual analysis:

Family nested variables (see Appendix 2 for Survey Codes):

- Q1: 1 or more (number of Children in the household)
- Q3: 1, 2, and 3 (location of the home: urban, suburban, or farm area)
- Q4: Year (decade home built)
- Q5: 1, 2,3,4,5 (frequency of pest control)
- Q6: 0, 1 (existence of cockroaches)
- Q7: 1, 2,3,4,5 (frequency of smoking in the house)
- Q8: 0, 1 (genetic history)

Individual Child Variables:

- Q10: Age of child
- Q11: 1, 2 (Male, Female)
- Q13: Age (age of diagnosis)
- Q14: 0, 1 (premature birth)
- Q15: 0, 1 (respiratory problems at birth)
- Q16: 0, ≥ 1 (breastfeeding duration)
- Q17: 0, ≥ 1 (household pets)
- Q20: 0, 1 (farm animal exposure)
- Q21: 0, 1 (day care attendance)
- Q22: 0, 1 (antibacterial product use)

⁴⁵ Statistical analysis was performed using a statistics consultant, Baowei Xu, PhD candidate, the Department of Statistics and Operations Research, University of North Carolina at Chapel Hill, March 28, 2007. The SAS software package was used to create a logistic regression analysis.

The asthma rate is modeled using a linear function of the variables as listed above:

$$\text{logit}(p_i) = \ln \frac{p_i}{(1-p_i)} = \alpha + \beta_1 \chi_{1,i} + \dots + \beta_k \chi_{k,i}$$

$I = 1, \dots, n,$

Initially all variables are included in the model. There are problems with this method in that some of the data is incomplete, which results in an incomplete model. The SAS software does not handle missing data, and will therefore discard any observation that has a missing value. In order to deal with this issue, backward variable selection technique was used. In using this technique, at each step, the least significant variable is deleted from the model, until all the variables in the model become significant. Once this technique is completed, the following variables are considered to be significant:

- Q1: number of children in household
- Q4: decade home built
- Q8: genetic history
- Q11: gender
- Q14: premature birth
- Q15: respiratory issues at birth
- Q21: day care attendance
- Q22: antibacterial product use

These results are consistent with the Chi Square test with the exception of Q1, Q4, Q11, Q15, and Q22, which are not included in the Chi Square analysis.

At this point, all variables found to be significant in the previous step are included in the logistic regression model. The following are the results of this analysis (note that those with negative coefficients are indicated here in red text – the negative coefficient indicates that the existence of these conditions will increase the chance of having asthma and the larger number, the more significant the relationship):

Table 5: Logistic Regression Analysis I

Parameter	DF	Estimate	Error	Chi-Square	P-value
Q1 (HH_Children)	1	0.160500	0.107400	2.233300	0.135100
Q4 (Age_Home)	1	0.000910	0.000391	5.478500	0.019300
Q8 (Genetic_Hist)	1	1.450900	0.238100	37.141300	<.0001
Q11 (Gender)	1	0.784000	0.228500	11.769300	0.000600
Q14 (Premature_Birth)	1	1.106300	0.307000	12.989100	0.000300
Q15 (Resp_Birth)	1	0.406200	0.415700	0.954700	0.328500
Q21 (Daycare)	1	0.636500	0.233400	7.439000	0.006400
Q22 (Antibacterial)	1	0.045900	0.256500	0.032000	0.858000

From this step, some variables are insignificant when including other variables. These variables are eliminated, and the analysis is repeated using only the significant variables: Q4, Q8, Q11, Q14, and Q21. The results of this analysis are below:

Table 6: Logistic Regression Analysis II

Parameter	DF	Estimate	Error	Chi-Square	P-value
Q4 (Age_Home)	1	0.001000	0.000369	7.309200	0.006900
Q8 (Genetic_Hist)	1	1.492100	0.233400	40.880600	<.0001
Q11 (Gender)	1	0.765800	0.225200	11.566700	0.000700
Q14 (Premature_Birth)	1	1.140200	0.290300	15.425100	<.0001
Q21 (Daycare)	1	0.587000	0.227600	6.651600	0.009900

From this analysis, it can be determined that Q4, decade in which the home was built, is very small. Once this variable is deleted, the results of the analysis are as follows:

Table 7: Logistic Regression Analysis III

Parameter	DF	Estimate	Error	Chi-Square	P-value
Q8 (Genetic_Hist)	1	1.219500	0.198200	37.863500	<.0001
Q11 (Gender)	1	0.577000	0.191500	9.080300	0.002600
Q14 (Premature_Birth)	1	1.211200	0.247800	23.885100	<.0001
Q21 (Daycare)	1	0.648100	0.200700	10.429100	0.001200

In addition, there are several variables that are not binary. For these variables, the possible answers are combined to create a smaller number of outcomes, and possibly yield a more significant result. These variables are Q3, Q5, Q7, Q13, and Q17. For example, for Q3, urban, suburban, or farm individually are not considered significant. However, when urban and suburban are combined to result in two levels – urban and farm, the variable becomes significant. The following is the result of this process:

Table 8: Data Transformations

	Q3 (HH-Location)	Q5 (Pest_Control)	Q7 (Smoking)	Q17 (Pets)
Original Observed Value	123	123456	012345	012346
P-Value	0.1668	0.6204	0.5953	0.9879
Transformed Value	(1,2)=1	(123)=1	(0)=1	0=0
	(3)=2	(456)=2	(12345)=2	(12345)=1
P-Value Post Transformation	0.0305	0.3259	0.062	0.4902

Although some variables remain insignificant, the p-values are smaller indicating that the transformation process may give improved results.

IV. Results of Spatial Analysis

SaTScan Results

Scanning occurred for high rates only, low rates only, and high and low rates, each yielding the same clusters. There are three potential clusters identified. Their results are outlined below:

Table 9: SaTScan Clusters

Cluster No	Centroid Latitude	Centroid Longitude	Radius (km)	Pop	Expected Cases	Observed Cases	Relative Risk	Likelihood Ratio	Monte Carlo Rank	P-Value
1	36.239300	-78.903700	7.38	8	1.460	5.466	5.756	13.792408	1/1000	0.001
2	36.221944	-79.048905	3.25	6	1.100	5.466	5.680	10.305239	18/1000	0.018
3	36.068205	-79.124072	1.14	6	1.100	5.466	5.680	11.305239	18/1001	1.018

Because Cluster 1 occurs outside of the study area, this cluster is excluded.

This occurrence may be due to the number of parents that pay tuition to the county to place their children within the county school district, or to those parents that have special permission from the Orange County Board of Education to voluntarily bring their children to a school within the county.

The clusters are located on the map below:

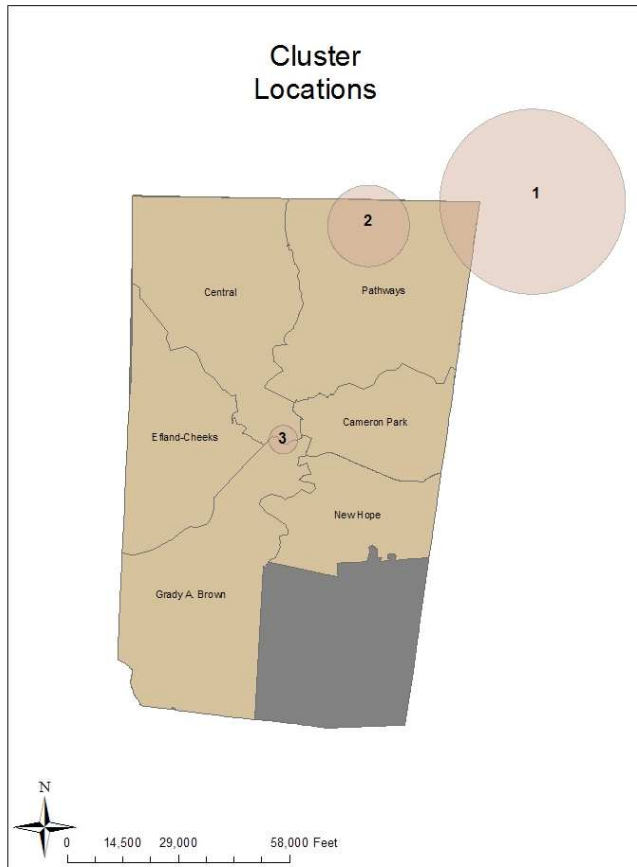


Figure 5: Cluster Locations

ArcGIS Results

Several maps generated in ArcGIS examine the population, the social context of the study area, and the spatial distribution of the variables. In addition an asthma surface map was created. Initially the number of children as a percentage of the population was examined using data from the 2000 U.S. Census covering census block groups in Orange County (see Figure 6):

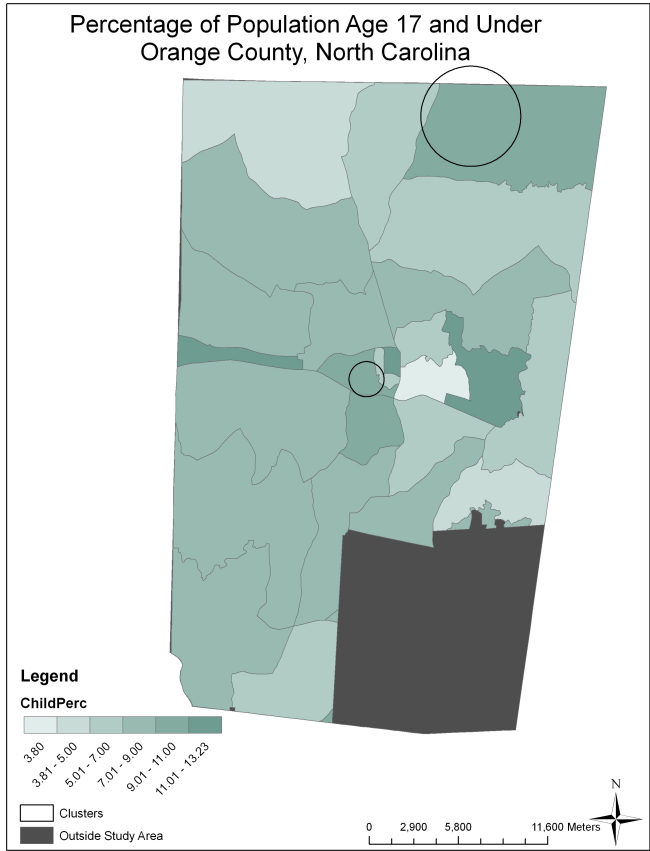


Figure 6: Children as a Percent of Total Population (Source: 2000 U.S. Census Bureau via UNC GIS Library)

Median Income figures are also compiled from the 2000 U.S. Census and displayed by block group (see Figure 7):

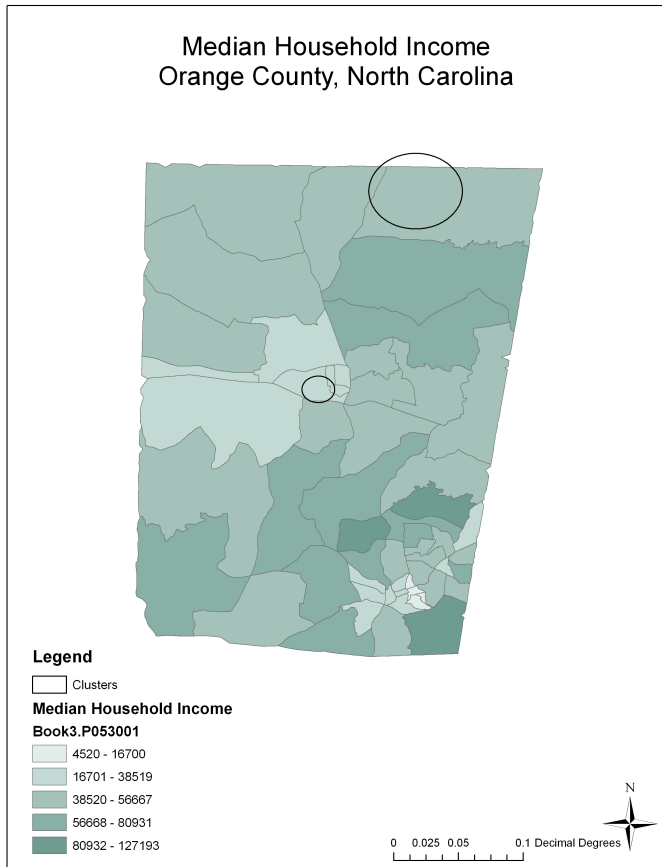


Figure 7: Median Income (Source: 2000 U.S. Census Bureau via UNC GIS Library)

A series of maps depicting the percentage of Urban, Rural Farm and Rural Non-Farm as outlined in the 2000 U.S. Census are created to understand the location of the clusters with respect to land usage (see Figure 8, Figure 9 and Figure 10):

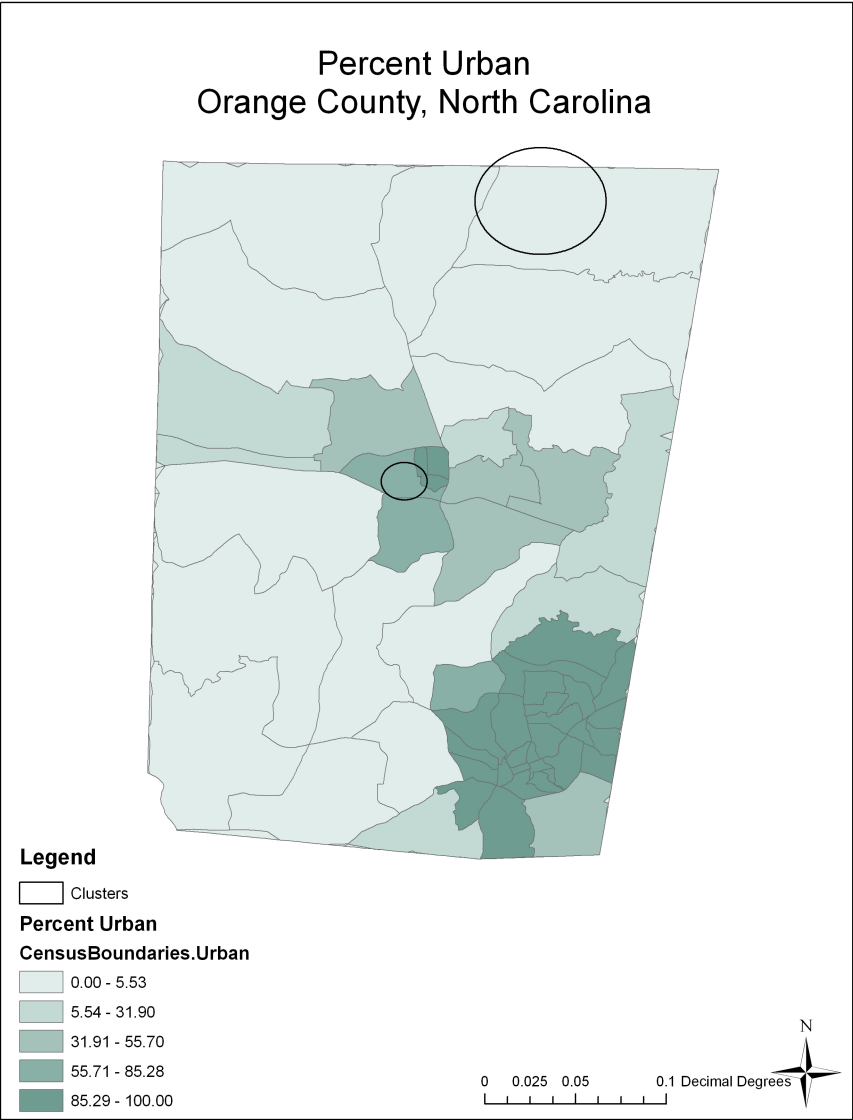


Figure 8: Percent Urban (Source: 2000 U.S. Census Bureau)

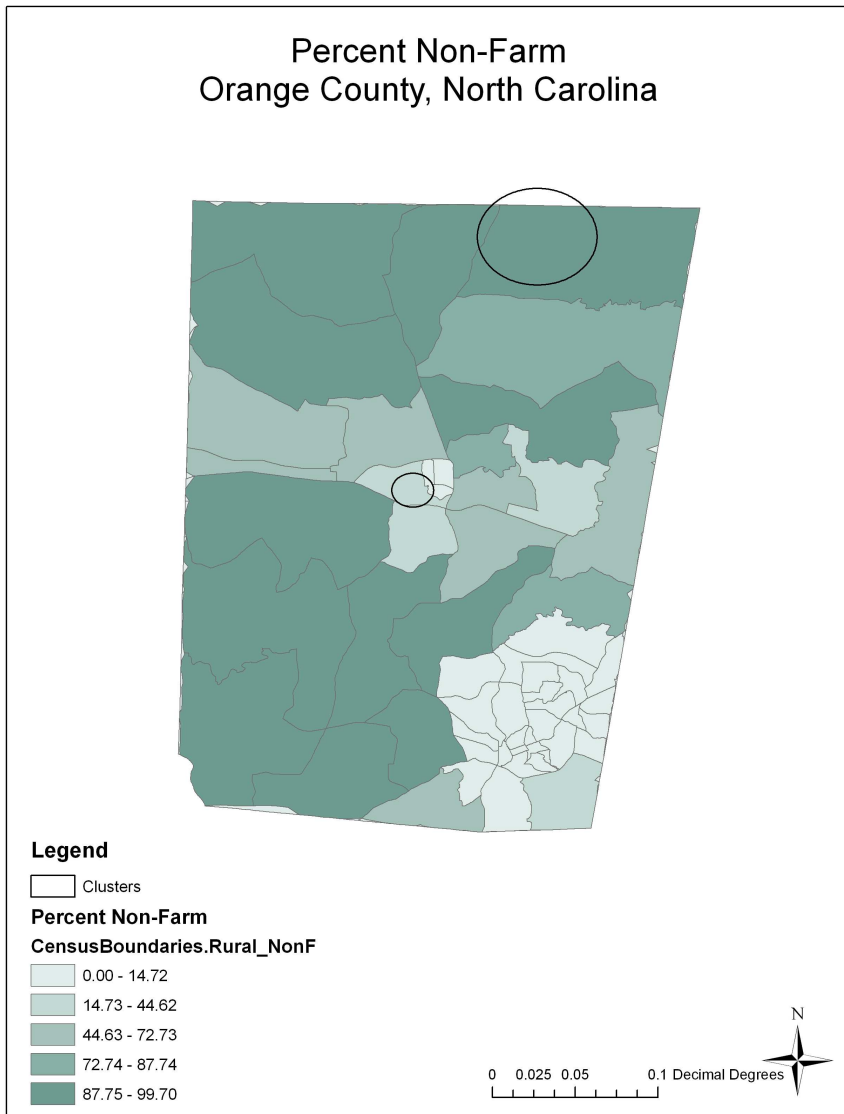


Figure 9: Percent Rural Non-Farm (Source: 2000 U.S. Census Bureau)

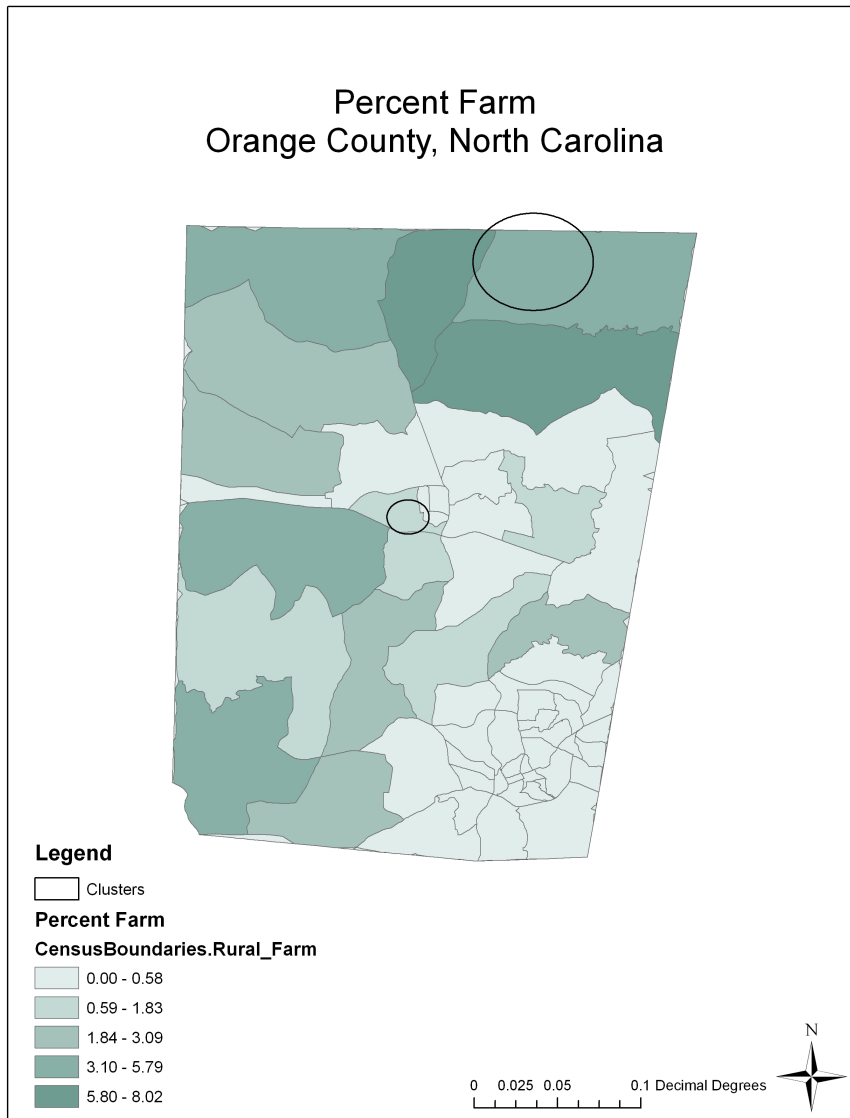


Figure 10: Percent Farm (Source: U.S. Census Bureau)

In order to create an asthma surface map from the point data, a grid is generated in ArcMap of the coverage area. The grid sizes are selected to be 1km X 1km. This determination is made to gain the most efficient distribution of data. In other words, larger grid cells would cover too much area, making very few grid cells with no data. Smaller grid cells would create

too many grid cells with no data. The points were then overlaid on the grid. At this point, statistics can be performed on the grid to sum how many asthma cases were represented in each grid cell by column and row. Finally, kriging was performed on the grid, initially consisting of the number of cases only (see Figure 11). However, because this does not consider an underlying population, a second grid is created in which the points represent a ratio of asthma cases to the total study population (see Figure 12). Kriging is one of four interpolation methods available in ArcGIS. This particular method was chosen because it reliably produced an output that was consistent with the actual data. The results are below:

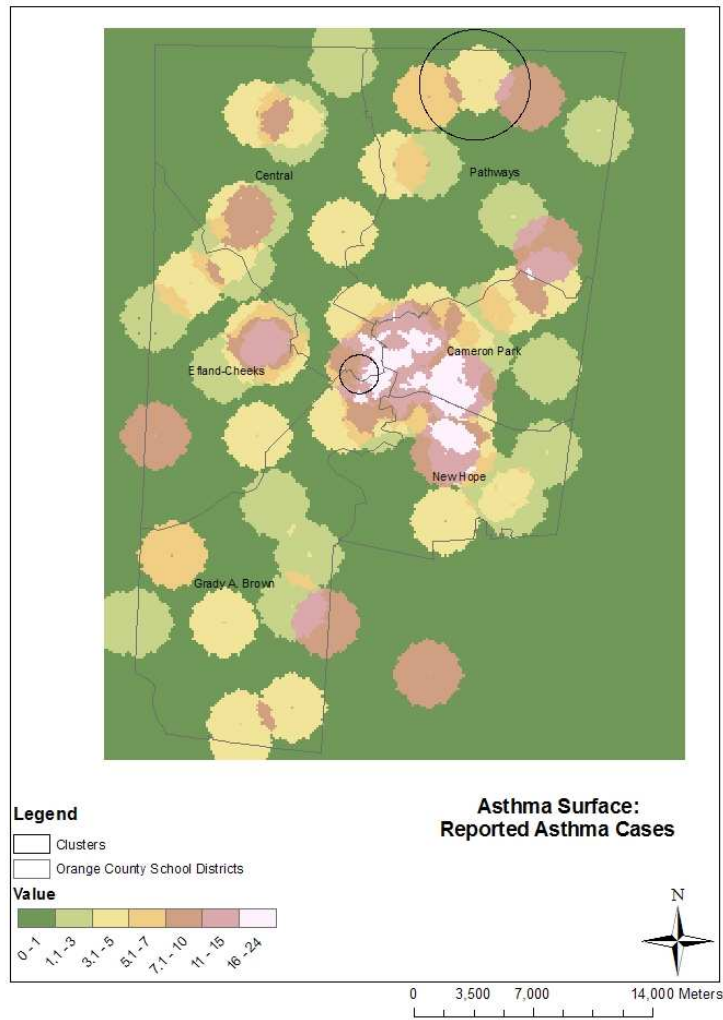


Figure 11: Asthma Surface: Cases

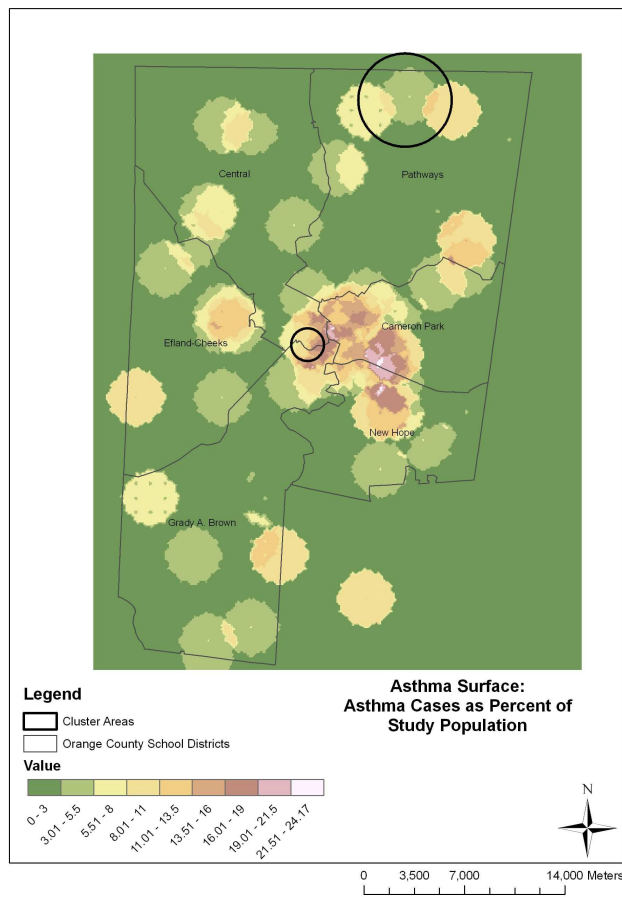


Figure 12: Asthma Surface: Cases as a Percentage of Study Population

V. Summary and Conclusion

Statistical Analysis

From the results as presented above, it can be determined that for this study population, living in an urban/suburban environment, having a genetic susceptibility to asthma, being born prematurely, and attending day care during the first year of life increase the risk of having asthma. In addition, males have a greater chance than females of having asthma, and children living in newer homes are less likely to have asthma. Of those factors that increase risk, genetic susceptibility and premature birth are long believed to be influential in having asthma. For the purposes of this study, the variables of interest are those that address living environment and day care attendance.

Since the factors “urban” and “suburban” are combined to achieve statistical significance, the ability to determine if there is a difference in significance between an urban or a suburban environment is not available with this data set. This finding does, however, support other research that farming environments provide protection against developing asthma, and is consistent with those factors outlined in the Hygiene Hypothesis. In addition, as indicated in Figure 8, Figure 9, and Figure 10, the study area consists

largely of the urban and rural non-farm environments as outlined in the U.S. Census. It should also be noted that the clusters are most present in the areas that fit the urban/rural non-farm categories. However, one concern regarding the urban-asthma relationship found in this study is the classification of the urban environment.

In past literature, asthma in urban environments is linked to outdoor air pollution like diesel fuel emissions and that from heavy industry; indoor pollution that is the result of poor housing; cockroach infestation and mold growth, also the result of poor housing; and low socioeconomic status. The research conducted in this manner is conducted in larger metropolitan areas. Some of these criteria appear to be inconsistent with the areas classified as urban in this particular study area. The higher rates, therefore, can be considered due to poverty. However, one possible issue for further study is to examine the factors that are classified in the traditional urban-asthma literature, and determine how these factors translate to a smaller urban scale.

The relationship between day care attendance and asthma is also supported in the literature, but is not specifically addressed in the Hygiene Hypothesis. However, as discussed earlier in the literature review, this finding coincides with more recent discussions about the Hygiene Hypothesis in that it is not any type of exposure that provides a protective benefit, but

particular exposures (like those present in farming environments). In this manner, the link between day care attendance and asthma is consistent. It may be that while day care centers are places where certain microbes are exchanged (like those that cause upper respiratory infections); the “old friends” as outlined earlier are not present in this environment due to the hygienic practices observed in these settings. However, there are other issues that should be considered.

One issue for further study, which cannot be determined with this data set, is to investigate in more detail the relationship between the length of time in day care, the age of first attendance, and the family and social structures which also influence the health of children that attend day care. It is a possibility that one of these factors is more contributory to the occurrence of asthma than simply the environment or potential exposures in a day care setting. In addition, for this study area, it is undetermined whether socio-economic status is linked to day care attendance. As discussed above in regard to the urban environment, with the data as presented, it is not possible to determine if poverty is an underlying factor here as well. However, it should be noted that as a whole, the study area is a middle income area with median household income above \$38,000 in majority of the households (as demonstrated in Figure 7). It should also be noted that while Cluster 3 (see

Figure 5) is located in a lower mid-income area, Cluster 2 is located in an area where median household income ranges from \$56,000 to \$80,000. Finally in order to better assess the relationship between reported asthma cases and median household income, the following map is produced:

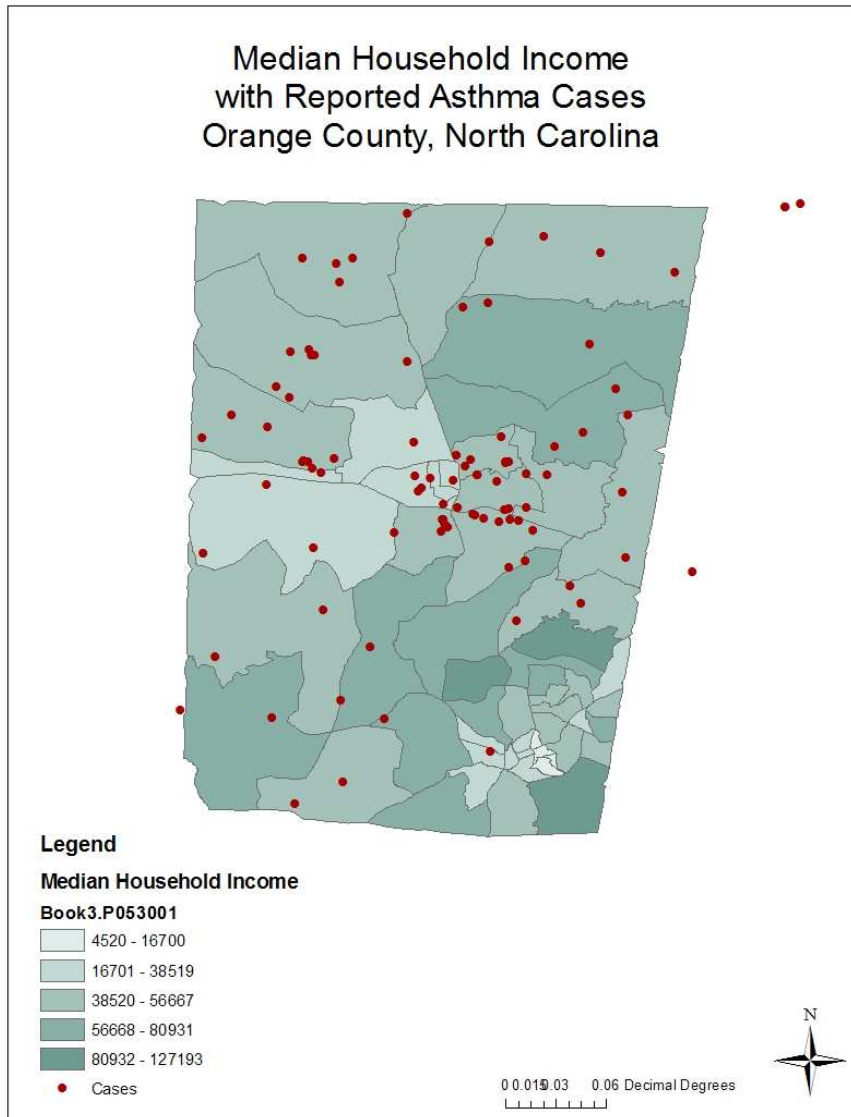


Figure 13: Median Household Income with Reported Asthma Cases (Source: U.S. Census Bureau)

While it is possible that there is a relationship in this study area between lower socio-economic status and reported cases of asthma, Figure 12 indicates that most all of the reported asthma cases are located within areas of median household income equal to or above \$38,000. Initially, a concern here could be a potential difference in response rate.

An examination of the responses of the school districts will assist in the determination of bias in response. One means through which to measure socio-economic status on a district basis is participation in the Free Lunch Program. This state program provides free lunch (and often breakfast) to students whose family qualifies based upon household income. As noted in Table 2, the response rates for each school district vary from 34.81% to 48.03%. While this does indicate a 14 point difference in response, Central Elementary, with 61.2% of the population participating in the Free Lunch Program, has a response rate of 44.86%. Efland-Cheeks Elementary, with 46.2% of the population participating in the Free Lunch Program, has a response rate of 36.11%. However, one potential explanation of a lower response rate at Efland-Cheeks Elementary is that the surveys distributed were in English only. A large Hispanic community is located within the Efland-Cheeks Elementary school district (see Figure 14). While problems

with language have not been verified, there is a possibility that some parents may not have participated in the survey due to a language barrier.

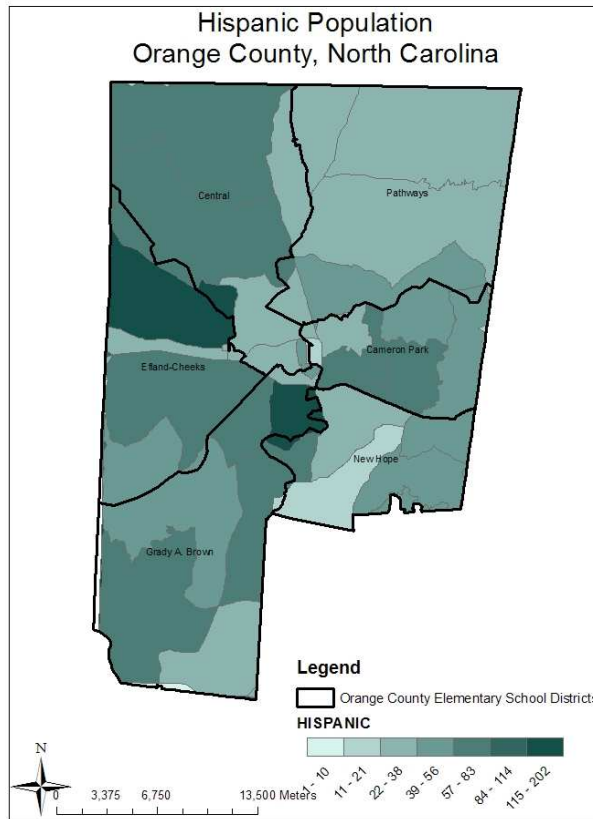


Figure 14: Hispanic Population (Source: U.S. Census Bureau)

Grady Brown Elementary school had the lowest response rate at 34.8%, but its Free Lunch participation is significantly less at 30.6%. Therefore, it is not clear that areas with high percentage rates of participation in the Free Lunch Program (as a means of measuring socio-economic status) are underrepresented in the sample.

Cluster Analysis

The cluster analysis revealed three potential clusters of significance. As discussed earlier, the first of the clusters has been excluded and discussion will focus on Clusters 2 and 3 as outlined in Figure 5. Cluster 2 is located in northern Orange County. The area containing and surrounding the cluster is a middle income area with median household income between \$38,000 and \$56,000 (see Figure 7). In addition 87.75% to 99.7% of the area is classified as rural non-farm by the 2000 U.S. Census. This finding is in line with the western lifestyle that is outlined in the Hygiene Hypothesis as a middle income, rural non-farm area. A concern regarding this cluster is the small number of households that comprise the cluster. Three households with a total of nine children are included in this cluster. While the SaTScan software does consider underlying population when determining clusters, there is a concern that one household has influenced this determination. One of the three households that are included in the cluster has six children, all of whom are reported to have asthma. Therefore, it is with reserve that this cluster be considered a true clustering of cases.

Cluster 3 is located centrally in the county just outside of the town of Hillsborough. This cluster is located within an area that's median income ranges from \$16,000 to \$38,000 and is determined to be 55.71% to 85.28%

urban by the 2000 U.S. Census. This cluster appears to be in agreement with traditional literature that emphasizes lower income, urban areas. However, as is the case with Cluster 2, there are concerns regarding the validity of Cluster 3 as well. The cluster is comprised of four households with a total of ten children. While there is not a single household that seems to dominate the cluster as there is in Cluster 2, the small number of households should be noted. In addition, as previously discussed, the components of the environment that are typical of larger urban areas may not be present in this area, classified as urban.

Asthma Surface Analysis

The production of two asthma surface maps assists in understanding the spatial distribution of the disease in the county. The initial map (Figure 11) consists only of cases of reported asthma. From this map it cannot be determined if an underlying population size impacts the distribution as shown. Therefore, a second map is presented that considers asthma cases as a percentage of the study population (Figure 12). The results are more concentrated areas of asthma, and a reduced number of high prevalence areas. Both clusters are visible on this map. However, an area of note can also be seen through this analysis that is not visible through the cluster analysis.

In the center of the county, to the immediate east of the town of Hillsborough is a significant area of high occurrence. Initially, this area was thought to be due to population size, but in Figure 12, once underlying population is accounted for, a large area of asthma occurrence greater than 11% is still visible. This area is classified as equal to/or greater than 44.63% rural non-farm (see Figure 9) with a median income equal to or greater than \$38,000 (see Figure 7). In addition, this area is one of the least concentrated in terms of the number of children as a percent of the total population (see Figure 6). Although any conclusion regarding this area would be speculative, this area of interest raises questions regarding the nature of the cases in this location as well as the nature of the physical and social environment. Further inquiry can resolve these questions, which cannot be determined from the data collected in this study.

Conclusion

The initial question guiding this research is “Can the Hygiene Hypothesis be used to explain childhood asthma prevalence in Orange County, North Carolina?” As expected, some of the reported asthma cases are due to factors outlined in traditional literature, like genetic susceptibility and premature birth. Otherwise, it is my belief that asthma in Orange County does not follow traditional literature insofar as it being a disease of poor,

urban populations. The Hygiene Hypothesis represents an addition to the traditional paradigm that considers the implication of broad scale changes in lifestyle. These changes are occurring at a relatively rapid rate, and possibly result in an alteration in the way the immune system functions, leading to increases in a variety of autoimmune disorders, asthma being one of many. In essence, while there are positive health benefits to the “western” environment, there also seem to be valid consequences to this change that have resulted in the alteration of a basic body function. The Hygiene Hypothesis cannot absolutely explain asthma in Orange County, however the premise of the hypothesis offers potential understanding of the etiology of the disease in areas that cannot be classified by traditional literature. More specifically, the recent variation of the Hygiene Hypothesis, as offered by Bjorksten,⁴⁶ Weinstock,⁴⁷ and Zaccane,⁴⁸ provide additional understanding of the impact of these large scale changes.

The second question under examination is “How is asthma prevalence affected by spatial differences in environmental factors in Orange County?”

⁴⁶ Bjorksten, Bengt. “Effects of Intestinal Microflora and the Environment on the Development of Asthma and Allergies.” Springer Seminars in Immunopathology. (2004) 25: 257-270.

⁴⁷ Weinstock, Joel V., Summers, Robert W., Elliott, David E. “Role of Helminths in Regulating Mucosal Inflammation.” Springer Seminars in Immunopathology. (2005) 27: 249-271.

⁴⁸ Zaccane, P., Fehervari, Z., Phillips, J.M., Dunne, D.W., Cooke, A. “Parasitic Worms and Inflammatory Disease.” Parasite Immunology. (2006) 28: 515-523.

The use of cluster analysis to resolve this question proved to be somewhat inconclusive as there are potential issues with both of the clusters determined to be significant. However, the asthma surface maps provide a view of asthma in the county that implies that there is a clear spatial distribution in the county, with areas of high prevalence congregating across space. Further analysis of these areas may advance understanding of the underlying causes of this distribution, but are not viable within the given data set.

Finally, because asthma is a disease of varying origin, variables that result in a positive outcome in one individual cannot be confidently linked to all individuals with asthma. This reality creates difficulty in determining cause and treatment. However, recent trends indicate additional diseases in the family known as autoimmune disorders are also increasing in prevalence and the growing concern regarding the origins of these diseases are becoming very similar to the concerns voiced in the debate about childhood asthma. While the reaction to the significant changes in environment may vary by individual, the theories that are emerging to explain the outcome of these diseases find their roots in the ecological approach, some of which has been outlined here. While there has been, and continues to be, research that examines these disease from an individual, microbiological perspective, research that examines change on the social, environmental, and cultural

levels can inform and contribute to this debate in ways not possible through research solely focused on the individual. From this perspective, the Hygiene Hypothesis and its variations have genuine contributions to the understanding of the prevalence and distribution of childhood asthma in Orange County, North Carolina.

Appendix I

Dear Parent,

Due to rapidly increasing asthma rates both worldwide and in our county, childhood asthma has become a major health care issue for children. In order to gain an understanding about the causes of this disease and its presence in Orange County, I am asking you to complete the enclosed survey. This survey will be distributed to all elementary school students in the first and fourth grades at every elementary school in the Orange County school system. Your participation in this study is completely voluntary. However, since the validity of the results depends upon obtaining a high rate of response, your participation is crucial to the success of this survey.

To participate, you would complete the enclosed survey and return it to me in the enclosed envelope. Please take the time to complete this survey *even if your child does not have asthma*. If you receive more than one survey, please only complete one survey per family. Your responses will be completely confidential; you are not asked to identify yourself or your child. The only persons that will have access to your information are the investigators overseeing this project. All information obtained in this study will be reported as group rather than individual results, further ensuring your privacy. Returning your completed survey indicates your consent to participate in this study.

This study is being conducted by Ashley Ward of the geography department at the University of North Carolina at Chapel Hill. If you have any questions or concerns regarding the survey please feel free to contact Ashley at (919) 563-0543 or by email at ward@mebtel.net. All research on human volunteers is reviewed by a committee at UNC-Chapel Hill that works to protect your rights and welfare. If you have any questions or concerns about your rights as a research subject you may contact, anonymously if you wish, the Institutional Review Board at (919) 966-3113. In addition, if you wish to be informed of the results of the survey, please provide the proper information where noted on the survey. All surveys should be returned to your child's school by **Friday, November 3, 2006**.

Thank you for considering participation in this survey. I hope that your responses can be used to further inform our county public health officials about the presence and experience of childhood asthma in the county, and what is locally affecting it.

Sincerely,

School Nurse

Principal Investigator

**Asthma and the Environment:
A Survey for Parents/Guardians**

Thank you for participating in this survey. The following are general questions about your household:

1. How many children do you have? _____

2. In order to create a map of childhood asthma in the county, and to gain an understanding of the risks of childhood asthma, please provide your street address below. Keep in mind this is an anonymous survey, and your privacy will be protected. You will not be contacted and your information will not be shared. It will only be used for mapping purposes, and will be anonymous on the map. A map depicting your home's location will not be displayed.

3. How would you label the location in which you live?

- a) Urban
- b) Suburban
- c) Farm area

4. In what year or decade was your home built?

5. Do you or a pest control expert spray pesticides or poisons to kill bugs or pests in your home?

- a) Never
- b) Annually
- c) Semi-Annually
- d) Quarterly
- e) Monthly
- f) Weekly

6. If you do use pesticides or poisons are they for any of the following (circle all that apply):

- a) Mice
- b) Ants
- c) Cockroaches
- d) Spiders
- e) Bees or Wasps

7. Does anyone smoke inside your home? This includes people who live in the home as well as those who visit on a regular basis.

- a) Never
- b) Occasionally
- c) Sometimes
- d) Frequently
- e) Daily

8. Does either parent of a child in the household have a respiratory disease? For example, asthma, emphysema, bronchitis, or other chronic respiratory disease?

- a) Yes
- b) No

9. If you answered "yes" to the previous question, please note which parent, and what type of respiratory disease:_____

Please answer the following questions about each of your children:

	Child 1	Child 2	Child 3	Child 4
10. Age				
11. Gender (Male/Female)				
12. Does he or she have any of the following conditions:				
Asthma				
Eczema				
Psoriasis				
Reactive Airway Disease (RAD)				
Chronic Bronchitis				
13. If you answered yes to any of the above conditions, at what age was he or she diagnosed?				
14. Was he or she born prematurely?				
15. Did he or she have severe respiratory problems at birth?				

Thinking back to the first year of life for each child, please answer the following questions:

	Child 1	Child 2	Child 3	Child 4
16. During the first year of life, did you breastfeed? If so, for how long?				
17. Were there pets in the home during his or her first year of life? If so, was the pet a cat, dog, other mammal, bird, or reptile?				
18. If you have moved during this time, since your child's first year of life was not spent at the address listed above, please provide the address if it was spent elsewhere in Orange County, NC. If it was outside of Orange County, NC it is not necessary that you provide the address, please simply note that it was outside of the county.				
19. What was the age of the home that you lived in during the first year of each child's life?				
20. Was he or she frequently exposed to farm animals in the first year of life?				
21. Did he or she attend day care during his or her first year of life?				
22. Did you regularly use products sold as "antibacterial" in his or her first year of life? For example, hand soaps, baby wipes, dish detergent, etc. commercially labeled "antibacterial."				

23. If one of your children currently has asthma, how are you treating his or her illness? Please select all that apply.

- a) Oral Medication
- b) Inhaler
- c) Not Treating at this Time
- d) Other _____

24. What do you believe is the cause of your child's asthma?

Thank you for participating. If you would like to receive the results of this survey, please list your name, mailing address, or email address below.

Appendix 2

Survey Codes

Q1: 1 or more (age)
Q2: Address
Q3: 1,2,3
Q4: Year
Q5: 1,2,3,4,5
Q6: 1,2,3,4,5
Q7: 1,2,3,4,5
Q8: 0,1
Q9: 1,2 (1=Male, 2=Female)
Q10: Age
Q11: 1,2 (1=Male, 2=Female)
Q12a – Q12e: 0,1 (0=No, 1=Yes)
Q13: Age
Q14: 0,1 (0=No, 1=Yes)
Q15: 0,1 (0=No, 1=Yes)
Q16: 0=No, ≥ 1 = number of months
Q17: 0=No, ≥ 1 = type of pet
Q18: Address
Q19: Age
Q20: 0,1 (0=No, 1=Yes)
Q21: 0,1 (0=No, 1=Yes)
Q22: 0,1 (0=No, 1=Yes)
Q23: 1,2,3,4
Q24: Text
Q25: Contact Info

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