Geo-Statistical Analysis of Possible Spirochetal Involvement in Multiple Sclerosis

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Abstract

Multiple Sclerosis (MS) is believed to have geographic factors, although the identity of those factors has eluded researchers for centuries. MS is most frequently found in temperate climates north of forty degrees latitude, especially in Europe and North America. Its etiology is unknown, but current mainstream thinking is that it is an autoimmune disorder caused by an unidentified virus. In the 1930s, a small group of researchers believed that MS was caused by a spirochete. This paper presents results of data visualization work done testing and expanding the latter hypothesis using ArcGIS 9. The geographic distribution of MS as plotted using mortality data was comparable to the distributions of known geography-dependent spirochetal diseases, including Lyme. We investigated population densities and how they vary with elevation. A geospatially indicated vector and reservoir host (ixodid tick and seabird, respectively) are also discussed.

Introduction

Throughout history, humans have sought to understand the world in which they live. Many tools and approaches have been used to develop this understanding with advances in understanding often following advances in the tools. The telescope, for example, allowed an understanding of astronomy not possible when the primary tool was the naked eye. The microscope allowed an understanding of disease processes not possible before its invention. And John
Snow, along with many others, showed that the map could advance an understanding of disease causal agents not possible without its use (Cliff, 2004; Koch, 2005). John Snow’s maps demonstrated that an understanding of the “where” of a disease outbreak can lead to effective ways to prevent the disease even if the “how” of the disease is not yet well understood. The closure of the Broad Street pump, resulting from Dr. Snow’s recommendation derived from his maps, showed that a successful intervention targeting a causal source could exist even if a specific causal agent was unknown. In fact, the bacterial causal agent of cholera, Vibrio cholerae, was not discovered and identified during Dr. Snow’s lifetime (UCLA, 2006).

Mapping tools have greatly progressed in the 150 years since Dr. Snow’s groundbreaking work. Today’s mapping tools, such as the Geographic Information System (GIS) products produced by ESRI, are sufficiently sophisticated to have made possible the discipline of health geography. Health geography is “the application of geographical information, perspectives, and methods to the study of health, disease, and healthcare” (Wikipedia, 2006). The GIS role in health geography is to provide a:

“… holistic approach to public health that promotes the well being of human populations through organizing data about who we are, where we live, and how we live within a geographic framework. The health of human populations reflects the complex interplay between population characteristics and the environment. Genetic makeup can predispose certain populations to chronic or acute conditions. Cultural factors, such as stress, economic status, and access to health care, can play a significant part in disease onset…GIS incorporates data that describes population characteristics, socioeconomic conditions, and the landscape, and analyzes the spatial relationship of these factors. In addition to integrating and analyzing health related data, this technology promotes data sharing through the use of standard formats and a highly efficient communication tool—the map” (ESRI, 2002).
The research discussed in this paper applies GIS to the health geographic study of Multiple Sclerosis (MS). It is generally agreed that the first written record of a case of MS dates from the early 1400s, yet the etiology of MS is currently unknown. Current understanding of the disease, however, specifies the importance of geographic factors in the incidence of MS. For example, MS is most frequently found in temperate climates north of forty degrees latitude, especially in Europe and North America. Yet GIS has never been systematically used to advance understanding of the etiology of MS. The research described in this paper is the start of such a systematic analysis. It is hoped that better understanding of the “where” of MS can lead to effective ways to prevent the disease, and possibly the solution to the 600-year-old mystery of the “how” of MS.

**Background**

Overview of Multiple Sclerosis (MS) and Its Diagnosis

MS is the “most common primary neurological disorder of young adults” (Warren, 2001, page 1). The National Multiple Sclerosis Society estimates that 400,000 people in the United States have MS (National Multiple Sclerosis Society, 2005c). It is an “old” disease with the first written record of the disease considered to be the description of the illness experienced by Lidwina of Schiedam, Holland (1380-1433). The record exists because her 37-years of suffering, acceptance of her situation, and mystical experiences attracted the attention of clergy who documented her condition. Pope Leo XIII canonized Lidwina in 1890. Because Lidwina’s first serious experience with her illness was a bone-breaking fall while skating on the frozen canal near her home at the age of sixteen, she is considered to be the patron saint of figure skaters (Murray, 2005).

The National Multiple Sclerosis Society (2005a) defines MS as a demyelinating “autoimmune disease that affects the central nervous system
(CNS). In MS, the peripheral nervous system is not affected. The symptoms of MS result from the patchy loss of myelin around CNS nerve fibers. The areas without myelin form scar tissue called sclerosis, plaques, and/or lesions. This scar tissue interferes with the nerve fiber's ability to transmit electrical impulses. The specific symptoms of MS experienced by an individual are specific to the way in which that person’s CNS electrical impulses are affected. The course of MS is generally divided into four categories:

- **Relapse-Remitting:** This is the most common form of MS and describes the disease course for approximately eighty-five percent of people initially diagnosed with MS. In this form, the person experiences a neurological “attack”, that is, a distinct, sudden, and clearly noticeable decrease in CNS/neurological function (relapse), followed soon thereafter by complete or nearly complete recovery (remitting) – until the next attack. The time separation and specific characteristics of the attacks are unique to each individual.

  - **Secondary-Progressive:** This can be considered an advanced stage of Relapse-Remitting because it is seen only in people who originally were diagnosed with the Relapse-Remitting form of the disease. Historically, approximately half of all people diagnosed with Relapse-Remitting develop this form within ten years of diagnosis. It is characterized by a continuing decline in CNS/neurological function with or without attacks/relapses. If attacks occur, there is little or no recovered function after the attack. Specific characteristics of the loss of functioning are unique to each individual.

- **Primary-Progressive:** Approximately ten percent of diagnosed MS patients have this form of the disease at initial diagnosis. It is similar to Secondary-Progressive, but without any attacks and without any
prior diagnosis of Relapse-Remitting MS. There is only a continuing worsening of CNS/neurological functioning. Specific characteristics of the continued worsening are unique to each individual.

- **Progressive-Relapsing**: Approximately five percent of diagnosed MS patients have this form of the disease at initial diagnosis. It is similar to both Relapse-Remitting and Secondary-Progressive. There are attacks, similar to Relapse-Remitting, but there may or may not be recovery after the attacks to the pre-attack level of functioning. Similar to Primary-Progressive, there is also only a continuing worsening of CNS/neurological functioning between attacks. Specific characteristics of the attacks, recovery, and continued worsening are unique to each individual.

Currently, there is no one diagnostic test that determines whether a person has MS. A diagnosis of MS is made only when the following two conditions exist:

1. “Objective evidence of at least two areas of myelin loss, or demyelinating lesions, ‘separated in time and space.’ This means lesions have occurred in different places within the brain, spinal cord, or optic nerve—at different points in time.

2. All other diseases that can cause similar neurologic symptoms have been objectively ruled out.” (National Multiple Sclerosis Society, 2003)

Data used to determine whether these two conditions exist include: 1) a person’s medical history and self-report of lost neurological functioning; 2) a clinical examination that includes neurological tests; and 3) laboratory tests. Laboratory tests usually include: 1) Magnetic Resonance Imaging (MRI) to determine if there are lesions in the brain (not all people who receive a diagnosis
of MS show lesions in the brain on an MRI); 2) evoked potential tests to
determine the speed with which electrical impulses move in the CNS; 3) test of
cerebrospinal fluid to determine if there is evidence of a CNS immune response
(such an antibody response is found is almost all individuals diagnosed with MS,
but is also present in people diagnosed with other diseases); and 4) blood tests
to rule out other diseases with similar symptoms, but for which there is a
definitive blood test (e.g., Lyme Disease).

**Geographic Factors in MS**

MS is a disease about which the recognized experts may be in general
agreement, but not total agreement. Much of what is “known” about MS is not
known with certainty. For example, there is general, but not total, agreement that
a cause of MS has not yet been definitively identified. There is more common
agreement that MS is an autoimmune disorder. There is also widespread
agreement that geographic factors play a role in MS, even if the role of those
factors is not yet understood. Studies indicate that: MS is more likely to occur in
temperate climates north of forty degrees latitude, especially in Europe and North
America; geographic clusters exist (e.g., Faroe Islands, Danish islands in the
North Atlantic; Galion, Ohio; DePue, Illinois; Rochester, New York; El Paso,
Texas); and the risk of acquiring MS coincides with the risk in the geographic
area in which a person lives before puberty – however, not everyone agrees with
the results of the studies (Jonew, 2006; Murray, 2005; National Multiple Sclerosis

People who receive a diagnosis of MS are also: much more likely to be
women rather than men, usually between the ages of 20 and 50, and much more
likely to be of northern European ancestry (National Multiple Sclerosis Society,
2005b). It was while studying the geographic factors of MS, that the primary
author (who has been studying MS for six years) noticed a similarity between the
geographic distribution of MS and the geographic distribution of Lyme Disease.
Given the mystery surrounding MS, the author decided to investigate further the
possible relationship between MS and Lyme to analyze whether MS might be a
form of Lyme or a disease caused by a spirochete similar to the one that causes Lyme.

**MS, Lyme, and Spirochetes**

A non-geographic testament to the possible link between MS and Lyme is the difficulty that doctors face in distinguishing between the two when making a diagnosis. Lyme Disease is a differential diagnosis for MS. In certain cases, patients are misdiagnosed with Lyme several times before receiving a diagnosis of MS. Both diseases can produce MRI’s marked by sclerotic plaques, and both manifest similar symptoms such as memory lapses, fatigue, and joint pain (Warren, 2001). Both diseases involve vascular inflammation within the CNS caused in part by inflammatory cytokines and chemokines (Pardridge, 1998; Rothwell, 2002).

Lyme resembles MS more and more as it progresses. In its most advanced stages, Lyme mimics an autoimmune attack against the myelin sheath, which is what most researchers believe MS to be (Filley, 2001). NINDS (2006a) defines MS as “An unpredictable disease of the central nervous system … in which the body, through its immune system, launches a defensive attack against its own tissues … the nerve-insulating myelin.” NINDS (2006b) also recognizes the neurological complications of Lyme, which usually occur in the second stage, and include “numbness, pain, weakness, Bell's palsy … visual disturbances, and meningitis symptoms … decreased concentration, irritability, memory and sleep disorders, and nerve damage in the arms and legs.”

Lyme has an identified spirochetal causal agent, *Borrelia Burgdorferi*. Some of the effects of Lyme are understood to be caused by *Borrelia Burgdorferi’s* presence in the CNS. The sensitive CNS is protected by the blood-brain barrier (BBB), which is supposed to keep CNS material inside of the CNS, and non-CNS material, such as *Borrelia Burgdorferi*, outside of the CNS. *Borrelia Burgdorferi*, however, crosses the BBB by using tissue plasminogen activator (tPA), which regenerates plasmin and degrades the collagen layer of the BBB. Once the protective collagen layer of the BBB is permeable, the
spirochete and other invaders can cross into the CNS. Likewise, tPA is found in the MS BBB, though its role is currently unknown (Pardridge, 1998). MS is also characterized by damage to the BBB endothelium and subsequent increased barrier permeability (Pardridge, 1998). The method of degradation in MS is not known (Russell, 1997). However, a CNS invader that depends on degradation of the BBB collagen layer to enter the CNS could explain observed disparities in MS incidence and prevalence by ethnic group. One would expect that ethnic groups known for high collagen levels might evidence a lower incidence of MS. For example, African-Americans have high levels of collagen and low rates of MS.

When a bacteria such as a spirochete crosses the BBB and invades the CNS, one of the first CNS responses is the clustering of macrophages around the invader. Macrophages have two main functions: to digest dead cell material and to digest bacteria by phagocytosis (Guyton, 1997). Macrophages can also secrete Nitric Oxide (NO) to kill the bacteria. This is seen in Leishmania, a parasitic disease that affects the body’s internal organs and immune system. The macrophages seen in Leishmania patients secrete NO to kill the antigen, a protozoan (CDC, 2004).

Macrophages and NO have been observed around the sclerotic plaques of MS. While the macrophages might be serving to break down remnants of myelin already attacked by the unknown antigen, the macrophages’ secretion of NO seems to suggest that some bacteria is also present. NO plays a number of different roles in disease, both positive and negative; it may induce axonal degeneration or vascular dilation, serve as a signaling molecule between neurons, affect memory and thought processes of the brain, or kill bacteria (Guyton, 1997). Among MS patients, the mysterious increase in lymphocyte movement across the BBB could be in response to a bacterial invader.

Both Lyme and MS also involve demyelination caused by what can resemble an autoimmune attack against the myelin sheath, and is considered an autoimmune attack in MS. An autoimmune attack is considered to be one where the body attacks itself in error; it “thinks” there is an invader to eliminate, but there is not and healthy tissue is destroyed. Healthy tissue is attacked in error.
But the general autoimmune theory, in the absence of a specific causal agent, does not explain very well the relapse-remitting progression common in both MS and Lyme. If, in fact, the T-cells and the body’s immune cells are “incorrectly” attacking the healthy Myelin Basic Protein (MBP) or some other feature of the fatty sheath surrounding the axons and not an invader, then one would not expect the disease to remit when there is still myelin left to be digested – as has been observed. For the autoimmune theory to be plausible, there would have to be some mechanism by which the immune system switches from the misidentification of healthy tissue as an invader to its correct identification, and a ceasing of the attack in mid-attack.

Both Lyme and MS can follow a relapse-remitting progression which, in Lyme, is thought to result from the many different forms that spirochetes such as *Borrelia Burgdorferi* are known to take. When the environment is positive for the spirochetal activity, the bacteria remain in a fully elongated form (about 5-20 μm in length), but in the presence of antibiotics many spirochetes defensively curl up into a granular form (about .3-.5μm) (Mattman, 2001). While in the granular form, the spirochetes are virtually undetectable even by electron microscopy, and the disease appears to be latent for some time. This latency period, though, is perhaps the most deleterious stage of disease. While in their highly minimized forms, the spirochetes are able to traverse many of the body’s pores and enter into cells and organs (Saier, 2001). When no longer threatened, they expand again into their elongated form.

**MS as a Zoonotic Disease**

Given the similarities of MS to Lyme Disease, it seems reasonable to ask: 1) Are MS and Lyme really the same disease? and 2) If not, are they similar zoonotic diseases? A zoonotic disease is one that is transmitted from animals to humans. For such transmission to occur, the following conditions must usually be met:
● Existence of a pathogen (i.e., bacteria, virus) that causes disease in humans and can survive in both humans and animals.

● Existence of a disease host/reservoir animal within which the pathogen lives (e.g., deer). Often the host is a carrier of the disease and never manifests any symptoms of the disease caused by the pathogen.

● Existence of a disease animal vector (e.g., tick) in proximity to both the animal host and the human that can transmit the pathogen from the animal host to the human. The vector, like the host, is often a carrier that does not exhibit symptoms. The vector and the host can be one and the same animal (e.g., raccoon with rabies).

● Transmission of the pathogen by the vector into the human's body.

Whether the infected human actually develops the disease caused by the pathogen is thought to depend on many factors such as a genetic predisposition and/or exposure to an environmental trigger. It is possible that not everyone who acquires the pathogen will acquire the disease.

Despite the similarities between MS and a spirochetal disease, however, most researchers today believe MS to be an autoimmune disease unrelated to the existence of any pathogen. Those who believe a pathogen is involved most commonly think it is a virus (National Institute for Neurological Disorders and Stroke, 2006a). Spirochetal involvement in MS, however, was a hypothesis gaining ground in Europe in the 1930s (Murray, 2005). Unfortunately, most of the research in support of this hypothesis, as well as the researchers themselves, were lost during World War II. A surviving researcher, Gabriel Steiner, published work after World War II that identified a spirochete, *Spirochaeta Myelophthora*, as the causal agent of MS with an unknown vector (Steiner, 1952; Steiner, 1954). Some of those who
worked with Steiner in the United States as well as other researchers hypothesize that MS and Lyme might in fact be either: 1) the same disease; or 2) different diseases caused by two different spirochetes carried by the same arthropod vector (Mattman, 2001; Rubel, 2003; Fritzsche, 2005).

**Hypotheses**

The hypothesis to be tested is that MS and Lyme Disease are triggered or influenced by a similar zoonotic spirochetal agent and spread by a tick-like vector. If a common etiology exists, then a geostatistical relationship between Lyme and MS should be observed at either the state-level or the county-level or both. The possibility of a common bacterial basis for both MS and Lyme is examined in this study using geostatistical analysis. Such analysis combines descriptive and inferential statistical techniques with data visualization (cartographics). The results have proven useful in understanding the etiology of many diseases including cholera, plague, malaria, smallpox, AIDS, and Lyme (Ormsby, 2001, Cliff, 2004; Koch, 2005;).

The analysis can be improved by using a control variable (disease) and at least one other condition in which the causal agent or geographic distribution might be similar to that of MS. The control variable in this study is accident/injury because this condition should be unrelated to a bacterial distribution. The two diseases with a suggested bacterial cause or geographic similarity to MS are Breast Cancer (Cantwell, 1998) and Amyotrophic Lateral Sclerosis (ALS, Lou Gehrig’s Disease) (Agency for Toxic Substances and Disease Registry, 2003).

**Methods**

Comparing disease distributions requires a database of the incidence and/or prevalence of the diseases under examination and their associated environmental variables. The data collection process began with a search for an authoritative source of incidence and prevalence data for Lyme, MS, Breast Cancer, ALS, and accidents/injuries. Deaths recorded with the Centers for Disease Control and Prevention (CDC) and other government agencies provide
an incidence measure of the given diseases. A useful dataset was found on TheDataWeb, which is an online set of data libraries. The dataset, “Mortality – Underlying Cause-of-Death – 1998” (United States Bureau of the Census (Census Bureau), 2005b; CDC, 2005c), was accessed via DataFerret, a data mining tool (Census Bureau, 2005a; CDC, 2005a). The United States Bureau of the Census (Census Bureau) and the Centers Disease Control and Prevention (CDC) make both TheDataWeb and DataFerrett available to the public without charge.

This “Mortality” dataset contains geographic, demographic, and cause-of-death variables obtained from the death certificates of people who died in 1998. Geographic variables include: county and state of residence, and county and state population. Cause-of-death-related variables include the underlying-cause-of-death coded using the International Classification of Diseases (ICD) Code (9th Revision).

The coding of death certificate information is standardized across all states. Death certificates are completed and filed at the state-level. (CDC, 2005b). The death certificate information is collected from the states at the federal level by the National Center for Health Statistics (NCHS) and published along with other vital statistics as part of the National Vital Statistics System, “the oldest and most successful example of inter-governmental data sharing in Public Health and the shared relationships, standards, and procedures form the mechanism by which NCHS collects and disseminates the Nation’s official vital statistics.” (CDC, 2005d, Introduction section). “The vital statistics general mortality data are a fundamental source of demographic, geographic, and cause-of-death information. This is one of the few sources of comparable health-related data for small geographic areas and a long time period in the United States.” (Census Bureau, 2005c, National Center for Health Statistics section).

DataFerrett returns information from TheDataWeb in aggregate form only. Upon submitting a DataFerrett query for data the following use restriction statement is displayed:
“WARNING! DATA USE RESTRICTIONS. Read Carefully Before Using The Public Health Service Act (Section 308 (d) ) provides that the data collected by the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC), may be used only for the purpose of health statistical reporting and analysis. Any effort to determine the identity of any reported case is prohibited by this law. NCHS does all it can to ensure that the identity of data subjects cannot be disclosed. All direct identifiers, as well as any characteristics that might lead to identifications, are omitted from the dataset. Any intentional identification or disclosure of a person or establishment violates the assurances of confidentiality given to the providers of the information. Therefore, users will:

- Use the data in this dataset for statistical reporting and analysis only.
- Make no use of the identity of any person or establishment discovered inadvertently and advise the Director, NCHS, of any such discovery.
- Not link this dataset with individually identifiable data from other NCHS or non-NCHS datasets.

By using the data you signify your agreement to comply with the above-stated statutorily based requirements.”

Because DataFerrett queries use the ICD (9th Revision; ICD-9) codes as a selection criteria, the appropriate ICD-9 codes for each disease were determined through review of an online version of this document available from the National Center for Health Statistics (NCHS, 2005). See Table 1 for a list of the ICD-9 codes used as selection criteria. The Disease/Condition DataFerrett Selection Codes were then used to extract the state of residence for those who died in the United States in 1998 from each of the five diseases/conditions of interest. Data
was obtained for each of the fifty (50) states and the District of Columbia (total N for the state-level analyses = 51). This data was downloaded into an Excel file.

Added to this Excel file was the population of each state according to both the 1990 Census and the 2000 Census obtained from the Census Bureau American FactFinder, Population Finder website/webtool (Census Bureau, n.d.). The total 1990 population from the Census Bureau and the total 1998 deaths from DataFerrett for each state were used to calculate the incidence variables used in the analyses. See Table 2. The completed Excel file was opened and saved in SPSS (SPSS, 2003), which was used to calculate the descriptive and inferential statistics. The SPSS file was saved as a Dbase IV file and then opened and saved in ArcGIS for the cartographic analyses.

The same general method was used to obtain data at the county level. However, in order to protect the privacy of individuals, DataFerrett does not return data for counties with less than 100,000 people according to the 1990 Census. Instead, all death data for a state from counties with less than 100,000 is lumped into one value. Wyoming, for example, has no counties with a population of more than 100,000 so the county-level death data for Wyoming is returned as one statewide number. Delaware’s three counties each have a population over 100,000 so county-level data is returned for all three Delaware counties. New Jersey has twenty-one counties, but three of these counties have a population less than 100,000. For New Jersey, data is returned for each of eighteen individual counties and then one number is returned for the three counties (combined) with a population of less than 100,000.

There are 3141 counties in the United States, but DataFerrett returns data on 504, which includes the combined values for a state’s less-than-100,000 counties. At the county-level, the population data was obtained from Census data available through the University of Virginia (n.d.). County-level analyses were also done using only those states generally considered to have a high Lyme incidence (Lyme-State). These 123 Lyme-State counties, which include those counties lumped together because of a less-than-100,000 population, are in the following ten states: Connecticut, Delaware, Maine, Maryland,
<table>
<thead>
<tr>
<th>Disease/Condition</th>
<th>Data Ferrett Selection Code</th>
<th>ICD-9 Categories and Code Descriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple Sclerosis (MS)</td>
<td>340</td>
<td>Diseases of the Nervous System and Sense Organs (VI: 320-389), Other Disorders of the Central Nervous System (340-349), Multiple Sclerosis (340) – Includes Disseminated or Multiple Sclerosis: Not Otherwise Specified (NOS), Brain Stem, Cord, Generalized</td>
</tr>
<tr>
<td>Lyme Disease</td>
<td>088.8</td>
<td>Infectious and Parasitic Diseases (I: 001-139), Rickettsioses and Other Arthropod-Borne Diseases (080-088), Other Arthropod-Borne Diseases (088), Other Specified Arthropod-Borne Diseases (088.8), Lyme Disease (088.81) – includes Erythema Chronicum Migrans, Babesiosis (088.82) – includes Babesiasis, Other (088.89). <strong>NOTE:</strong> Lyme could not be selected individually because DataFerrett does not allow more detail in selection than 088.8, so analyses were done with this dataset for the category Other Specified Arthropod-Borne Diseases (OSABD) rather than Lyme alone.</td>
</tr>
<tr>
<td>Breast Cancer</td>
<td>174.0 – 174.9</td>
<td>Neoplasms (II: 140-239), Malignant Neoplasm of the Female Breast (174) –Includes Nipple and Areola (174.0), Central Portion (174.1), Upper-Inner Quadrant (174.2), Lower-Inner Quadrant (174.3), Upper-Outer Quadrant (174.4), Lower-Outer Quadrant (174.5), Axillary Tail (174.6), Other (174.8), and Breast, Unspecified (174.9)</td>
</tr>
<tr>
<td>Amyotrophic Lateral Sclerosis (ALS, Lou Gehrig’s Disease)</td>
<td>335.2</td>
<td>Diseases of the Nervous System and Sense Organs (VI: 320-389), Hereditary and Degenerative Diseases of the Central Nervous System (330-337), Anterior Horn Cell Disease (335), Motor Neuron Disease (335.2) – includes Amyotrophic Lateral Sclerosis, Progressive Muscular Atrophy (Pure), and Motor Neuron Disease (Bulbar) (Mixed Type). <strong>NOTE:</strong> ALS could not be selected individually because ALS does not have its own ICD-9 code. The code for Motor Neuron Disease, which includes ALS was used for the analyses done with this dataset.</td>
</tr>
<tr>
<td>External Cause (CONTROL)</td>
<td>E800 - E999</td>
<td>Supplementary Classification of External Causes of Injury and Poisoning (E800 -E999). <strong>NOTE:</strong> Used as the Control Variable in the analyses.</td>
</tr>
</tbody>
</table>

**Table 1. ICD-9 Code Used as the DataFerret Selection Criteria and Reasoning**
<table>
<thead>
<tr>
<th>Variables</th>
<th>Calculation of Variable</th>
</tr>
</thead>
<tbody>
<tr>
<td>MS Death Incidence per 100,000 Live (1990)</td>
<td>Number of deaths from MS in 1998 as reported by DataFerrett in that geographic unit (state, county) divided by the 1990 Census population for that geographic unit.</td>
</tr>
<tr>
<td>MS Death Incidence per 100,000 Deaths (1998)</td>
<td>Number of deaths from MS in 1998 as reported by DataFerrett in that geographic unit (state, county) divided by the total number of 1998 deaths from all causes reported by DataFerrett for that geographic unit.</td>
</tr>
<tr>
<td>OSABD Death Incidence per 100,000 Live (1990)</td>
<td>Number of deaths from OSABD in 1998 as reported by DataFerrett in that geographic unit (state, county) divided by the 1990 Census population for that geographic unit.</td>
</tr>
<tr>
<td>OSABD Death Incidence per 100,000 Deaths (1998)</td>
<td>Number of deaths from OSABD in 1998 as reported by DataFerrett in that geographic unit (state, county) divided by the total number of 1998 deaths from all causes reported by DataFerrett for that geographic unit.</td>
</tr>
<tr>
<td>1998 Lyme Incidence per 100,000 Live (1990)</td>
<td>Number of new Lyme cases reported by State Epidemiologists to the CDC for 1998 for that geographic unit (state, county) divided by the 1990 Census population for that geographic unit.</td>
</tr>
<tr>
<td>1992-1998 Lyme Incidence per 100,000 Live (1990)</td>
<td>Total of the number of new Lyme cases reported by State Epidemiologists to the CDC for each of the years between 1992 and 1998 for that geographic unit (state, county) divided by the 1990 Census population for that geographic unit.</td>
</tr>
<tr>
<td>Breast Cancer Death Incidence per 100,000 Live (1990)</td>
<td>Number of deaths from Breast Cancer in 1998 as reported by DataFerrett in that geographic unit (state, county) divided by the 1990 Census population for that geographic unit.</td>
</tr>
<tr>
<td>Breast Cancer Death Incidence per 100,000 Deaths (1998)</td>
<td>Number of deaths from Breast Cancer in 1998 as reported by DataFerrett in that geographic unit (state, county) divided by the total number of 1998 deaths from all causes reported by DataFerrett for that geographic unit.</td>
</tr>
<tr>
<td>Motor Neuron Death Incidence per 100,000 Live (1990)</td>
<td>Number of deaths from Motor Neuron Disease in 1998 as reported by DataFerrett in that geographic unit (state, county) divided by the 1990 Census population for that geographic unit.</td>
</tr>
<tr>
<td>Motor Neuron Death Incidence per 100,000 Deaths (1998)</td>
<td>Number of deaths from Motor Neuron Disease in 1998 as reported by DataFerrett in that geographic unit (state, county) divided by the total number of 1998 deaths from all causes reported by DataFerrett for that geographic unit.</td>
</tr>
<tr>
<td>External Cause Death Incidence per 100,000 Live (1990)</td>
<td>Number of deaths from External Causes in 1998 as reported by DataFerrett in that geographic unit (state, county) divided by the 1990 Census population for that geographic unit.</td>
</tr>
<tr>
<td>External Cause Death Incidence per 100,000 Deaths (1998)</td>
<td>Number of deaths from External Causes in 1998 as reported by DataFerrett in that geographic unit (state, county) divided by the total number of 1998 deaths from all causes reported by DataFerrett for that geographic unit.</td>
</tr>
</tbody>
</table>

Table 2. Calculation of Variables Used in the Dataset of Variables for Data Analysis
All statistical calculations were done using SPSS. Counts of disease deaths provided by the CDC were normalized by the 1990 Census population information, yielding number of deaths due to a certain disease per 100,000 people in that state or county. See Table 2. But normalizing disease deaths by the number of living people in a state or county produced the confounding factor of that geographic unit’s demographics and age. So a new measurement was introduced: the number of deaths from each disease was divided over the total deaths of each county or state (incidence of death due to a specific disease per 100,000 deaths in that geographic unit). See Table 2. Another confounding factor was the exclusion of counties with fewer than 100,000 residents due to CDC privacy policy. To accommodate for this, the total deaths from all of these smaller counties was smeared proportionally across each county included in the set. This set of all the counties with fewer than 100,000 people was labeled a “super-county”. The analysis could use these blocks in combination or independently.

To this data, in both the state and county files, was added the number of new Lyme cases reported each year from 1992-1998, centroid latitude, centroid longitude, and population elevation (the elevation of the county seat or the nearest population center to the county seat for which there is elevation data). Centroid latitude and longitude were averaged over all counties in a state to calculate the state value. The same method was used to calculate each state’s population elevation. Centroid latitude, centroid longitude, and most population elevation information were obtained from the United States Geological Survey (USGS, n.d.). The Lyme case data was added because the death data from DataFerrett includes more than Lyme (See Table 1). The DataFerrett category that includes Lyme deaths is “Other Specified Arthropod Borne Diseases” in ICD-9. This category variable is named OSABD in this study.

The number of Lyme cases in each state for the years 1992-1998 is available from CDC publications (CDC, 2002). The number of Lyme cases per year by county is not, however, available from the CDC. Although the CDC publishes some multi-year cartographic material by county, the CDC does not
report county-level, annual numerical data for a state to the public. County-level Lyme incidence data is only available to the public by contacting each state’s department of health, specifically, the state epidemiologist. In this study, Lyme data available by county was subsequently compiled to match the super-counties data available for DataFerrett death data.

The process of obtaining Lyme incidence data by county for the years 1992 through and including 1998 was labor-intensive. Each state’s Department of Health website was visited to see if the needed Lyme data was available on the website. If the data was not available, that state’s epidemiologist was emailed using contact information from the Council of State and Territorial Epidemiologists (n.d.) website provided by the CDC. Most epidemiologists contacted via email responded and provided the necessary data. All of these sources were recorded and the data compiled and added to the database. As of this writing, this appears to be the most comprehensive database of Lyme in existence.

**Results**

Descriptive statistics for the variables in each of the three basic datasets can be found in Table 3, Table 4, and Table 5. As many statistical tests assume that the data are normally distributed, each variable’s skewness and kurtosis values and standard errors were examined. A normally distributed variable has a value of 0 for both skewness (a measure of symmetry) and kurtosis (a measure of clustering around a central point). If the ratio of the skewness value to its standard error is between −2 and +2, then the distribution is symmetrical (normal). If the ratio of the kurtosis value to its standard error is between −2 and +2, then the data are normally distributed. (SPSS, 2003; Norusis, 2003).

Few of the variables are normally distributed. In the State-Level variables, only MS Death Incidence per 100,000 Live (1990), MS Death Incidence per 100,000 Deaths (1998), Motor Neuron Death Incidence per 100,000 Live (1990), Motor Neuron Death Incidence per 100,000 Deaths (1998), and External Cause Death Incidence per 100,000 Live (1990) are normally distributed. In the Lyme-
State County Level (Population >= 100,000) variables, only MS Death Incidence per 100,000 Live (1990) and Breast Cancer Death Incidence per 100,000 Deaths (1998) are normally distributed.

The next step in the analysis was a correlation analysis. Calculating a Pearson correlation coefficient \( r \) is appropriate for variables that are normally distributed. (SPSS, 2003, page 379). Calculating a Kendall’s tau-b or Spearman’s rho is appropriate when the data are not normally distributed. Because all three of these correlation analyses assume a linear relationship between the variables, a scatterplot graph was constructed for each pair of variables to be analyzed. Each scatterplot was linear so a Pearson’s, Kendall’s, or Spearman’s coefficient was calculated as appropriate for pairs of variables in each of the three datasets. The results can be seen in Table 6, Table 7, and Table 8.

Multiple regression was also used to find the model that would best predict the MS Death Incidence per 100,000 Deaths. All variables contained in the dataset were entered into the regression analysis using the stepwise feature. All variable values were converted to z-scores for use in the regression analysis. These results can be seen in Table 9. Lastly, cartographic analyses were completed. These can be seen in Figure 1, Figure 2, and Figure 3. They show the normalized distribution of MS Deaths, OSABD Deaths, and External Causes Deaths, respectively.
Figure 1. Normalized Count of MS Deaths by County (1998 Deaths Divided by 1990 Census Population)

Figure 2. Normalized Count of Other Specified Arthropod-Borne Diseases (OSABD) Deaths by County (1998 Deaths Divided by 1990 Census Population)
Figure 3. Normalized Count of External Causes of Death by County (1998 Deaths Divided by 1990 Census Population)
<table>
<thead>
<tr>
<th>Dataset of State-Level Disease and Geographic Variables</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>Std. Dev.</th>
<th>Skewness Value</th>
<th>Std. Err. Value</th>
<th>Kurtosis Std. Err.</th>
</tr>
</thead>
<tbody>
<tr>
<td>MS Death Incidence per 100,000 Live (1990)</td>
<td>51</td>
<td>0.1</td>
<td>2.0</td>
<td>1.1</td>
<td>0.4</td>
<td>0.2</td>
<td>0.3</td>
<td>0.5</td>
</tr>
<tr>
<td>MS Death Incidence per 100,000 Deaths (1998)</td>
<td>51</td>
<td>12.4</td>
<td>219.6</td>
<td>112.8</td>
<td>43.7</td>
<td>0.3</td>
<td>0.3</td>
<td>-0.1</td>
</tr>
<tr>
<td>OSABD Death Incidence per 100,000 Live (1990)</td>
<td>51</td>
<td>1.5</td>
<td>7.2</td>
<td>3.6</td>
<td>1.6</td>
<td>0.8</td>
<td>0.3</td>
<td>-0.5</td>
</tr>
<tr>
<td>OSABD Death Incidence per 100,000 Deaths (1998)</td>
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<td>159.0</td>
<td>803.9</td>
<td>385.0</td>
<td>166.6</td>
<td>0.9</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>1998 Lyme Incidence per 100,000 Live (1990)</td>
<td>51</td>
<td>0.0</td>
<td>104.5</td>
<td>6.7</td>
<td>18.6</td>
<td>4.2</td>
<td>0.3</td>
<td>18.9</td>
</tr>
<tr>
<td>1992-1998 Lyme Incidence per 100,000 Live (1990)</td>
<td>51</td>
<td>0.0</td>
<td>472.2</td>
<td>33.6</td>
<td>83.7</td>
<td>3.9</td>
<td>0.3</td>
<td>16.8</td>
</tr>
<tr>
<td>Breast Cancer Death Incidence per 100,000 Live (1990)</td>
<td>51</td>
<td>8.9</td>
<td>22.1</td>
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<td>-0.6</td>
<td>0.3</td>
<td>1.9</td>
</tr>
<tr>
<td>Breast Cancer Death Incidence per 100,000 Deaths (1998)</td>
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<td>1377.7</td>
<td>2213.4</td>
<td>1772.1</td>
<td>186.6</td>
<td>0.3</td>
<td>0.3</td>
<td>2.1</td>
</tr>
<tr>
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<td>51</td>
<td>0.7</td>
<td>2.7</td>
<td>1.8</td>
<td>0.5</td>
<td>0.0</td>
<td>0.3</td>
<td>-0.4</td>
</tr>
<tr>
<td>Motor Neuron Death Incidence per 100,000 Deaths (1998)</td>
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<td>98.9</td>
<td>303.1</td>
<td>187.1</td>
<td>45.1</td>
<td>0.2</td>
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<td>-0.0</td>
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<tr>
<td>External Cause Death Incidence per 100,000 Live (1990)</td>
<td>51</td>
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<td>109.8</td>
<td>66.1</td>
<td>15.8</td>
<td>0.4</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>External Cause Death Incidence per 100,000 Deaths (1998)</td>
<td>51</td>
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<td>16802.8</td>
<td>7067.0</td>
<td>2068.1</td>
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<td>0.3</td>
<td>9.0</td>
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<tr>
<td>Population Elevation (feet)</td>
<td>51</td>
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<td>6305.4</td>
<td>1337.7</td>
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<td>1.8</td>
<td>0.3</td>
<td>2.3</td>
</tr>
<tr>
<td>Centroid Latitude</td>
<td>51</td>
<td>21.0</td>
<td>60.3</td>
<td>39.5</td>
<td>5.9</td>
<td>0.1</td>
<td>0.3</td>
<td>3.2</td>
</tr>
<tr>
<td>Centroid Longitude</td>
<td>51</td>
<td>-157.3</td>
<td>-69.5</td>
<td>-93.4</td>
<td>19.0</td>
<td>-1.3</td>
<td>0.3</td>
<td>2.1</td>
</tr>
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</table>

Table 3. Descriptive Statistics for the Dataset of State-Level Disease and Geographic Variables
<table>
<thead>
<tr>
<th>Dataset of County-Level (Population &gt;=100,000) Disease and Geographic Variables</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>Std. Dev.</th>
<th>Skewness Value</th>
<th>Std. Err.</th>
<th>Kurtosis Value</th>
<th>Std. Err.</th>
</tr>
</thead>
<tbody>
<tr>
<td>MS Death Incidence per 100,000 Live (1990)</td>
<td>504</td>
<td>0.0</td>
<td>4.3</td>
<td>1.0</td>
<td>0.7</td>
<td>0.9</td>
<td>0.1</td>
<td>1.5</td>
<td>0.2</td>
</tr>
<tr>
<td>MS Death Incidence per 100,000 Deaths (1998)</td>
<td>504</td>
<td>0.0</td>
<td>523.6</td>
<td>112.2</td>
<td>81.4</td>
<td>0.9</td>
<td>0.1</td>
<td>1.9</td>
<td>0.2</td>
</tr>
<tr>
<td>OSABD Death Incidence per 100,000 Live (1990)</td>
<td>504</td>
<td>0.0</td>
<td>14.9</td>
<td>3.3</td>
<td>2.1</td>
<td>1.5</td>
<td>0.1</td>
<td>4.0</td>
<td>0.2</td>
</tr>
<tr>
<td>OSABD Death Incidence per 100,000 Deaths (1998)</td>
<td>504</td>
<td>0.0</td>
<td>1905.0</td>
<td>354.2</td>
<td>221.5</td>
<td>1.6</td>
<td>0.1</td>
<td>5.2</td>
<td>0.2</td>
</tr>
<tr>
<td>1998 Lyme Incidence per 100,000 Live (1990)</td>
<td>504</td>
<td>0.0</td>
<td>485.8</td>
<td>10.3</td>
<td>43.2</td>
<td>7.3</td>
<td>0.1</td>
<td>61.0</td>
<td>0.2</td>
</tr>
<tr>
<td>1992-1998 Lyme Incidence per 100,000 Live (1990)</td>
<td>504</td>
<td>0.0</td>
<td>2743.6</td>
<td>51.1</td>
<td>213.4</td>
<td>7.6</td>
<td>0.1</td>
<td>71.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Breast Cancer Death Incidence per 100,000 Live (1990)</td>
<td>504</td>
<td>1.8</td>
<td>35.1</td>
<td>16.7</td>
<td>4.1</td>
<td>0.5</td>
<td>0.1</td>
<td>1.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Breast Cancer Death Incidence per 100,000 Deaths (1998)</td>
<td>504</td>
<td>221.0</td>
<td>3081.5</td>
<td>1815.4</td>
<td>368.6</td>
<td>0.0</td>
<td>0.1</td>
<td>0.8</td>
<td>0.2</td>
</tr>
<tr>
<td>Motor Neuron Death Incidence per 100,000 Live (1990)</td>
<td>504</td>
<td>0.0</td>
<td>6.4</td>
<td>1.8</td>
<td>1.1</td>
<td>0.7</td>
<td>0.1</td>
<td>0.9</td>
<td>0.2</td>
</tr>
<tr>
<td>Motor Neuron Death Incidence per 100,000 Deaths (1998)</td>
<td>504</td>
<td>0.0</td>
<td>661.0</td>
<td>193.5</td>
<td>112.8</td>
<td>0.8</td>
<td>0.1</td>
<td>1.2</td>
<td>0.2</td>
</tr>
<tr>
<td>External Cause Death Incidence per 100,000 Live (1990)</td>
<td>504</td>
<td>25.0</td>
<td>140.2</td>
<td>59.4</td>
<td>17.9</td>
<td>1.0</td>
<td>0.1</td>
<td>1.8</td>
<td>0.2</td>
</tr>
<tr>
<td>External Cause Death Incidence per 100,000 Deaths (1998)</td>
<td>504</td>
<td>2970.3</td>
<td>18308.1</td>
<td>6477.6</td>
<td>1831.9</td>
<td>1.3</td>
<td>0.1</td>
<td>4.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Population Elevation (feet)</td>
<td>504</td>
<td>-40.0</td>
<td>6485.9</td>
<td>753.6</td>
<td>1090.8</td>
<td>3.0</td>
<td>0.1</td>
<td>9.6</td>
<td>0.2</td>
</tr>
<tr>
<td>Centroid Latitude</td>
<td>504</td>
<td>19.5</td>
<td>61.2</td>
<td>38.3</td>
<td>5.2</td>
<td>-0.38</td>
<td>0.1</td>
<td>1.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Centroid Longitude</td>
<td>504</td>
<td>-158.0</td>
<td>-68.7</td>
<td>-89.6</td>
<td>16.0</td>
<td>-1.3</td>
<td>0.1</td>
<td>1.7</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Table 4. Descriptive Statistics for the Dataset of County-Level (Population >= 100,000) Disease and Geographic Variables
<table>
<thead>
<tr>
<th>Dataset of Lyme State County-Level (Population &gt;=100,000) Disease and Geographic Variables</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>Std. Dev.</th>
<th>Skewness Value</th>
<th>Std. Err.</th>
<th>Kurtosis Value</th>
<th>Std. Err.</th>
</tr>
</thead>
<tbody>
<tr>
<td>MS Death Incidence per 100,000 Live (1990)</td>
<td>123</td>
<td>0.0</td>
<td>2.8</td>
<td>1.0</td>
<td>0.6</td>
<td>0.4</td>
<td>0.2</td>
<td>2.0</td>
<td>0.4</td>
</tr>
<tr>
<td>MS Death Incidence per 100,000 Deaths (1998)</td>
<td>123</td>
<td>0.0</td>
<td>412.1</td>
<td>107.2</td>
<td>71.5</td>
<td>0.8</td>
<td>0.2</td>
<td>2.0</td>
<td>0.4</td>
</tr>
<tr>
<td>OSABD Death Incidence per 100,000 Live (1990)</td>
<td>123</td>
<td>0.0</td>
<td>7.2</td>
<td>2.6</td>
<td>1.3</td>
<td>1.0</td>
<td>0.2</td>
<td>1.6</td>
<td>0.4</td>
</tr>
<tr>
<td>OSABD Death Incidence per 100,000 Deaths (1998)</td>
<td>123</td>
<td>0.0</td>
<td>815.3</td>
<td>275.0</td>
<td>139.8</td>
<td>0.9</td>
<td>0.2</td>
<td>1.4</td>
<td>0.4</td>
</tr>
<tr>
<td>1998 Lyme Incidence per 100,000 Live (1990)</td>
<td>123</td>
<td>0.0</td>
<td>485.8</td>
<td>35.4</td>
<td>73.3</td>
<td>3.7</td>
<td>0.2</td>
<td>16.0</td>
<td>0.4</td>
</tr>
<tr>
<td>1992-1998 Lyme Incidence per 100,000 Live (1990)</td>
<td>123</td>
<td>2.4</td>
<td>2743.6</td>
<td>176.6</td>
<td>378.7</td>
<td>4.0</td>
<td>0.2</td>
<td>19.9</td>
<td>0.4</td>
</tr>
<tr>
<td>Breast Cancer Death Incidence per 100,000 Live (1990)</td>
<td>123</td>
<td>9.9</td>
<td>35.1</td>
<td>18.3</td>
<td>3.7</td>
<td>0.9</td>
<td>0.2</td>
<td>3.1</td>
<td>0.4</td>
</tr>
<tr>
<td>Breast Cancer Death Incidence per 100,000 Deaths (1998)</td>
<td>123</td>
<td>1061.0</td>
<td>3081.5</td>
<td>1957.8</td>
<td>339.1</td>
<td>0.2</td>
<td>0.2</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>Motor Neuron Death Incidence per 100,000 Live (1990)</td>
<td>123</td>
<td>0.0</td>
<td>4.8</td>
<td>1.8</td>
<td>1.1</td>
<td>0.7</td>
<td>0.2</td>
<td>0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Motor Neuron Death Incidence per 100,000 Deaths (1998)</td>
<td>123</td>
<td>0.0</td>
<td>632.2</td>
<td>198.4</td>
<td>120.9</td>
<td>1.1</td>
<td>0.2</td>
<td>1.8</td>
<td>0.4</td>
</tr>
<tr>
<td>External Cause Death Incidence per 100,000 Live (1990)</td>
<td>123</td>
<td>25.0</td>
<td>118.5</td>
<td>47.7</td>
<td>12.6</td>
<td>1.6</td>
<td>0.2</td>
<td>7.2</td>
<td>0.4</td>
</tr>
<tr>
<td>External Cause Death Incidence per 100,000 Deaths (1998)</td>
<td>123</td>
<td>2970.3</td>
<td>10056.5</td>
<td>5077.8</td>
<td>1126.6</td>
<td>1.6</td>
<td>0.2</td>
<td>5.5</td>
<td>0.4</td>
</tr>
<tr>
<td>Population Elevation (feet)</td>
<td>123</td>
<td>9.0</td>
<td>2140.0</td>
<td>341.7</td>
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<td>1.9</td>
<td>0.2</td>
<td>5.0</td>
<td>0.4</td>
</tr>
<tr>
<td>Centroid Latitude</td>
<td>123</td>
<td>38.5</td>
<td>45.2</td>
<td>41.3</td>
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<td>0.5</td>
<td>0.2</td>
<td>-0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Centroid Longitude</td>
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<td>-80.5</td>
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<td>-74.9</td>
<td>2.6</td>
<td>-0.1</td>
<td>0.2</td>
<td>-0.3</td>
<td>0.4</td>
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</table>

Table 5. Descriptive Statistics for the Dataset of Lyme State County-Level (Population >= 100,000) Disease and Geographic Variables
Statistically Significant Correlations in the Dataset of State-Level Disease and Geographic Variables (MS Variables and Other Variables)  

<table>
<thead>
<tr>
<th>Variable Description</th>
<th>N</th>
<th>Kendall’s tau_b</th>
<th>Spearman’s rho</th>
<th>Pearson</th>
<th>Kendall’s tau_b</th>
<th>Spearman’s rho</th>
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</thead>
<tbody>
<tr>
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<td>0.213*</td>
<td>0.293*</td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sig. (2-tailed): 0.028</td>
<td>Sig. (2-tailed): 0.037</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Breast Cancer Death Incidence per 100,000 Deaths (1998)</td>
<td>51</td>
<td></td>
<td></td>
<td></td>
<td>0.222*</td>
<td>0.330*</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sig. (2-tailed): 0.022</td>
<td>Sig. (2-tailed): 0.018</td>
</tr>
<tr>
<td>Motor Neuron Death Incidence per 100,000 Live (1990)</td>
<td>51</td>
<td>0.569**</td>
<td>0.404**</td>
<td>0.569**</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sig. (2-tailed): 0.000</td>
<td>Sig. (2-tailed): 0.003</td>
<td>0.569**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor Neuron Death Incidence per 100,000 Deaths (1998)</td>
<td>51</td>
<td>0.628**</td>
<td>0.401**</td>
<td>0.628**</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sig. (2-tailed): 0.000</td>
<td>Sig. (2-tailed): 0.004</td>
<td>0.628**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Population Elevation (feet)</td>
<td>51</td>
<td>0.269**</td>
<td>0.404**</td>
<td>0.269**</td>
<td>0.286**</td>
<td>0.401**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sig. (2-tailed): 0.005</td>
<td>Sig. (2-tailed): 0.003</td>
<td>0.269**</td>
<td>Sig. (2-tailed): 0.003</td>
<td>Sig. (2-tailed): 0.004</td>
</tr>
<tr>
<td>Centroid Latitude</td>
<td>51</td>
<td>0.522**</td>
<td>0.669**</td>
<td>0.522**</td>
<td>0.529**</td>
<td>0.692**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sig. (2-tailed): 0.000</td>
<td>Sig. (2-tailed): 0.000</td>
<td>0.522**</td>
<td>Sig. (2-tailed): 0.000</td>
<td>Sig. (2-tailed): 0.000</td>
</tr>
</tbody>
</table>

Table 6. Statistically Significant Correlations in the Dataset of State-Level Disease and Geographic Variables (MS Variables and Other Variables)
<table>
<thead>
<tr>
<th>Statistically Significant Correlations in the Dataset of County-Level (Population &gt;=100,000) Disease and Geographic Variables (MS Variables and Other Variables)</th>
<th>N</th>
<th>MS Death Incidence per 100,000 Live (1990)</th>
<th>MS Death Incidence per 100,000 Deaths (1998)</th>
</tr>
</thead>
</table>
| OSABD Death Incidence per 100,000 Live (1990) | 504 | Kendall’s tau_b: 0.119**  
        Sig. (2-tailed): 0.000  
        Spearman’s rho: 0.174**  
        Sig. (2-tailed): 0.000 | Kendall’s tau_b: 0.068*  
                                      Sig. (2-tailed): 0.023  
                                      Spearman’s rho: 0.101**  
                                      Sig. (2-tailed): 0.024 |
| OSABD Death Incidence per 100,000 Deaths (1998) | 504 | Kendall’s tau_b: 0.064*  
      Sig. (2-tailed): 0.035  
      Spearman’s rho: 0.094*  
      Sig. (2-tailed): 0.0360 | Kendall’s tau_b: 0.079**  
                          Sig. (2-tailed): 0.009  
                          Spearman’s rho: 0.114**  
                          Sig. (2-tailed): 0.010 |
| Breast Cancer Death Incidence per 100,000 Live (1990) | 504 | Kendall’s tau_b: 0.144**  
       Sig. (2-tailed): 0.000  
       Spearman’s rho: 0.209**  
       Sig. (2-tailed): 0.000 | No statistically significant correlation. |
| Breast Cancer Death Incidence per 100,000 Deaths (1998) | 504 | No statistically significant correlation. | Kendall’s tau_b: 0.099**  
                         Sig. (2-tailed): 0.001  
                         Spearman’s rho: 0.146**  
                         Sig. (2-tailed): 0.001 |
| Motor Neuron Death Incidence per 100,000 Live (1990) | 504 | Kendall’s tau_b: 0.134**  
       Sig. (2-tailed): 0.000  
       Spearman’s rho: 0.183**  
       Sig. (2-tailed): 0.000 | Kendall’s tau_b: 0.076*  
                        Sig. (2-tailed): 0.011  
                        Spearman’s rho: 0.106*  
                        Sig. (2-tailed): 0.017 |
| Motor Neuron Death Incidence per 100,000 Deaths (1998) | 504 | Kendall’s tau_b: 0.091**  
       Sig. (2-tailed): 0.002  
       Spearman’s rho: 0.125**  
       Sig. (2-tailed): 0.005 | Kendall’s tau_b: 0.114**  
                        Sig. (2-tailed): 0.000  
                        Spearman’s rho: 0.155**  
                        Sig. (2-tailed): 0.000 |
| External Cause Death Incidence per 100,000 Live (1990) | 504 | No statistically significant correlation. | Kendall’s tau_b: -0.073*  
                        Sig. (2-tailed): 0.016  
                        Spearman’s rho: -0.108*  
                        Sig. (2-tailed): 0.015 |
| External Cause Death Incidence per 100,000 Deaths (1998) | 504 | Kendall’s tau_b: -0.079**  
       Sig. (2-tailed): 0.009  
       Spearman’s rho: -0.117**  
       Sig. (2-tailed): 0.008 | No statistically significant correlation. |
| Centroid Latitude | 504 | Kendall’s tau_b: 0.173**  
      Sig. (2-tailed): 0.000  
      Spearman’s rho: 0.249**  
      Sig. (2-tailed): 0.000 | Kendall’s tau_b: 0.203**  
                        Sig. (2-tailed): 0.000  
                        Spearman’s rho: 0.296**  
                        Sig. (2-tailed): 0.000 |

Table 7. Statistically Significant Correlations in the Dataset of County-Level (Population >=100,000) Disease and Geographic Variables (MS Variables and Other Variables)
| Breast Cancer Death Incidence per 100,000 Deaths (1998) | 123 | No statistically significant correlation. | Kendall’s tau_b: 0.152*  
Sig. (2-tailed): 0.014  
Spearman’s rho: 0.221*  
Sig. (2-tailed): 0.014 |
| External Cause Death Incidence per 100,000 Live (1990) | 123 | No statistically significant correlation. | Kendall’s tau_b: -0.152*  
Sig. (2-tailed): 0.013  
Spearman’s rho: -0.221*  
Sig. (2-tailed): 0.014 |
| Centroid Latitude | 123 | Kendall’s tau_b: 0.136*  
Sig. (2-tailed): 0.027  
Spearman’s rho: 0.199*  
Sig. (2-tailed): 0.027 | Kendall’s tau_b: 0.134*  
Sig. (2-tailed): 0.029  
Spearman’s rho: 0.196*  
Sig. (2-tailed): 0.029 |
| Centroid Longitude | 123 | Kendall’s tau_b: 0.129*  
Sig. (2-tailed): 0.035  
Spearman’s rho: 0.192*  
Sig. (2-tailed): 0.033 | Kendall’s tau_b: 0.149*  
Sig. (2-tailed): 0.016  
Spearman’s rho: 0.226*  
Sig. (2-tailed): 0.012 |

Table 8. Statistically Significant Correlations in the Dataset of Basic Set of Lyme State County-Level (Population >=100,000) Disease and Geographic Variables (MS Variables and Other Variables)
Table 9. Multiple Regression Analysis of Z-Score of MS Death Incidence per 100,000 Deaths (1998) Variable at the State-Level, County-Level, and Lyme State County-Level: All Basic Set Variables Included in the Stepwise Analysis

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Independent Variables</th>
<th>R Square</th>
</tr>
</thead>
</table>
| State-Level (N=51) Z-Score of MS Death Incidence per 100,000 Deaths (1998) | Constant = -4.539E-16  
Z-Score of Motor Neuron Death Incidence per 100,000 Deaths (1998) (B = .354)  
Z-Score of Centroid Latitude (B = .378)  
Z-Score of OSABD Death Incidence per 100,000 Deaths (1998) (B = .259) | .554 |
| County-Level (N=504) Z-Score of MS Death Incidence per 100,000 Deaths (1998) | Constant = .196  
Z-Score of Centroid Latitude (B = .406)  
Z-Score of OSABD Death Incidence per 100,000 Deaths (1998) (B = .200)  
Z-Score of Breast Cancer Death Incidence per 100,000 Deaths (1998) (B = .099) | .109 |
| Lyme State County-Level (N=123) Z-Score of MS Death Incidence per 100,000 Deaths (1998) | Constant = -.867  
Z-Score 1992-1998 Lyme Incidence per 100,000 Live (1990) (B = .176)  
Z-Score of Breast Cancer Death Incidence per 100,000 Deaths (1998) (B = .210)  
Z-Score of Centroid Latitude (B = 1.051) | .134 |

Discussion

The results of the statistical analyses support geographically the proposed connection between Multiple Sclerosis, Lyme, and related diseases. The cartographic display in Figure 1 and Figure 2 show a clear similarity between MS and OSABD, which includes Lyme. Figure 3, which displays the control variable, is very different. The correlations and regression analyses also show a clear geographic co-occurrence of MS and Lyme. Because there is no such relationship with the control variable, External Deaths, a common cause for MS and Lyme is suggested. The strong association of MS with Motor Neuron Disease (ALS) and the weaker, but significant, association with Breast Cancer,
also suggest a possible common environmental, spirochetal, mechanism for these diseases. The well-known relationship between latitude and MS (Warren, 1998) is also seen in these analyses. This relationship is also statistically significant for both Breast Cancer and Motor Neuron Disease at the state and county level as well as Lyme at the county level.

The study, though, is not free of confounding factors. One is the lack of TheDataWeb data for every county because the data for counties with less than 100,000 people in a given state are combined into one number for all such counties. Because Lyme is known to be transmitted by ticks in wooded areas, much of the Lyme incidence occurs in more rural counties in which the boundary between people and nature is less well defined. The lack of data for individual rural counties (those with a population less than 100,000) may have introduced a smearing effect in which some vital Lyme incidence information may have been washed out.

Secondly, the geographical distribution of MS and Lyme deaths might represent not only the presence of a common etiological agent, but common social trends as well. States which have higher rates of diagnosis, in fact, sometimes display lower death rates, because, with experience, doctors in those areas often are more familiar with treating the disease. In addition, often people diagnosed with chronic illnesses move to other, more hospitable regions of the United States like Florida or California, or to regions with better healthcare such as states along the East Coast, particularly for MS. The use of death rates rather than diagnosis rates provided more definitive information, though it introduced the variable of healthcare.

**Conclusions and Next Steps**

Nonetheless, sufficient similarities exist in this study to suggest, but not confirm, a common spirochetal basis for MS and Lyme. This suggests that MS might develop from a secondary spirochete bite, though other factors such as stress and natural aging could also trigger its onset. Spirochetes thrive upon steroids, yet most MS medications use steroids to reduce neural inflammation...
The steroids could be playing additional roles if MS is in fact influenced by spirochetes. Although spirochetes thrive in the presence of steroids, the steroids could bring about the bacteria’s destruction. Acting as a sort of bait, often steroids cause spirochetes expand into their elongated forms, though in this form the bacteria are much more susceptible to T-cell attack (Mattman, 2001). This could explain the success of steroids as a medication and provide some insight for developing more permanent solutions. Spirochetes may also act as a gateway for certain types of cancer. Because the spirochetes are so amorphous, they can mimic the body’s own cells. Looking life self-material, the bacteria manage to fuse with the cell walls and from there eventually control the activities of the cell, often resulting in cancer (Mattman, 2001). The statistical correlations agree with this; the correlation between MS and breast cancer is significant.

The next steps for this work include further geostatistical analysis of existing data as well as an expansion of the dataset. Attempts will be made, for example, to find mortality data for each of the counties with a population under 100,000. It would also be advantageous to be able to add incidence and/or prevalence data for MS to this dataset. Zoonotic vector and host distribution data by county are also critical to the geostatistical analyses. It is fairly well accepted that the tick, specifically the *Ixodes scapularis* (deer tick), is the zoonotic vector for Lyme. Obtaining a detailed distribution of this tick as well as other ticks such as *Amblyomma americanum* (lone star tick) and *Dermacentor variabilis* (dog tick) and comparing the distribution against that of MS is also important.

Because the zoonotic vector cannot transmit a disease without a zoonotic host, a geostatistical analysis which includes the known distribution of possible hosts, should provide valuable information. Suggested hosts include small animals such as mice, deer, and birds. Some studies suggest that birds, especially migratory seabirds might be the zoonotic host for MS spirochetes (Fritzche, 2002). Should migratory seabirds or water foul prove to be the zoonotic host for MS, then it would seem that the first serious experience/attack of MS for history’s first recorded case (Lidwina’s bone-breaking fall while skating
on the frozen canal near her home) might also have been history’s first clue regarding the etiology of the disease. The ponds on which this patron saint of figure skaters loved to skate must have been home to many migratory birds. A geostatistical analysis involving the migratory patterns of birds which traditionally inhabited the area of Ludwina’s home might finally lead to a solution to the 600-year old mystery about the cause of MS.

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