CAMPYLOBACTERIOSIS IN GEORGIA: DEMOGRAPHICS, GEOGRAPHY, LANDUSE, AND WEATHER

by

TIFFIANI JOY MILLER ONIFADE

(Under the Direction of Erin K. Lipp)

ABSTRACT

Campylobacter, the most commonly reported cause of bacterial enteritis in the U.S., is generally considered a foodborne pathogen associated with poultry. In rural agricultural areas, as found in parts of Georgia, environmental transmission associated with land use and other drivers may contribute to campylobacteriosis patterns. We analyzed trends in *Campylobacter* case rates in Georgia, with respect to demographics, geography, landuse, weather, and climate evaluating the importance of environmental drivers in transmission. Annual rates in Georgia have declined 68% from 1987-2003. Case rates were significantly greater for children <5, peaked in summer months, and were greatest in forest and wooded areas. Models were developed, using key weather and climate parameters, to explain the variability in case rates for key areas of the state. Results indicate a significant relationship between environmental variables and case rates in Georgia suggesting that transmission routes in rural areas may be related to factors other than food.

INDEX WORDS: Campylobacter, Campylobacteriosis, Landuse, Weather, El Niño, Climate

CAMPYLOBACTERIOSIS IN GEORGIA: DEMOGRAPHICS, GEOGRAPHY, LANDUSE, AND WEATHER

by

TIFFIANI JOY MILLER ONIFADE

B.S., University of South Carolina, 2002

A Thesis Submitted to the Graduate Faculty of The University of Georgia in Partial Fulfillment of the Requirements for the Degree

MASTER OF SCIENCE

ATHENS, GEORGIA

2005

CAMPYLOBACTERIOSIS IN GEORGIA: DEMOGRAPHICS, GEOGRAPHY, LANDUSE, AND WEATHER

by

TIFFIANI JOY MILLER ONIFADE

Major Professor: Erin Lipp

Committee: Luke Naeher
Dana Cole

Electronic Version Approved:

Maureen Grasso
Dean of the Graduate School
The University of Georgia
December 2005

TABLE OF CONTENTS

Page

CHAPTER

CHAPTER 1

INTRODUCTION

This study seeks to describe and understand the history, trends, and potential drivers of campylobacteriosis in Georgia by examining the literature, performing an epidemiologic analysis, and modeling environmental factors in relation to incidence of the disease in Georgia. Campylobacteriosis is the most commonly reported cause of bacterial enteritis in the United States and the burden of the disease is great. This research has been conducted with the goal of describing particular trends and geographical patterns with the hopes that this research can be used to predict variability in incidence of campylobacteriosis for key areas of Georgia, so that in the future public health measures can be put into place to lessen the transmission. This paper is arranged with a Literature Review (Chapter 2), the analysis of the Epidemiology of Campylobacteriosis in Georgia (Chapter 3), and the modeling of Environmental Factors Influencing Incidence of Campyolbacteriosis in Georgia (Chapter 4).

The aim of the literature review is to formulate the background and history of campylobacteriosis to better understand the known trends in the burden of the disease. It has been reported that *Campylobacter* is the leading cause of diarrheal illness in the United States and worldwide (Allos, 2001), causing more cases in the U.S. than *Shigella* spp. and *Salmonella* combined (USDA, 2003, Altekruse et al., 1999). It is estimated that 1% of the U.S. population is infected yearly by the disease, which primarily causes diarrhea, nausea, and bloody stool, but could lead to life threatening illnesses (WHO, 2003, Buzby and Roberts, 1997, Medema et al., 1996, Nachamkin, 2002, USDA, 2003, Mead et al., 2004). Poultry, milk, and water have been implicated as the major sources of infection (Blaser et al., 1979, Blaser et al., 1983, Palmer et al., 1983, Skirrow, 1991, Fahey et al., 1995, Ashbolt, 2004). This is of particular concern in

Georgia, given the importance of the state's agriculture industry and the role of Georgia as the largest poultry producer in the country. Many efforts have been made to curb the foodborne and nationally a decline in cases has been seen (Van Gilder et al., 1999 Samuel et al., 2000, Samuel et al., 2004). This national decline is significant with a 23% decrease in case rate between 1996 and 2000 (Samuel et al., 2004, CDC, 2004); however, annual case rates remain high (21 per 100,000 persons). A strong seasonal effect has been observed in the United States and elsewhere, where cases peak in the summer months (Padungton and Kaneene, 2003, Miller et al., 2004, Louis et al., 2005, Nylen, 2002, Lindback and Svensson, 2001, Potter et al., 2002). The relationship between infection rates and season of the year suggests a possible link to climate and regional and global weather patterns. Determining the factors that influence transmission of the disease in Georgia as a case study may provide critical information for understanding the epidemiology of this important disease in other rural areas.

The aim of Chapter 3 (Epidemiology of Campylobacteriosis) is to describe the demographic trends of the disease in Georgia. Given the high prevalence of campylobacteriois and the potential for the infection to lead to more serious illnesses, it is important to fully understand the patterns and trends in the demographics of those infected. Most epidemiological studies in the United States have relied on the Centers for Disease Control and Prevention's (CDC) Food Net data (beginning in 1996) for analysis and description of trends in the United States. There are ten states that participate in the FoodNet Program, and although the states are diverse, all the data in some states comes from only a few counties in that state. According to studies done using FoodNet data, Georgia (which includes all 153 counties) reports the lowest case rates annually among the FoodNet states; however, the state claims the highest percentage of hospitalizations due to campylobacteriosis (Samuel et al. 2004). In the United States the incidence rates for camplyobacteriosis are estimated to be 21 cases per 100,000 people, but these rates vary, depending on the food net state, from a high of 48.3 cases per 100,000 people in California to a low of 12.2 cases per 100,000 people in Georgia. Like the variation in incidence rates seen across the United States, there is similar variation in incidence rates across Georgia. The aim here is to evaluate trends over a longer time period (1987-2003) and to look specifically at Georgia because of its diverse environments (urban and rural areas), demographics (gender, race, and age group), completeness of climatological and case data, to provide a more comprehensive analysis of temporal trends and the epidemiology of campylobacteriosis.

The aim of Chapter 4 (Environmental Factors Influencing Incidence of Campylobacteriosis) is to evaluate environmental influences with the goals of explaining additional variability in incidence of campylobacteriosis in Georgia that is not related to demographics. While much is known about the epidemiology of *Campylobacter* the literature is incomplete. The cause of the distinct seasonal pattern with incidence rates peaking in the summer months is still not understood, and the variations between incidence rates across the country has not been fully explained. This seasonal pattern and variation across geographic areas is seen in Georgia and with Georgia's range of land uses from agricultural to urban makes for an informative model for environmental factors on incidence rates. The aim here is to evaluate the clinical cases in Georgia (1987-2003) with respect potential environmental drivers to determine the relationship between large-scale climatic events, weather, land use, water impairment, drinking water source, and campylobacteriosis in Georgia.

REFERENCES

Allos, B.M., 2001. *Campylobacter Jejuni* infections: update on emerging issues and trends. Clinical Infectious Diseases. 32:1201-1206.

Altekruse, S.F., Stern, N.J., Fields, P.I., Swerdlow, D.L., 1999. *Campylobacter jejuni*--an emerging foodborne pathogen. Emerging Infectious Diseases. 5:28-35.

Ashbolt, N.J., 2004. Microbial contamination of drinking water and disease outcomes in developing regions. Toxicology. 198(1-3):229-238.

Blaser, M.J., Cravens, J., Powers, B.W., Laforce, F.M., Wang, W.L., 1979. *Campylobacter* enteritis associated with unpasturized milk, Short communication. The American Journal of Medicine, 67(4):715-718.

Blaser, M.J., Taylor, D.N., Feldman, R.A., 1983. Epidemiology of *Campylobacter Jejuni* Infections. Epidemiology Review. 5:157-176.

Buzby, J.C., Roberts, T., 1997. Estimated Annual Cost of *Campylobacter*-Associated Guillain-Barre Syndrome. USDA/ERS report, Washington DC.

CDC, 2004. Preliminary Food Net Data on the Incidence of Infection with Pathogens Transmitted Commonly Through Food --- Selected Sites, United States, 2003, MMWR. 53(16):338-343.

Fahey, T., Morgan, D., Gunneburg, C., Adak, G.K., Majid, F., Kaczmarski, E., 1995. An outbreak of *Campylobacter jejuni* enteritis associated with failed milk pasteurization. Journal of Infection, 31(2):137-143.

Lindback, J., Svensson, A., 2001. *Campylobacter* infections in Sweden-A statistical analysis of temporal and spatial distributions of notified sporadic campylobacter infections. Mathematical Statistics Stockholm University, Research report 2001:4. ISSN 1650-0377.

Louis, V., Gillespie, I., O'Brien, S., Russek-Cohen, E., Pearson, A., Colwell, R., 2005. Temperature-Driven Campylobacter Seasonality in England and Wales. Applied and Environmental Microbiology. 71(1): 85–92.

Mead, P.S., Slutsker, L., Dietz, V., McCaig, L.F., Bresee, J.S., Sharpiro, C., Griffin, P.M., Tauxe, R.V., Food-Related Illness and Death in the United States, Emerging Infectious Diseases. 5(5):607-625.

Medema, G.J., Teunis, P.F.M., Havelaar, A.H., Haas, C.N., 1996. Assessment of the dose-response relationship of *Campylobacter Jejuni*. International Journal of Food Microbiology, 30(1-2):101-111.

Miller, G., Dunn, G., Smith-Palmer, A., Ogden, I., Strachan, N., 2004. Human camoylobacteriosis in Scotland: seasonality, reagional trends and bursts of infection. Epidemiology Infection. 132:585-593.

Nachamkin, I., 2002. Chronic effects of *Campylobacter* Infection. Microbes and Infection. 4(2002):399-403.

Nylen, G., Dunstan, F., Palmer, S., Andersson, Y., Bager, F., Cowden, J., Feierl, G., Galloway, Y., Kapperud, G., Megraud, F., Molbak, K., Petersen, L., Ruutu, P., 2002, The seasonal distribution of *Campylobacter* infection in nine European countries and New Zealand. Epidemiology infections. 128(3):383-390.

Palmer, S.R., Gulley, P.R., White, J.M., Pearson, A.D., Suckling, W.G., Jones, D.M., Rawes, J.C.L., Penner, J.L., 1983. Water-Borne Outbreak of *Campylobacter* Gastroenteritis. The Lancet. 321(8319):287-290.

Padungton, P., Kaneene, J.B., 2003. *Campylobacter* spp. in human, chickens, pigs and their antimicrobial resistance. Journal of Veterinary Medical Science. 65(2):161-170.

Potter, R., Kaneene, J., Gardiner, J., 2002. A comparison of *Campylobacter jejuni* enteritis incidence rates in high and low poultry density counties: Michigan 1992-1999. Vector Borne Zoonitic Dis. 2(3):137-143.

Samuel, M. Reilly, K., Shallow, S., Marcus, R., Segler, S., McGivern, T., Kassenborg, H., Hollinger, K., Vose, D., Bartholomew, M., Kennedy, M., Vugia, D., 2000. Burden of *Campylobacter* Infection in United States and Declining Trend in California, FoodNet 1996-1998. 2nd International Conference on emerging Infectious Diseases, Atlanta, GA, July.

Samuel, M.C., Vugia, D.J., Shallow, S., Marcus, R.,Segler, S., McGivern, T., Kassenborg,H., Reilly, K., Kennedy, M., Angulo, F., Tauxe, R.V., 2004. Epidemiology of Sporadic *Campylobacter* Infection in the United States and Declining Trend in Incidence, Food Net 1996-1999. CID, 38, S165-S174.

Skirrow, M.B., 1991, Epidemiology of *Campylobacter* enteritis. International Journal of Food Microbiology, 12(1):9-16.

USDA (US Food and Drug Administration), 2003, posting date. Foodborne Pathogenic Microorganisms and Natural Toxins Handbook. <http://vm.cfsan.fda.gov/~mow/chap4.html>. Online.

Van Gilder, T., Vugia, D., Fiorentino, T., Segler, S., Carter, M., Smith, K., Morse, D., Cassidy, M., Angulo, F., 1999. Decline in *Salmonella* and *Campylobacter* but not *E. coli* O157 isolation rates in FoodNet sites: Farm, food, or fluctuation? 37th Annual Meeting of the Infectious Disease Society of America, Philadelphia, PA, November.

WHO (World Health Organization), 2003. Quantifying selected major risks to health. The world health report 2002. World health Organization. Geneva. (Chapter 4).

CHAPTER 2

LITERATURE REVIEW

INTRODUCTION

The notion that climate and health are linked was suggested as far back as Hippocrates, where he related the two around 400 BC (Rees, 1996). Through the years the idea lingered and in the Middle Ages herbalists would prescribe different remedies depending on the season. Today, we no longer believe that weather itself causes disease, but we are beginning to understand how it can create conditions for disease-causing organisms to thrive and migrate into areas where human exposure may occur, such as water sources. These types of relationships and the links to a changing global climate have been identified for diseases ranging from malaria and dengue fever to cholera (Lipp et al., 2002).

Campylobacter is the leading cause of diarrheal illness in the United States and worldwide (Allos, 2001), causing more cases in the U.S. than *Shigella* spp. and *Salmonella* combined (USDA, 2003, Altekruse et al., 1999). It is estimated that 1% of the U.S. population is infected yearly by the disease, which primarily causes diarrhea, nausea, and bloody stool, but could lead to life threatening illnesses (WHO, 2003, Buzby and Roberts, 1997, Medema et al., 1996, Nachamkin, 2002, USDA, 2003, Mead et al., 2004). Poultry (Blaser et al., 1983, Skirrow, 1991), milk (Blaser et al., 1979, Fahey et al., 1995), and water have been implicated as the major sources of infection (Blaser et al., 1983, Palmer et al., 1983, Ashbolt, 2004). This is of particular concern in Georgia, given the importance of the state's agriculture industry and the role of Georgia as the largest poultry producer in the country. Many efforts have been made to curb transmission via the food borne route, and nationally a decline in cases has been seen (Van Gilder et al., 1999, Samuel et al., 2000, Samuel et al., 2004). This decline is significant 23% between 1996 and 2000 (Samuel et al., 2004, CDC, 2004) however, case rates remain high (12.6 per 100,000 persons). A strong seasonal effect has been observed in the United States and elsewhere, where cases peak in the summer months (Padungton and Kaneene, 2003, Miller et al., 2004, Louis et al., 2005, Nylen, 2002, Lindback and Svensson, 2001, Potter et al., 2002). The relationship between infection rates and season of the year suggests a possible link to climate and regional and global weather patterns. Determining the factors that influence transmission of the disease in Georgia as a case study may provide critical information for understanding the epidemiology of this important disease in other rural areas.

CAMPYLOBACTER spp.

Campylobacter has been reported as a cause of human enteric disease for over 100 years and it has probably existed for many centuries (Kist, 1985). The first mention of a *Campylobacter*-like bacterium occurs in 1886 when Theodor Escherich isolated a spiral bacterium from the intestinal mucus of people who died of diarrheal disease and from the stool of others with enteric diseases (Kist, 1985). Because of its similar comma-shaped appearance it was classified in the *Vibrio* genus (Sebald, 1963). In 1913, the same bacterium was isolated from bovine fetuses (Kist, 1985). It was not until 1957, that King described this "*Vibrio*" as the agent for the enteritis and later linked it to animals (Kist, 1985). With further investigation, Sebald and Veron (1963) found that the metabolism of this *Vibrio* was very different from others in the genus; this lead to the classification of a new genus, *Campylobacter* (from Greek meaning curved rod) (Sebald and Veron, 1963). In 1968, a technique was developed, and then improved in 1977, to isolate *Campylobacter* from feces. (Kist, 1985) This procedure allowed for further study of *Campylobacter* leading to more diagnoses and treatment. For more than thirty years, *Campylobacter* has been the leading cause of diarrheal illness in the United States, causing more disease than *Shigella* spp. and *Salmonella* spp. combined (USDA, 2003, Altekruse et al., 1999).

Campylobacter spp. are motile, Gram-negative slender bacteria with a curved rod-shape. They range in size from 0.2-0.9 µm in width to 0.5-5 µm in length (Nachamkin, 2002). The flagellum can be monotrichous or amphitrichous and moves by corkscrew motion. Members of this genus are microaerophillic and thrive in an environment with 3-5% oxygen, 2-10% carbon dioxide, and 85% nitrogen. They are also thermopihlic, with optimum growth conditions at temperatures between 37 and 42° C, with better growth at the upper end of this range. *Campylobacter* are susceptible to environmental stresses such as freezing, drying, acidic conditions, and salinity (Altekruse, 1999).

The campylobacteria (which includes the genera *Campylobacter* and *Arcobacter*), also knows as campylobacters can be divided into two classes based on a positive or negative catalase reaction. Catalase-negative campylobacters are sensitive to oxygen and require lower oxygen content (3% O_2) for growth. They are also able reduce nitrates and nitrites. Catalase-positive campylobacters can thrive in environments with higher oxygen content (5% O_2) and are able to reduce nitrates but not nitrites. *Campylobacter jejuni* and *C. coli,* the major causes of campylobacteriosis, are both catalase-positive campylobacters (Butzler, 1984).

Various warm-blooded animals serve as *Campylobacter* reservoirs including poultry, cattle, swine, sheep, dogs, cats, and rodents (Atwill, 1995, Stanley and Jones, 2003). The USDA estimates that between 20 and 100% of retail chicken is contaminated with *Campylobacter*

(USDA, 2003). Additionally, natural waters, sediment and sewage sludge have been found to contain this pathogen (Lucey et al., 2000, Ashbolt, 2004, Sahlstrom et al., 2004, Jones, 2001).

Campylobacteriosis occurs as sporadic cases or outbreaks. Outbreaks come from a single source such as in the town of Bennington, VT where 200 people were infected by consumption of non-chlorinated drinking water (USDA, 2003). Sporadic cases are often thought to have a foodborne or waterborne origin such as eating undercooked poultry or drinking unpasturized milk or untreated water (CDC, 2004). The infectious dose is low (400-500 bacteria) so one drop of juice from raw meat can cause infection (CDC, 2004).

RESERVOIRS AND TRANSMISSION OF CAMPYLOBACTER

Because the ideal growing environment for *Campylobacter* is at a temperature of 42° and has an obligate host requirement (Altekruse et al., 1999), it does not proliferate easily outside of the gut (Ketley, 1997). Therefore, reservoirs provide critical links to human disease. Livestock, domestic animals, and birds are some of the commonly known reservoirs for *Campylobacter* spp. (Atwill, 1995, Stanley and Jones, 2003) and are shed in the feces of these animals in various concentrations throughout the year. *Campylobacter jejuni* can be isolated year round from slurry tanks around sheep farms (Stanley and Jones, 2003). Land application of fecal waste could lead to further contamination of the environment and possible runoff into nearby waterways.

Despite its obligate host requirement, *Campylobacter* are routinely found in environmental sources such as water and sewage (Buswell et al., 1998, Lucey et al., 2000, Ashbolt, 2004, Sahlstrom et al., 2004, Jones, 2001). For short periods of time, *Campylobacter* spp. can survive in sterile water but their survival increases when associated with a biofilm and at lower temperatures (Bruswell et al. 1998). In sterile water at 37^{o} C *Campylobacter* survived an average of 21.8 hours while at lower temperatures the survival times went up with highest survival in sterile water at 4^{o} C (201.6 hours). When autochthonous microflora were added to the microcosms to better represent the natural environment, survival rates increased significantly to ~ 200 hours at 30^{o} C and ~ 550 hours at 4 ^{o} C (Bruswell et al. 1998). Furthermore, by infecting protozoa (i.e., *Acanthamoeba polyphaga*) *C. jejuni* is able to prolong its survival in the environment and outside of a vertebrate host (Axelsson-Olsson et al., 2005).

One proposed environmental model for the transmission of campylobacteriosis to humans (Skelly and Weinstre, 2003) suggests that humans are exposed to the pathogen through feces, food, and aquatic environments. While *Campylobacter* has been found in all these environments, the modes of movement between them are not fully understood.

CAMPYLOBACTERIOSIS

The disease caused by any member of the *Campylobacter* genus is termed campylobacteriosis or *Campylobacter* enteritis. *Campylobacter jejuni* causes over 99% of human cases (CDC, 2004). *Campylobacter* enteritis is a disease of interest to public health because of its high frequency in the population and potential chronic effects. The symptoms of the disease include mild or severe diarrhea often accompanied with fever and traces of blood in the stool. Symptoms often appear within two to five days of exposure and last for one week. In immunocompromised persons, the bacteria can spread to the bloodstream and cause life-threatening infection. *Campylobacter* infection is also believed to be a precursor to Guillian-Barré Syndrome, an autoimmune disorder that can cause paralysis (Nachamkin, 2002, Takanhashi, 2005). One in 1,000 campylobacteriosis cases lead to Guillian-Barré syndrome (Allos, 1997).

Campylobacteriosis patients are treated with antibiotics and generally recover within one to two days. Without treatment, *Campylobacter* continues to be excreted even after a patient has recovered; cells may be shed in the feces for days to several weeks post-infection (Bulzer, 1984). Due to the amount of time that the organism is excreted there are potential environmental ramifications such that if sewage is not properly treated further transmission of disease is possible.

Campylobacteriosis is a global health concern. In developing countries, rates for *Campylobacter* infection are high, with 5% to 20% of the population infected annually, depending on the country (Oberhelman and Taylor, 2000). The incidence of campylobacteriosis for children under five years old in developing countries is 40,000 cases per 100,000 children under five (40% of the <5 population; Coker et al. 2002). In general, there is an increasing incidence of the disease in developing countries and an expanding spectrum of related diseases caused by *Campylobacter*. With the high incidence of HIV in developing countries there is consequently a greater potential for HIV-related deaths due to *Campylobacter* (Coker et al. 2002).

In developed countries, the rate of infection is lower, for example 1% of the United States population is infected each year (WHO, 2004). In the United States and other developed countries, *Campylobacter* remains the most frequently isolated bacterial enteric pathogen from clinical samples (WHO, 2004). In 1997, the reported incidence of campylobacteriosis in the United States was 25.2 people for every 100,000 people; however, it is estimated that about 1% of the United States population are actually infected each year with *Campylobacter* (WHO, 2004). In the U.S., U.K., Canada, Denmark case rates are declining (Samuel et al., 2004, FDSCG, 2002, Samuelsson, 2004); however, in Australia cases have risen dramatically (CDA, 2005). The prevalence of the disease among children under 5 is also noted in developed nations but this peak is less dramatic and the disease is still common among other age groups (Coker et al. 2002, Padungton and Kaneene, 2003).

TRENDS IN CAMPYLOBACTERIOSIS

Demographics

Gender. In general, *Campylobacter* prevalence is higher in males (Potter et al., 2002, Samuel et al. 2004). This trend is not well understood; however, it has been suggested that this is due to poor food handling practices more common among men or physiological differences between the genders (Altekruse et al, 1999, Louis et al., 2005).

Age. Prevalence of *Campylobacter* infections is distributed bimodally across age groups with the greatest number of cases reported for children under the age of five and a second, smaller, peak in the 20-29 age group (Potter et al., 2002, Samuel et al., 2004). Several hypotheses have been proposed to explain this trend. First, parents are more likely to take their young children and infants to the doctor for symptoms of gastroenteritis (Friedman et al., 2000). Furthermore, children get sick more frequently due to an immature immune system. Subsequently, infections in childhood act to build immunity such that infection is less likely in later years (Perez-Perez and Blaser, 2005). The second peak in campylobacteriosis among the 20-29 year olds has not been explained.

Race. There has been little research in the area of race and campylobacteriosis. However, in one study in the U.S., Blacks were noted to have significantly lower rates than Whites, Hispanics, and Asians (Samuel et al. 2004).

Seasonality

In the U.S. and other parts of the world, there is a distinct peak in cases in the summer months (Miller et al., 2004, Louis et al., 2005, Nylen, 2002, Lindback and Svensson, 2001, Potter et al., 2002). The cause of this apparently universal seasonal trend is not fully understood. Some hypotheses have included increased risk of infection during peak summer travel times (Miller et al. 2004), increased consumption of poultry products in warmer weather and a higher likelihood of eating outdoors and outside of the home, in general (Friedman et al. 2000), and spread of the pathogen via flies (Hald et al., 2004). In a more systematic analysis, Louis et al. (2005) found a significant relationship between temperature change in England and Wales and seasonal campylobacteriosis rates.

Declining Cases in the United States

Between 1996 and 2003, there was a significant decline in *Campylobacter* cases in the United States (Van Gilder et al., 1999, Samuel et al., 2000, Samuel et al., 2004). This is noteworthy because the incidence rates are on the rise in other countries (Altekruse, 1999), particularly Austrailia and New Zealand. Data from states participating in the Centers for Disease Control and Prevention (CDC) FoodNet program show a 23% decline in *Campylobacter* cases from 1996-2000, with similar declines across all races, age groups, and genders (Samuel et al. 2004). Possible explanations for this decline include improvements in the meat processing and poultry industries due to Hazard Analysis and Critical Control Points (HACCP) and Pathogen Reduction (PR) rule implementations (Buchanan and Whiting, 1998, Hariharan et al., 2004, Keener, 2004). These rules, which went into effect in 1997, require the use of more water when processing and disinfection of that water with trisodium phosphate.

THE ROLE OF CLIMATE IN INFECTIOUS ENTERIC DISEASE

El Niño-Southern Oscillation

The term el niño means small boy in Spanish; capitalized it refers to the infant Jesus (El Niño). In 1882, Carrillo (as described by Glantz, 2001), reported unusually warm ocean currents off the coast of Peru at the Geographical Society Conference. He named the phenomenom El Niño due to its consistent occurrence around Christmas time. Later other scientists observed its association with regional climatological changes, such as increased rainfall and higher temperatures in Peru (Glantz, 2001). By the late 1800s researchers were beginning to correlate these El Niño events to interannual climate anomalies in other parts of the world, including India and Australia (Glantz, 2001).

The term Southern Oscillation was given by Gilbert Walker in 1923 (Glantz, 2001). This name was based on the apparent see-saw in surface pressure between the eastern and western portions of the Pacific Ocean. In 1937, Walker and Bliss also found that these periodic pressure oscillations were related to weather changes such as rainfall patterns and wind fields in the Pacific (Glantz, 2001). In the 1960s, synoptic observations of sea surface temperature and air pressure over the Pacific allowed scientists to link El Niño and the Southern Oscillation phenomena. El Niño events (warm water) corresponded to the negative pressure phase of the Southern Oscillation (i.e., high pressure over the western and low pressure over the eastern Pacific Ocean between Tahiti, French Polynesia, and Darwin, Australia). This phase also brought relaxed trade winds and heavy rainfall in the central and eastern equatorial Pacific. Conversely, La Niña events (cool water) corresponded to the positive pressure phase of the Southern Oscillation, with low pressure over the western and high pressure over the eastern Pacific Ocean and increased trade winds and decreased rainfall over central and eastern equatorial Pacific

(Philander 1990). Because these terms described the same phenomena, it is now known as El Niño-Southern Oscillation (ENSO).

The effects of global climatic events, such as ENSO, have varying influence on local weather throughout the world, from monsoons to drought. For example, during El Niño events, disruption of the ocean-atmosphere system in the tropical Pacific causes the trade winds to relax and reduce upwelling. This causes an increase in ocean surface temperature in the eastern equatorial Pacific. Rainfall then follows the warm water eastward resulting in changes in atmospheric circulation and changes in weather around the world (NOAA, 1997).

ENSO EFFECTS

ENSO events have immediate effects around the Pacific which include rain in South America and drought in Australia during El Niño conditions (Zimmer, 1999).These events also have far reaching effects that result in anomalies in local climate patterns around the world (e.g., in El Niño years 35 per 1000 people are affected by natural disasters globally) (Kovats et al. 2003). Today much research has been done to further examine these teleconnections, and the effects on rainfall have been studied in many parts of the world.

Based on reports from National Oceanographic and Atmospheric Administration (NOAA) there is a general trend to the weather patterns caused by ENSO. The strongest connections, globally, are noted in the winter when the sea surface temperatures or sea surface pressures reach their peak anomalies related to ENSO. For example in the southeast U.S., El Niño winters are associated with extreme increases in precipitation whereas La Niña winters are linked to significant decreases in precipitation relative to 'neutral' conditions (NOAA, 1997). Conversely, El Niño summers (when the ENSO is less dramatic), are associated with slight decrease in precipitation and La Niña summers show a slight increase in precipitation (NOAA, 1997).

While regional precipitation anomalies such as those reported for the southeast U.S. have been frequently correlated with ENSO indices (either measured by sea surface temperature anomalies (SSTA) in the eastern equatorial Pacific or the pressure difference described by the Southern Oscillation Index (SOI)), some recent studies show that local scale changes in precipitation may be more variable (e.g., Schmidt et al. 2001, El-Askary et al., 2004). These studies are of particular importance because they reveal that the connections between ENSO and local weather patterns exist and given that these patterns are not uniform it further suggests that local ENSO effects are specific to geographic areas. Understanding local precipitation response to predictable climate anomalies, such as ENSO, provides an important tool for effective management of water resources and protection of water supplies (Chen et al., 2004).

PRECIPITATION EFFECTS ON PATHOGEN LOADING IN WATERSHEDS

Changes in precipitation can affect the loading of enteric pathogens in waterways. Significant runoff and subsequent contamination of waterways after extreme rain events is a common occurrence (e.g., Lipp et al. 2001, Lipp et al. 2002, Leeming et al. 1998; Patz, 2001). The presence of waterborne disease agents, including *Giardia* cysts, *Cryptosporidium* oocysts, and enteric viruses, have been positively correlated with rainfall (Graczyk et al. 1999, Patz, 2001, Kristemann et al., 2002, Lipp et al., 2001). Microbial contamination in drinking water reservoirs in parts of Germany has been shown to increase by as much as 1- to 2-logs during extreme rainfall and runoff events (Kristemann et al., 2002). In areas, such as Florida, where wet winters are correlated with El Niño events, a direct relationship between the ENSO state and water quality (measured by fecal coliform bacteria) has been noted (Lipp et al. 2001). This is one of the only studies that has been able to relate ENSO events to the change in local weather patterns and then to discrete changes in water quality (Tampa Bay, FL).

LANDUSE

The transport of pathogens via runoff can increase concentrations of waterborne pathogens in impacted watersheds (Ferguson el al., 2003); in turn the amount and quality of run off is directly related to land use. Runoff is affected by the amount and intensity of precipitation, surrounding land use, soil type, and topography (USGS, 2005, Tsubo, 2005, Sheresta, 2003). Sherestha (2003) suggested that urban land use resulted in the highest level of runoff followed by residential (village) areas, agricultural land, pasture land, and forests. These are related to land cover by impervious surfaces. Changes in land use have been associated with the emergence of pathogenic diseases in many regions of the world (Patz, 2001). Some of the land use changes include human settlement, commercial development, and road construction. Combinations of these types of changes have been linked with emergence of diseases such as malaria and schistosomiasis (Patz, 2001). Several studies have further implicated land use in the contamination of waterways (Interlandi & Crockett, 2002). Significant concentrations of fecal indicator microbes are found in waters that drain from confined livestock farming operations (Crowther et al., 2001). This information suggests that along with weather factors, the use of the land is an important factor in the amounts of pathogens in watersheds.

Sewage disposal

Proper disposal of wastewater is also an important consideration when investigating modes of disease transmission. In Georgia, 62% of homes use public means for sewage disposal

(U.S. Census, 1990). This type of disposal is regulated by local, state, or federal agencies. The remainder of the State uses other means of disposal, usually a private on-site disposal system (OSDS; e.g., septic systems and cess pits), which do not include a mechanism for disinfection of waste. Septic systems include a tank which allows solid material to collect and scum to surface while the liquid portion is allowed to go into a leach field where the soil can assist in the filtration of microbes and organics from the waste water (American Ground Water Trust, 2005). Cesspools are less common and are simply pits where sewage is dumped. Local ordinances provide guidelines on how to properly locate these private systems but beyond that it is the homeowner's responsibility to ensure it is working properly. This is of particular importance because of the known links between sewage-contaminated water and human illness (Haflinger, 1999, Kambole, 2003, Exner, 2001). Public sewage treatment facilities have more stringent guidelines; however, all facilities are not required to perform tertiary levels of treatment which may be necessary to kill many microbial contaminants. Sahlstrom et al. (2004) found that 55% of sludge samples treated by common methods for secondary treatment (sedimentation, mesophilic or thermophilic aerobic digestion, composting, and storage) were positive for *Salmonella* and other potentially harmful microbes. Sludge, also known as biosolids, is often applied directly to land for use as fertilizer and may present a risk for infectious diseases (Sahlstrom et al., 2004).

Drinking Water Source

Waterborne disease agents have been identified as a major concern for human health (Patz, 2001). It has been estimated that in North America, 15-30% of gastrointestinal disease is a result of contaminated water (Ashbolt, 2004). Once pathogens are in the watersheds, proper treatment of the water is required before consumption to prevent human infection and disease, including, campylobacteriosis (Ashbolt, 2004).

Waterborne disease outbreaks have been a problem in the United States for many years. The US Environmental Protection Agency (EPA) regulates public drinking water systems that serve over 25 people; nationwide, these public systems serve 90% of the population (US Census, 1990). For those that are not served by public sources, individual wells are used. These wells are not regulated by the EPA but suggestions are given to prevent contamination of the water and each state determines the exact ordinances for that state. Some of the EPA's suggestions are for wells to be placed at least 50 feet from septic tanks and leach fields, silos, and livestock yards, 100 feet from petroleum tanks, liquid tight manure storage, and fertilizer storage and handling, and 250 feet from manure stocks (EPA, 2005). The regulation of these water sources are the responsibility of the homeowner who must carry out any testing to ensure water safety. The depth of private wells can also indicate likelihood of becoming contaminated. Drilled wells (deep wells of 100-1000 feet), are drilled below the bedrock and get water from confined ground water sources, while dug wells (10-30 feet deep) and bored or driven wells (30-100 feet deep), tap water from the saturated zone above the bedrock (an unconfined water source) which is more easily contaminated (EPA, 2005).

CONCLUSIONS

Published literature has shown the relationship of climate to health and disease. Large climatic events (e.g., ENSO) affect global and local weather patterns resulting in increased precipitation and runoff. Based on the type of land use this runoff can be great and can contain pathogens such as *Campylobacter*. This pathogen is able to persist in natural waters, where humans may be exposed. The source of the drinking water may also be a key factor in the transmission of the disease. The goal of the research, presented in this thesis, is to relate land use, weather, and other environmental factors with changes in Georgia *Campylobacter* case rates with the long term aim of linking key environmental drivers with climate change and variability (i.e., ENSO).

REFERENCES

American Ground Water Trust, 2005, <http://www.agwt.org/SepticSystems.htm.> Online.

Allos, B.M., 1997. Association between *Campylobacter* infecection and Guillan-Barré syndrome. Journal of Infectious Diseases. 176:S125-128.

Allos, B.M., 2001. *Campylobacter jejuni* infections: update on emerging issues and trends. Clinical Infectious Diseases. 32:1201-1206.

Altekruse, S.F., Stern, N.J., Fields, P.I., Swerdlow, D.L., 1999. *Campylobacter jejuni*--an emerging foodborne pathogen. Emerging Infectious Diseases. 5:28-35.

Ashbolt, N.J., 2004. Microbial contamination of drinking water and disease outcomes in developing regions. Toxicology. 198(1-3):229-238.

Atwill, E.R., 1995, Microbial Pathogens Excreted by livestock and Potentially Transmitted to Humans through Water. Veterinary Medicine Teaching and Research Center, University of California Davis.

Axelsson-Olsson, D., Waldenstrom, J., Broman, T., Olsen, B., Holmberg, M. 2005. Protozoan *Acanthamoeba polyphaga* as a Potential Reservior for *Campylobacter jejuni*. Applied and Environmental Microbiology. 71(2):987-992.

Blaser, M.J., Cravens, J., Powers, B.W., Laforce, F.M., Wang, W.L., 1979. *Campylobacter* enteritis associated with unpasturized milk, Short communication. The American Journal of Medicine, 67(4):715-718.

Blaser, M.J., Taylor, D.N., Feldman, R.A., 1983. Epidemiology of *Campylobacter jejuni* Infections. Epidemiology Review. 5:157-176.

Buchanan, R.L., Whiting, R.C., 1998. Risk Assessment: A Means for Linking HACCP Plans and Public Health. Journal of Food Prot. 61:1531-1534.

Buswell, C.M., Herlihy, Y.M., Lawrence, L.M., McGuiggan, J.T.M., Marsh, P.D., Keevil, C.W., Leach, S.A., 1998. Extended Survival and Persistence of *Campylobacter* spp. in Water and Aquatic Biofilms and their Detection by Immunoflourescent-Antibody and –rRNA Staining. Applied and Environmental Microbiology. 64, 733-741.

Butzler. 1984. *Campylobacter* infection in man and animals. P 6. Boca Raton Florida, CRC Press.

Buzby, J.C., Roberts, T., 1997. Estimated Annual Cost of *Campylobacter*-Associated Guillain-Barré Syndrome. USDA/ERS report, Washington DC.

CDA (Communicable diseases Australia). 2005. National Notifiable Diseases Surveillance System. < http://www1.health.gov.au/cda/Source/Rpt_2_sel.cfm> online.

CDC (Center for Disease Control), 1991. *Campylobacter* enteritis—New Zeland, 1990, MMWR. 40(7):116-117,123.

CDC, 2004. Preliminary Food Net Data on the Incidence of Infection with Pathogens Transmitted Commonly Through Food --- Selected Sites, United States, 2003, MMWR. 53(16):338-343.

CDC, 2004. *Campylobacter* Infections. <Http://www.cdc.gov/ncidid/dbmd/diseaseinfo/campylobacter_t.htm>. Online.

Chen, Z., Grasby,S.E., Osadetz, K.G., 2004. Relation between climate variability and ground water levels in the upper carbonate aquifer, southern Manitoba Canada. Journal of Hydrology, 290, 43-62.

Coker, A.O., Isokpehi, R.D., Thomas, B.N., Amisu, K.O., Obi, C.L., 2002. Human Campylobacteriosis in Developing Countries. Emerging Infectious Diseases. 8(3):237-243.

Crowther, J., Kay, D., Wyer, M.D., 2002. Faecal-indicator concentrations in waters draining lowland pastoral catchments in the UK: relationships with land use and farming practices. Water Research. 36 (7), 1725-1734.

EL-Askary, H., Sarkar, S., Chiu, L., Kafatos, M., El-Ghazawi, T., 2004. Rain gauge derived precipitation variability over Virginia and its relation with the El Niño Southern Oscillation. Advances in Space Research 33 (3), 338-342.

EPA (Environmental Protection Agency) 2005. Private drinking water wells. <http://www.epa.gov/safewater/privatewells>. Online.

Exner, M., Hartemann, P., Kistemann, T., 2001, Hygiene and health—the need for a holistic approach., Association for Professionals in Infection Control and Epidemiology, Inc. 29, 228-231.

Fahey, T., Morgan, D., Gunneburg, C., Adak, G.K., Majid, F., Kaczmarski, E., 1995. An outbreak of *Campylobacter Jejuni* enteritis associated with failed milk pasteurization. Journal of Infection, 31(2):137-143.

Ferguson, C., de Roda Husman, A.M., Altavilla, N., Deere, D., Ashbolt, N., 2003. Fate and Transport of Surface Water Pathogens in Watersheds. Critical Reviews in Environmental Science and Technology. 33 (3), 299-361.

FDSCG (Foodborne Disease Strategy Consultative Group). 2002. Incidence and trends in foodborne disease in the UK in the years 2001-2002. <www.foodstandards.gov.uk/multimedia/pdfs/foodbornediseasetrends.pdf.>. Online.

Friedman, C., Neimann, J., Wegener, H., Tauxe, R., 2000. Epidemiology of *Campylobacter jejuni* infections in the United States and Other Industrialized nations, p. 121-138. In: Campylobacter, 2nd Ed. (Nachamkin, I. and Blaser, M. eds.), ASM Press, Washington, DC.

Glantz, 2001. Currents of Change, Cambridge university press2001 NY, NY pg 1-43.

Graczyk, T., Evans, B., Shiff, C., Karreman, H., Patz, J., 2000. Environmental and Geographical Factors Contributing to Watershed Contamination with *Cryptosporidium parvum* Oocysts. Academic Press, Environmental Research Section A. 82:263-271.

Hafliger, D., Huber, Ph., Luthy, J. 1999. Outbreak of viral gastroenteritis due to sewage-contaminated drinking water. International Journal of Food Microbiology. 54, 123-126.

Hald, B., Skovgard, H., Bang, D., Pedersen, K., Dybdahl, J., Jespersen, J., Madsen, M. 2004. Flies and *Campylobacter* Infection of Broiler Flocks. Emerging Infectious Diseases. 10(8):1490-1492.

Hariharan, H., Murphy, G.A, Kempp, I., 2004. *Campylobacter Jejuni*: Public health Hazards and potential control methods in poultry: a review. Vet Med. 49(11):441-446.

Interlandi, S.J., Crockett, C.S., 2003. Recent water quality trends in the Schuylkill River, Pennsylvania, USA: a preliminary assessment of the relative influences of climate, river discharge and suburban development. Water Research. 37 (8), 1737-1748.

Jones, K., 2001. The *Campylobacter* Conundrum. Trends in Microbiology. 9(8):365-366.

Jones, K., 2001. *Campylobacters* in water, sewage and the Environment. Journal of Applied Microbiology. 90,68S-79s.

Kambole, M.S., 2003. Managing the water quality of Kafue River. Physics and Chemistry of the Earth. 28, 1105-1109.

Keener, K.M., Bashor, M.P., Curtis, P.A., Sheldon, B.W., Kathariou, S., 2004. Comprehensive Review of *Campylobacter* and Poultry Processing. Comprehensive Reviews in Food Science and Food Safety. 3:105-116.

Ketley, J.M., 1997. Pathogenesis of enteric infection by *Campylobacter*. Microbiology. 143:5-21.

Kist, M. 1985. The historical background of *Campylobacter* infection: new aspects p. 23-27. In A.D. Pearson, M.B. Skirrow, H. Lior, and B. Rowe (ed.), *Campylobacter* III. Public Health Laboratory Service, London, United Kingdom.

Kistemann, T., Claben, T., Koch, C., Dangendorf, F., Fischeder, R., Gebel, J., Vacata, V., Exner, M., 2002, Microbial load of Drinking Water Reservoir Tributaries during extreme Rainfall and Runoff. Applied and Environmental Microbiology. 68, 2188-2197.

Kovats, R., Bouma, M., Hajat, S., Worrall, E., Haines, A., 2003. El Nino and Health. Lancet. 362: 481-489.

Lindback, J., Svensson, A., 2001. *Campylobacter* infections in Sweden-A statistical analysis of temporal and spatial distributions of notified sporadic campylobacter infections. Mathematical Statistics Stockholm University, Research report 2001:4. ISSN 1650-0377.

Lipp, E.K., Schmidt, N., Luther, M.E., Rose, J.B., 2001, Determining the effects of El Nino-Southern Oscillation events on Coastal Water Quality. Estuaries. 24. 491-497.

Lipp, E.K., Huq, A., Colwell, R.R., 2002. Effects of Global Infectious Disease: the Cholera Model. Clinical Microbiology Reviews. 15, 757-770.

Leeming, R., Bate, N., Hewlett, R., Nichols, P.D., 1998. Discriminating faecal pollution: a case study of stormwater entering Port Phillip Bay, Australia. Water Science and Technology. 38 (10), 15-22.

Louis, V., Gillespie, I., O'Brien, S., Russek-Cohen, E., Pearson, A., Colwell, R., 2005. Temperature-Driven *Campylobacter* Seasonality in England and Wales. Applied and Environmental Microbiology, In Review.

Lucey, B., Crowley, D., Moloney, P., Cryan, B., Daley, M., O'Halloran, F., Threlfall, E.J., Fanning, S., 2000. *Campylobacter* spp. of human and Animal Origin. Emerging Infectious Diseases. 6(1):.

Mead, P.S., Slutsker, L., Dietz, V., McCaig, L.F., Bresee, J.S., Sharpiro, C., Griffin, P.M., Tauxe, R.V. 2004, Food-Related Illness and Death in the United States, Emerging Infectious Diseases. 5(5):607-625.

Medema, G.J., Teunis, P.F.M., Havelaar, A.H., Haas, C.N., 1996. Assessment of the dose-response relationship of *Campylobacter Jejuni*. International Journal of Food Microbiology, 30(1-2):101-111.

Miller, G., Dunn, G., Smith-Palmer, A., Ogden, I., Strachan, N., 2004. Human camoylobacteriosis in Scotland: seasonality, reagional trends and bursts of infection. Epidemiology Infection. 132:585-593.

Nachamkin, I., 2002. Chronic effects of *Campylobacter* Infection. Microbes and Infection. 4(2002):399-403.

NOAA (National Oceanic and Atmospheric Asscoiation), 1997. Our Changing Climate. Reports to the Nation on Our Changing Planet. 4, 1-28.

Nylen, G., Dunstan, F., Palmer, S., Andersson, Y., Bager, F., Cowden, J., Feierl, G., Galloway, Y., Kapperud, G., Megraud, F., Molbak, K., Petersen, L., Ruutu, P., 2002, The seasonal distribution of *Campylobacter* infection in nine Euroean countries and New Zeland. Epidemiology infections. 128(3):383-390.

Oberhelman RA, Taylor DN. *Campylobacter* infections in developing countries. In: Nachamkin I, Blaser MJ, editors. *Campylobacter*, 2nd edition. Washington: American Society for Microbiology; 2000. p.139-53.

Palmer, S.R., Gulley, P.R., White, J.M., Pearson, A.D., Suckling, W.G., Jones, D.M., Rawes, J.C.L., Penner, J.L., 1983. Water-Borne Outbreak of *Campylobacter* Gastroenteritis.. The Lancet. 321(8319):287-290.

Padungton, P., Kaneene, J.B., 2003. *Campylobacter* spp. in human, chickens, pigs and their antimicrobial resistance. Journal of Veterinary Medical Science. 65(2):161-170.

Patz, J.A., 2001. Public Health Risk Assessment Linked to Climatic and Ecological Change. Human and Ecological Risk Assessment. 7 (5), 1317-1327.

Perez-Perez, G.I., Blaser, M.J., 2005. *Campylobacter* and *Helicobacter*. Medmicro. Ch 23. <http://gsbs.utmb.edu/microbook/ch023.htm.>. Online.

Philander, 1990. *El Niño, La Niña, and the Southern Oscillation.* Academic Press, San Diego.

Potter, R., Kaneene, J., Gardiner, J., 2002. A comparison of *Campylobacter jejuni* enteritis incidence rates in high and low poultry density counties: Michigan 1992-1999. Vector Borne Zoonitic Dis. 2(3):137-143.

Rees, R., 1996. Under the weather: climate and disease, 1700-1900 History Today. 46:35-42.

Sahlstrom, L., Aspan, A., Bagge, E., Danielsson-Tham, M., Albihn, A., 2004. Bacterial pathogen Incidences in Sludge from Swedish Sewage treatment Plants. Water Research. 38, 1989-1994.

Samuel, M. Reilly, K., Shallow, S., Marcus, R., Segler, S., McGivern, T., Kassenborg, H., Hollinger, K., Vose, D., Bartholomew, M., Kennedy, M., Vugia, D., 2000. Burden of *Campylobacter* Infection in United States and Declining Trend in California, FoodNet 1996-1998. 2nd International Conference on emerging Infectious Diseases, Atlanta, GA, July.

Samuel, M.C., Vugia, D.J., Shallow, S., Marcus, R.,Segler, S., McGivern, T., Kassenborg,H., Reilly, K., Kennedy, M., Angulo, F., Tauxe, R.V., 2004. Epidemiology of Sporadic

Campylobacter Infection in the United States and Declining Trend in Incidence, Food Net 1996-1999. CID, 38, S165-S174.

Samuelsson, Susanne. 2004. Zoonotic Enteric Infections 2003. Epi-News. No 9.

Schmidt, N., Lipp, E.K., Rose, J. B., Luther,M. E., 2001. Enso Influences on Seasonal Rainfall and River discharge in Florida. American Meterological Society. 14, 615-628.

Sebald, M., and M. Veron. 1963. DNA base content in the classification of vibrios. Ann. Inst. Pasteur 105: 897-910.

Shrestha, M.N., 2003. Spatially Distributed Hydrological Modelling considering Land-use changes using Remote Sensing and GIS. Map Asia Conference 2003. GIS development.net, 1-8.

Skelly, C., Weinstein, P., 2003. Pathogen Survival Trajectories: And eco-environmental approach to the modeling of Human Campylobacteriosis Ecology. Environmental Health Perspectives. 111, 19-28.

Skirrow, M.B., 1991, Epidemiology of *Campylobacter* enteritis. International Journal of Food Microbiology, 12(1):9-16.

Stanley, K., Jones, K., 2003. Cattle and Sheep Farms as Reservoirs of *Campylobacter.* Journal of Applied Microbiology. 94,104s-113s.

Takahanshi, M., Koga, M., Yokoyama, K., Yuki, N., 2005, Epidemiology of *Campylobacter* jejuni Isolated from Patents with Guillian-Barre and Fisher Syndromes in Japan. Journal of Clinical Microbiology. 43(1):335-339.

Tsubo, M., Walker, S., Hensley, M., 2005. Quantifying risk for water harvesting under semi-arid conditions: Part I. Rainfall intensity generation. Agricultural Water Management. 76(2):77-93.

U.S. Census Bureau, 1990. Georgia-DP-5 Housing Characteristics. <Http://factfinder.census.gov/servlet/QTTable?_bm=n&_lang=en&qr_name=DEC_1990_ST >. Online.

USDA (US Food and Drug Administration), 2003, posting date. Foodborne Pathogenic Microorganisms and Natural Toxins Handbook. <http://vm.cfsan.fda.gov/~mow/chap4.html>. Online.

USGS, 2005. The Water Cycle-Surface Runoff. <http://ga.water.usgs.gov/edu/watercyclerunoff.html>. Online.

Van Gilder, T., Vugia, D., Fiorentino, T., Segler, S., Carter, M., Smith, K., Morse, D., Cassidy, M., Angulo, F., 1999. Decline in *Salmonella* and *Campylobacter* but not *E. coli* O157 isolation rates in FoodNet sites: Farm, food, or fluctuation? 37th Annual Meeting of the Infectious Disease Society of America, Philadelphia, PA, November.

WHO (World Health Organization), 2003. Quantifying selected major risks to health. The world health report 2002. World health Organization. Geneva. (Chapter 4).

Zimmer, 1999. The El Nino Factor- El nino weather patter may be beginning of new weather patterns. Discover 1.

CHAPTER 3

THE EPIDEMIOLOGY OF CAMPYLOBACTERIOSIS IN GEORGIA, USA, 1987-2003[1]

[1] Tiffiani Joy Miller Onifade, Erin Lipp, and Dana Cole. To be submitted *Emerging Infectious Diseases.*

ABSTRACT

Campylobacter spp. are the most commonly reported cause of bacterial enteritis in the United States; however, relatively little is known about regional and local scale variability of the disease. Here we describe demographic, seasonal, and geographic trends of campylobacteriosis in Georgia, USA. Data were analyzed on culture-confirmed cases of campylobacteriosis from 1987-2003. The average annual incidence of the disease in Georgia was 13.4 cases per 100,000 people (ranging from a high of 22.5 cases per 100,000 in 1989 to a low of 6.8 cases per 100,000 in 2003). Incidence among the 0-4 age group (20.7 cases per 100,000) was significantly higher than all other groups. Males had significantly higher rates than females (12.7 and 10.3 cases per 100,000, respectively). Counties with a large white population (>70%) had significantly higher incidences (10.2 cases per 100,000) than those with a small percentage of whites (5.9 cases per 100,000). A marked seasonal trend was also evident with rates peaking in the summer months. Geographically, incidence varied across the state among counties with no cases reported (Stewart and Webster) to a mean annual high of 40.6 cases per 100,000 in Ware County. While case rates state-wide were significantly higher in high population density counties, a distinct cluster of high incidence counties that were most frequently noted as the highest case rate counties in the state (1987-2003) (top quartile) were noted in very low population density areas in the southeast portion of the state. Despite a state-wide decline in rates over the period of record, disease prevalence remained high in this cluster and above both the state-wide and national averages. Results suggest that non-demographic factors, including environmental influences, may affect the rates of campylobacteriosis in these rural areas.

INTRODUCTION

Campylobacteriosis has been a well-studied disease due to its high incidence, the changing trends in rates of illness, and health outcomes that increase its economic burden to the population. Since reliable culture techniques were developed in 1977 (Kist 1985), *Campylobacter* has been recognized as the leading cause of diarrheal illness in the United States and worldwide. Rates have been on the rise around the world, causing more cases than *Shigella* spp. and *Salmonella* combined (USDA, 2003, Altekruse et al., 1999). In developing countries, rates for *Campylobacter* infection are also high, with 5% to 20% of the population infected annually, depending on the country (Oberhelman and Taylor, 2000, Coker et al., 2002). This is of particular concern given its increasing incidence, expanding spectrum of infections, and the potential of HIV-related deaths associated with campylobacteriosis (Coker et al., 2002). In developed countries, the rate of infection is lower, for example 1% of the United States population is infected each year (Oberhelman and Taylor, 2000); but the disease is still responsible for the greatest portion of diarrheal disease due to bacteria and in many countries (i.e., Sweden, Australia, and the United States) case rates are declining (Lindback and Svensson, 2001, Samuel et al., 2004).

Cases of campylobacteriosis have been linked to poultry (Blaser et al., 1983, Skirrow, 1991), milk (Blaser et al., 1979, Fahey et al., 1995), and water (Blaser et al., 1983, Palmer et al., 1983, Ashbolt, 2004). Upon infection, *Campylobacter* causes diarrhea, nausea, and bloody stool, but could lead to life threatening illnesses (Medema et al., 1996, Nachamkin, 2002, USDA, 2003, Mead et al., 2004) such as Guillain-Barré Syndrome (1 in 1,000 cases develop this syndrome) (CDC 2004), which costs the United States up to 1.8 billion dollars annually (Buzby et al., 1997).

A 23% decline in case rates between 1996 and 2003 in the U.S. has been attributed to efforts to curb *Campylobacter* infection by improving poultry processing (Buchanan and Whiting, 1998, Hariharan et al., 2004, Keener, 2004, Van Gilder et al, 1999, Samuel et al., 2000, Samuel et al., 2004, CDC, 2004); Epidemiologic studies of campylobacteriosis have found that the incidence is higher in males and among children under five and among young adults (20-29yrs); and white persons are disproportionately affected when compared to blacks (Potter et al., 2002, Samuel et al. 2004). None of these trends are well understood. Consequently, detailed epidemiological investigations are needed to understand non-foodborne routes of transmission.

Given the high prevalence of campylobacteriois and the potential for the infection to lead to more serious illnesses, it is important to fully understand the patterns and trends in the demographics of those infected. Many epidemiological studies in the United States have relied on Food Net data (beginning in 1996) for analysis and description of trends in the United States (CDC, 2005). Ten states participate in the FoodNet Program, and although the states are diverse, all of the data in some states come from only a few counties in that state. According to studies conducted using FoodNet data, Georgia reports the lowest case rates annually among the FoodNet states; however, the state claims the highest percentage of hospitalizations due to campylobacteriosis (Samuel et al. 2004). In the United States the incidence rates for camplyobacteriosis are estimated to be 21 cases per 100,000 people, but these rates vary, depending on the Food Net state, from a high of 48.3 cases per 100,000 people in California to a low of 12.2 cases per 100,000 people in Georgia (Samuel et al. 2004).

In this study, we evaluated trends of campylobacteriosis in Georgia, USA, as a case study. While statewide rates are low compared to other Food Net states (CDC, 2005), hospitalization rates are high. Additionally, Georgia is an attractive study site given that disease data are available beginning in beginning in 1987, nine years prior to data collection by Food Net (Samuel et al., 2004). Like the variation in incidence rates seen across the United States, there is similar variation in incidence rates across Georgia. The aim here is to evaluate trends over a longer time period (1987-2003) and to look specifically at Georgia because of its diverse geographic area to provide a more comprehensive analysis of demographic, temporal and geographic trends in the epidemiology of campylobacteriosis.

METHODS

Data Sources

Georgia's 159 counties are divided into 19 Health Districts (as of 2002) (Fig.1), which are responsible for supervising the collection and reporting of notifiable disease data from county health boards and private practitioners in their district. The Georgia Division of Public Health, Notifiable Disease Section, receives all reports of laboratory confirmed cases of campylobacteriosis from health care providers, health districts and laboratories. Information from the records of all culture-confirmed *Campylobacter* cases reported to Georgia between 1987 to 2003 were abstracted from the Georgia Division of Public Health Notifiable Disease Section database. Abstracted data included county and city of residence, age, gender, race and date of specimen collection. Monthly county case rates and population densities were calculated using annual county population estimates obtained from the Real Estate Center at Texas A & M University (TAMU) (http://recenter.tamu.edu/data/popc/popcs13.html). These case rates were used to examine individual differences in demographic and geographic characteristics of *Campylobacter* cases across Georgia.

To evaluate the relationship between county-level case rates and the demographic characteristics of Georgia counties, population estimates and demographic information for each county in Georgia were obtained from the U.S. Census Bureau (http://www.census.gov/popest/datasets.html). This data was only available for the years 1990 to 2003. The demographic characteristics evaluated were gender, age group, and race (Table 1). In addition, annual county population density estimates were also calculated using the annual county population estimates obtained from the TAMU Real Estate Center and county land area data from the U.S. Census Bureau.

Data Analysis

Descriptive analyses of annual case rates (per 100,000 people) among categories of gender, age group, race, month and season were performed for the entire state of Georgia and for each of 159 counties and the 19 Public Health Districts. Monthly case rates for age group, gender, and race were also calculated for each county. In instances where there was a missing identifier, the case was excluded from calculation based on that identifier. For seasonal analyses, months were collapsed into seasons defined as spring (March, April, and May), summer (June, July, and August), fall (September, October, and November), and winter (December, January, and February). Data were analyzed for differences in mean rates between counties and districts and for temporal trends.

The distributions cases among all demographic variables were calculated for each county and public health district and compared to that county's or public health district's case rates in the general population. Counties were grouped according to the distribution of demographic variables (deciles) by age, gender, race, and geographic location. Population density was calculated as the number of people per square mile in a given county. Quartiles for population density were determined by the evaluating the distribution of total number of data points (all counties for all years). Percent distributions of county populations were calculated for each age group, gender, and race. Due to data entry errors in the years 1990 and 1991, age data could only be analyzed among reported *Campylobacter* cases from 1992-2003. Differences in county case rates were analyzed among deciles for population demographic distribution and quartiles for population density analysis.

To determine statistically significant differences in case rates among study variables, an analysis of variance (PROC ANOVA) was performed using SAS software (version 8) and post hoc Least Significant Difference (LSD) or Student-Newman-Keuls (SNK) tests were used to determine the pair-wise differences. In all measures, statistical significance was declared when $p<0.05$.

RESULTS

Temporal Trends

Between 1987 and 2003, Georgia received 16,119 reports of campylobacteriosis. The average annual number of reported cases during the study period was 948. The overall annual incidence of culture confirmed *Campylobacter* infection was 13.4 ± 5.7 (mean ± standard deviation) cases per 100,000 people, ranging from a high of 22.5 cases per 100,000 in 1989 to a low of 6.8 cases per 100,000 in 2003 (Fig. 2).

Annual incidence declined through the period of record, with an average of 1.1 fewer cases per 100,000 people per year and an average annual 12.8% decline in rates. The rate of decline was not constant over time; data show a steep drop of 11.3 cases per 100,000 people between 1990 and 1993 (22% annual average decrease), a small increase from 1993 to 1996, followed by a steady decline of 3.9 cases per 100,000 people from 1996 to 2003 (8.4% annual average decrease) (Fig. 2). Over the period where food net reported the 23% decline in national rates (1996-2000) Georgia reported a larger 45% decline.

State-wide, case rates peaked in the summer months. Mean rates in June, July, and August were significantly greater ($p<0.0001$) than those reported in other months (Fig. 3a). Rates were greatest in July (1.6 cases per 100,000), followed by June (1.5 per 100,000), and August (1.4 per 100,000). The lowest rates were reported in December (0.8 cases per 100,000). When monthly data were combined for seasonal analysis, the mean summer rate was 4.6 cases per 100,000 and was significantly greater ($p=0.0007$) than all other seasons (Fig. 3b). The lowest rate was noted for winter, with 2.4 cases per 100,000.

Declines were seen in all months over the period of record, with the largest declines in October (5.3% average annual decline) and February (5.2% average annual decline). Likewise, rates declined in all seasons with fall and winter having the greatest declines (5.6% and 4.2% average annual declines, respectively), which were significantly higher than declines noted in spring and summer (3.3% and 2.3%, respectively).

Demographic Patterns (State-wide)

Age. A bimodal distribution of case rates was observed across age categories (Fig. 4). Mean annual case rates for children under 5 were significantly higher than any other group (20.7 cases per 100,000; $p<0.0001$) (Fig. 4). This group was followed by those aged 20-29 and 30-39, with means of 16.3 and 13.7 cases per 100,000, respectively. The lowest rates were seen in the ≥60 age group, with a mean rate of 5.9 cases per 100,000 people. Between 1992 and 2003, all but the 50-59 and ≥60 age groups reported an overall decline in annual case rates. The average annual change in case rates over the study period for all other age groups ranged from a decrease of 9.6% among the 20-29 age group and a 6.7% increase among the 50-59 age group.

Gender. Annual campylobacteriosis incidence was significantly higher for males than females, with 12.7 and 10.3 cases per 100,000, respectively ($p<0.001$). Across the state, annual rates for both males and females declined at similar rates with 7% and 6.4% average annual declines, respectively (1990–2003).

Race. There was a significant difference in incidence between races (white, black, and other) ($p=0.0008$). Case rates for whites and others were significantly greater than rates for blacks (7.2, 5.6, and 2.8 mean cases per 100,000 per year, respectively) (Fig. 5).

Geographic Patterns

County. Case rates varied significantly between counties ($p<0.0001$). Ware, located in southeast Georgia, and Clarke, in north central Georgia, had significantly higher mean case rates than all other counties except for Clinch, in southeast Georgia, with rates of 40.6, 38.7 and 35.9 cases per 100,000 people, respectively ($N = 17$). Counties with the lowest annual rates were Stewart and Webster, in west Georgia, with no cases reported in either county over the time period. Over the 17 year period, the counties Clinch, Charlton, Appling, Ben Hill, Oglethorpe, Lanier, Pierce, Schley, and Ware were consistently noted in the top quartile of frequency in having for highest monthly incidence rates and Laurens, Muscogee, Stewart, Webster, Chattahoochee, Dekalb, Glasscock, Gwinnett, and Wheeler were consistently in the bottom quartile. Of the counties consistently in the upper quartile, 80% (7/9) were located in the southeast portion of the state (Fig. 6) where much of the land is used for farmland and grazing. The populations of these counties were also significantly lower (mean 13,630 people, and a density of less than 118 people per square mile) than the counties consistently found in the lowest quartile (mean 154,590 people, and a density greater than 118 people per square mile). The racial makeup of these groups of counties were also different in that the high case rate counties had significantly higher percentages of whites (mean 72.9%) than the lower case rate counties and significantly lower percentages of blacks (25.2%) than the lower case rate counties.

Health District. Mean annual incidence also varied significantly between health districts ($p<0.0001$). District 3.2, located in the metro-Atlanta area, reported a mean of 22.6 cases per 100,000 (N=17), which was significantly higher than all other districts except for District 10 (northeast Georgia), which reported a mean of 19.8 cases per 100,000 (Fig. 7). The lowest rates were in districts 7, 5.1, and 9.3, with rates of 4, 5, and 5.9 cases per 100,000, respectively (Fig. 7). Over the 17 year period, the health districts 10, 3.2, and 1.2 were consistently noted in the top quartile for highest annual incidence rates (>58% of the time) and districts 7, 9.3, and 5.1 were consistently in the bottom quartile (>64% of the time) (Fig. 7).

Population Density. There were significant differences in incidence rates for counties based on population density ($p<0.0001$). Counties with population densities in the highest quartile (> 118 people mi^{-2}) had significantly greater rates (12.3 cases per 100,000) than counties in all other population density quartiles (Table 2). There were notable exceptions to this trend; as a cluster of counties in the southeastern portion of the state (consistently high rates counties) had low population densities (< 68 people mi^{-2}).

Age. Following the observed statewide trends, there were significant differences in mean incidence for counties based on age group distribution. Counties with <10% of its population in the 0-4 age group had significantly higher incidences (8.9 cases per 100,000; $p=0.0025$) than counties with >10% in this age group (2.7 cases per 100,000 people). Counties with >30% of their population in the 20-29 age group also had significantly higher rates (17.4 cases per 100,000 people) than counties with <30% in that age groups (average 5.7 cases per 100,000) (p<0.0001). There were no significant differences in incidence rates between counties based on percent population in other age groups (Table 3).

Race. County case rates were also associated with racial distribution (white, black, and other). Counties with large white populations (>70%) had the highest incidences (10.2 cases per 100,000 people) of campylobacteriosis. Inversely, counties with the highest percentages of blacks (>60%) had the lowest incidences (3.6 cases per 100,000). There was also a significant difference in incidence rates for counties based on percentage of the population that was classified as “other” such that counties with >20% “other” had significantly higher incidences (12.6 cases per 100,000 people) than counties with lower percentages of “others” (Table 4).

DISCUSSION

During the 17 year period of analysis (1987-2003), 16,119 culture-confirmed cases of *Campylobacter* infection were reported in Georgia, at a mean of 948 cases per year and a mean incidence of 13.4 cases per 100,000 people. Between 1996 and 2003, the national (U.S) average was 21 cases per 100,000 people. During this period, the incidence rate in Georgia declined from 21.2 to 6.8 cases per 100,000 people, a 68% decrease (average annual decrease of 5.4%). Nationally, a smaller decline in rates has been observed since 1996 (23% through 2000) with similar declines across all races, age groups, and genders (Samuel, 2004). Over this same time period (1996-2000) the decline in Georgia was 45%. These declines are significant due to the fact that around the world in both developed and developing countries the incidence of campylobacteriosis has risen substantially over the past 20 years (Coker et al. 2002). Several possible explanations for this disparity have been suggested, including improvements in the meat processing and poultry industries due to Hazard Analysis and Critical Control Points/ Pathogen

Reduction (HACCP/PR) rule implementations (Buchanan and Whiting, 1998). These rules require the use of more water when processing and disinfection of that water with trisodium phosphate; however, these practices were implemented in 1997 and cannot explain the significant decline noted in Georgia prior to 1993. Another possible reason for the decline is better education of the public on food safety (Samuel, 2004).

There was a high degree of variability in campylobacteriosis rates within the state over the period of record, which was related in part to the demographic makeup of each county. High case rates were found in counties with highly dense populations (12.3 cases per 100,000), counties with >30% of their population in the 20-29 age groups, and counties with >70% white in their populations. Although, case rates were found to be significantly higher in the 0-4 year old age group this did not affect the county rates due to the small contribution of this age group to the total county population.

The counties with the high incidences were not always located in the health districts with high incidences. High incidence health districts were located in urban areas with only a few counties assigned to them. Other health districts, which had lower rates and contained high incidence counties included a broader area and many more counties; therefore, the high rate may have been localized in a few counties but distributed over a larger district area, effectively masking the high incidence area. This may also be indicative of reporting differences between the health districts. This finding suggests that a county level analysis is more effective at pin pointing high incidence areas.

In this study we found a significant difference between the rates of campylobacteriosis in males and females in Georgia, with males having higher rates. This is consistent with previous studies although this trend is not well understood (Potter et al., 2002, Samuel et al. 2004). It has been suggested that this is due to poor food handling practices more common among men; however, this seems unlikely given that the trend was evident among all age groups including those <5 years old (Samuel et al. 2004). Therefore, physiological differences between the sexes may explain this trend (Altekruse et al, 1999).

A bimodal distribution of rates with a major peak in the 4 and under group and a minor peak in the young adult category (between 20 and 29 years old) was evident in our study, which is similar to previous reports (Friedman et al., 2000, Louis et al., 2005, Perez-Perez and Blaser, 2005). Campylobacters, as well as other pathogens that cause gastroenteritis are vastly underreported in the general population (Gillespie et al., 2002). It has been speculated that high rates noted in the under five age group may be a reporting bias, with parents being more likely to take their young children to the doctor for symptoms of gastroenteritis (Friedman et al., 2000). Because of this Louis et al. (2005) suggested that this group may better represent the actual case load. In addition to a reporting bias, children get sick more frequently due to an immature immune system (Perez-Perez and Blaser, 2005). Subsequently, infections in childhood act to build immunity such that infection is less likely in later years (Perez-Perez and Blaser, 2005). It is unclear what factors may have lead to the second peak in campylobacteriosis among the 20-29 year olds.

There was a significant difference in incidence of campylobacteriosis based on race, with rates for blacks significantly lower than for whites and other races. This is consistent with previous findings (Samuel et al., 2004); however, it is unclear what may drive this trend. One explanation may be cultural differences that result in different consumption and food preparation patterns. Samuel et al. (2004) speculate that blacks may be less likely to be seen by a physician for mild *Campylobacter* infection. This is suspected because blacks have the highest rates of hospitalizations due to the disease (Samuel et al., 2004).

Despite state-wide demographic trends, the counties with the highest mean case rates for both the total population and the under 5 group were clustered in the southern portion of the state. This suggests that other factors not identified here may be affecting the case rates in these areas. Case rates in these counties averaged 25 cases per 100,000 people, well above both the Georgia and national averages. One explanation for this trend may be related to environmental factors associated with the agrarian nature of these counties (Jones, 2001, GASS, 2004). Many of the homes acquire their drinking water from private (often untested) wells (EPA, 2005). Given that *Campylobacter* spp. is readily found in the guts of animals and livestock and are often shed in feces into the surrounding environment it is likely that some of these environmental influences may affect the incidence of the disease (Jones, 2001).

Campylobacteriosis cases peak in the summer months (from May to July in the northern hemisphere) across the U.S. and around the world (Miller et al. 2004, Louis et al, 2005, Nylen, 2002, Lindback and Svensson, 2001, Potter et al, 2002). The cause of this apparently universal seasonal trend is not fully understood. Some hypotheses have suggested an increased risk of infection during peak summer travel times (Miller et al. 2004, Coker et al. 2002; Louis et al., 2005), increased consumption of poultry products in warmer weather and a higher likelihood of eating outdoors and outside of the home, in general (Friedman et al. 2000). Jones (2001) suggests that the seasonal trends are due to variations in *Campylobacter* infections of livestock and poultry flocks, which could be due to increased transmission by flies in the summer months along with variations in environmental loading (Rosef and Kapperud, 1983; Hald et al., 2004; Nichols, 2005). In this study, highest rates in Georgia were also reported in the summer, particularly in July, followed by August and June. In a systematic analysis, Louis et al. (2005) found a significant relationship between temperature change in England and Wales and seasonal campylobacteriosis rates suggesting that environmental factors such as climate affect case rates.

CONCLUSIONS

Many studies to date have relied on Food Net data to describe and identify trends in campylobacteriosis (CDC, 2005); however, these data only represent a very small portion of the U.S. population (5.4% in 1996 and 9.5% in 1999), the state samples are not representative of the entire state, and the data are only available starting in 1996. With these data, extrapolations have been made to describe many trends, particularly the decline in incidence (Samuel et al. 2004). This decline in case rates from Food Net states has been noted from 1996-2003 and has been attributed to improvements in the poultry industry (Buchanan and Whiting, 1998, Samuel et al. 2004); however, in Georgia where data are available beginning in 1987, the majority of the declines were seen prior to 1995 (before the HACCP/PR was implemented in 1997). The rate of decline in Georgia actually slowed from 1996 through 2003. The present study is important because it examines trends prior to the collection of data by the Food Net program. Additionally, Georgia is an important study site for analysis of geographic and demographic trends due to its wide variability across the state in population density, race, and age. Each of these factors were significantly associated with campylobacteriosis incidences state-wide. Counties with high population densities, predominantly white populations, or large populations in the 20-29 age group had significantly higher case rates over the period of record. It is important to note, however, that a cluster of counties with the greatest frequency of highest reported rates did not follow all of these trends. Although they had largely white populations, these counties tended to be in rural areas with low population density and older populations, clustered in the southern portion of the state. These findings suggest that non-demographic factors, including environmental influences, may have an important effect on cases in these areas. Further research should investigate the role of environmental factors on disease rates in high case rate regions.

REFERENCES

Altekruse, S.F., Stern, N.J., Fields, P.I., Swerdlow, D.L., 1999. *Campylobacter jejuni*--an emerging foodborne pathogen. Emerging Infectious Diseases. 5:28-35.

Ashbolt, N.J., 2004. Microbial contamination of drinking water and disease outcomes in developing regions. Toxicology. 198(1-3):229-238.

Blaser, M.J., Cravens, J., Powers, B.W., Laforce, F.M., Wang, W.L., 1979. *Campylobacter* enteritis associated with unpasturized milk, Short communication. The American Journal of Medicine, 67(4):715-718.

Blaser, M.J., Taylor, D.N., Feldman, R.A., 1983. Epidemiology of *Campylobacter jejuni* Infections. Epidemiology Review. 5:157-176.

Buchanan, R.L., Whiting, R.C., 1998. Risk Assessment: A Means for Linking HACCP Plans and Public Health. Journal of Food Prot. 61:1531-1534.

Buzby, J.C., Allos, B.M., Roberts, T., 1997. The economic burden of *Campylobacter*-associated Guillian-Barré syndrome. J Infect Dis. 176 Suppl 2:S192-197.

CDC, 2004. Preliminary Food Net Data on the Incidence of Infection with Pathogens Transmitted Commonly Through Food --- Selected Sites, United States, 2003, MMWR. 53(16):338-343.

CDC, 2004. *Campylobacter* Infections. Http://www.cdc.gov/ncidid/dbmd/diseaseinfo/campylobacter_t.htm. [online]

CDC (FoodNet), 2005. http://www.cdc.gov/foodnet/index.htm [online].

Coker, A.O., Isokpehi, R.D., Thomas, B.N., Amisu, K.O., Obi, C.L., 2002. Human Campylobacteriosis in Developing Countries. Emerging Infectious Diseases. 8(3):237-243.

EPA (Environmental Protection Agency) 2005. Private drinking water wells. http://www.epa.gov/safewater/privatewells [online]

Fahey, T., Morgan, D., Gunneburg, C., Adak, G.K., Majid, F., Kaczmarski, E., 1995. An outbreak of Campylobacter Jejuni enteritis associated with failed milk pasteurization. Journal of Infection, 31(2):137-143.

Friedman, C., Neimann, J., Wegener, H., Tauxe, R., 2000. Epidemiology of Campylobacter Jejuni infections in the United States and Other Industrialized nations, p. 121-138. In: Campylobacter, 2nd Ed. (Nachamkin, I. and Blaser, M. eds.), ASM Press, Washington, DC.

GASS (Georgia Agricultural Statistics Service), 2004, Number of Farms and Land in Farms. Georgia Farm Report. 4(3):3.

Gillespie, I., O'Brien, S., Frost, J., Adak, G., Horby, P., Swan, A., Painter, M., Neil, K., 2002. A case-case Comparison of *Campylobacter coli* and *Campylobacter jejuni* Infection: A tool for generating Hypotheses. Emerging Infectious Diseases. 8:937-942.

Hald, B., Skovgard, H., Bang, D.D., Pedersen, K., Dybdahl, J., Jespersen, J., Madsen, M., 2004. Flies and Campylobacter infection of Broiler Flocks. EID. 10(8)1490-1492.

Hariharan, H., Murphy, G.A, Kempp, I., 2004. Campylobacter Jejuni: Public health Hazards and potential control methods in poultry: a review. Vet Med. 49(11):441-446.

Jones, K., 2001. The Campylobacter Conundrum. Trends in Microbiology. 9(8):365-366.

Jones, K., 2001. Campylobacters in water, sewage and the Environment. Journal of Applied Microbiology. 90,68S-79s.

Keener, K.M., Bashor, M.P., Curtis, P.A., Sheldon, B.W., Kathariou, S., 2004. Comprehensive Review of Campylobacter and Poultry Processing. Comprehensive Reviews in Food Science and Food Safety. 3:105-116.

Kist, M. 1985. The historical background of *Campylobacter* infection: new aspects p. 23-27. In A.D. Pearson, M.B. Skirrow, H. Lior, and B. Rowe (ed.), *Campylobacter* III. Public Health Laboratory Service, London, United Kingdom.

Lindback, J., Svensson, A., 2001. Campylobacter infections in Sweden-A statistical analysis of temporal and spatial distributions of notified sporadic campylobacter infections. Mathematical Statistics Stockholm University, Research report 2001:4. ISSN 1650-0377.

Louis, V., Gillespie, I., O'Brien, S., Russek-Cohen, E., Pearson, A., Colwell, R., 2005. Temperature-Driven Campylobacter Seasonality in England and Wales. Applied and Environmental Microbiology. 71(1): 85–92.

Mead, P.S., Slutsker, L., Dietz, V., McCaig, L.F., Bresee, J.S., Sharpiro, C., Griffin, P.M., Tauxe, R.V., Food-Related Illness and Death in the United States, Emerging Infectious Diseases. 5(5):607-625.

Medema, G.J., Teunis, P.F.M., Havelaar, A.H., Haas, C.N., 1996. Assessment of the dose-response relationship of Campylobacter Jejuni. International Journal of Food Microbiology, 30(1-2):101-111.

Miller, G., Dunn, G., Smith-Palmer, A., Ogden, I., Strachan, N., 2004. Human camoylobacteriosis in Scotland: seasonality, reagional trends and bursts of infection. Epidemiology Infection. 132:585-593.

Nichols, G., 2005. Fly Transmission of Campylobacter. EID. 11(3);March 2005.

Nachamkin, I., 2002. Chronic effects of Campylobacter Infection. Microbes and Infection. 4(2002):399-403.

Nylen, G., Dunstan, F., Palmer, S., Andersson, Y., Bager, F., Cowden, J., Feierl, G., Galloway, Y., Kapperud, G., Megraud, F., Molbak, K., Petersen, L., Ruutu, P., 2002, The seasonal distribution of *camoylobacter* infection in nine European countries and New Zealand. Epidemiology infections. 128(3):383-390.

Oberhelman RA, Taylor DN. *Campylobacter* infections in developing countries. In: Nachamkin I, Blaser MJ, editors. *Campylobacter*, 2nd edition. Washington: American Society for Microbiology; 2000. p.139-53.

Palmer, S.R., Gulley, P.R., White, J.M., Pearson, A.D., Suckling, W.G., Jones, D.M., Rawes, J.C.L., Penner, J.L., 1983. Water-Borne Outbreak of *Campylobacter* Gastroenteritis. The Lancet. 321(8319):287-290.

Perez-Perez, G.I., Blaser, M.J., 2005. *Campylobacter* and *Helicobacter*. Medmicro. Ch 23. http://gsbs.utmb.edu/microbook/ch023.htm

Potter, R., Kaneene, J., Gardiner, J., 2002. A comparison of *Campylobacter jejuni* enteritis incidence rates in high and low poultry density counties: Michigan 1992-1999. Vector Borne Zoonitic Dis. 2(3):137-143.

Rosef, O., Kapperrud, G., 1983. House Flies (*Musca domestica*) as Possible Vectors of *Campylobacter fetus* subsp. *Jejuni*. Applied and Environmental Microbiology. Feb:381-383.

Samuel, M. Reilly, K., Shallow, S., Marcus, R., Segler, S., McGivern, T., Kassenborg, H., Hollinger, K., Vose, D., Bartholomew, M., Kennedy, M., Vugia, D., 2000. Burden of *Campylobacter* Infection in United States and Declining Trend in California, FoodNet 1996-1998. 2nd International Conference on emerging Infectious Diseases, Atlanta, GA, July.

Samuel, M.C., Vugia, D.J., Shallow, S., Marcus, R.,Segler, S., McGivern, T., Kassenborg,H., Reilly, K., Kennedy, M., Angulo, F., Tauxe, R.V., 2004. Epidemiology of Sporadic *Campylobacter* Infection in the United States and Declining Trend in Incidence, Food Net 1996-1999. CID, 38, S165-S174.

Skirrow, M.B., 1991, Epidemiology of *Campylobacter* enteritis. International Journal of Food Microbiology, 12(1):9-16.

USDA (US_Food_and _Drug_Administration), 2003, posting date. Foodborne Pathogenic Microorganisms and Natural Toxins Handbook http://vm.cfsan.fda.gov/~mow/chap4.html [Online]

Van Gilder, T., Vugia, D., Fiorentino, T., Segler, S., Carter, M., Smith, K., Morse, D., Cassidy, M., Angulo, F., 1999. Decline in Salmonella and Campylobacter but not E. coli O157 isolation rates in FoodNet sites: Farm, food, or fluctuation? 37th Annual Meeting of the Infectious Disease Society of America, Philadelphia, PA, November.

Table 1. Description of demographic data.

Data Type	Categories Assigned								
Age (years)	0-4	5-9	10-14	15-19	20-29	30-39	40-49	50-59	≥60
Gender	Male	Female							
Race	Black	White	Other[1]						

1. Data collected from the Georgia's Division of Public Health reported the race as Black or African American, White, Asian, American Indian/Alaskan Native, or Multiracial. These groups were collapsed into three groups: Black which included Black/African American reports, White which included White reports, and Other which included Asian, American Indian/Alaskan Native, and multiracial.

Table 2. Incidence (per 100,000 people) within counties by quartiles of population density.

Quartile[a]	County Population Density people/mi^2	Incidence
>75%-ile	>118	12.3*
51-75%-ile	49-118	10.2
26-50%-ile	31-49	9.2
≤25%-ile	<31	8.3

* This incidence was significantly higher than all other quartiles.
[a] Population density quartiles were based on intervals of all data points. Density is reported as the number of people per square mile for all counties and all years.

Table 3. Incidence (per 100,000 people) by percent distribution of county by age group.

Percentage of County Population	Age Group								
	0-4	5-9	10-14	15-19	20-29	30-39	40-49	50-59	≥60
>30%	-	-	-	-	17.4*	-	-	-	12.3
21-30%	-	-	-	14.2	4.3	9.9	-	7.2	8.3
10-20%	2.7	-	-	5.1	8.8	8.8	8.9	7.7	9.0
<10%	8.9*	8.8	8.8	8.7	7.6	6.6	5.2	10.2	7.3

* This incidence was significantly higher than all others in that age group.
- There were no counties with populations for this age group within this percentage range.

Table 4. Incidence (per 100,000 people) by percent distribution of county by race.

Percentage of County Population	Race		
	White	Black	Other
>90%	11.4*	-	-
81-90%	11.4*	-	-
71-80%	9.8*	3.8	-
61-70%	7.9	3.4	-
51-60%	6.4	8.6	-
41-50%	7.6	6.8	-
31-40%	5.3	7.0	-
21-30%	3.9	9.8*	12.6*
11-20%	-	9.8*	6.3
≤10%	-	11.5*	8.9

* This incidence was significantly higher than all others in that racial group.
- There were no counties with populations for this racial group within this percentage range.

Figure 1. Map of Georgia counties and health districts.

Figure 2. Annual incidence of campylobacteriosis in Georgia

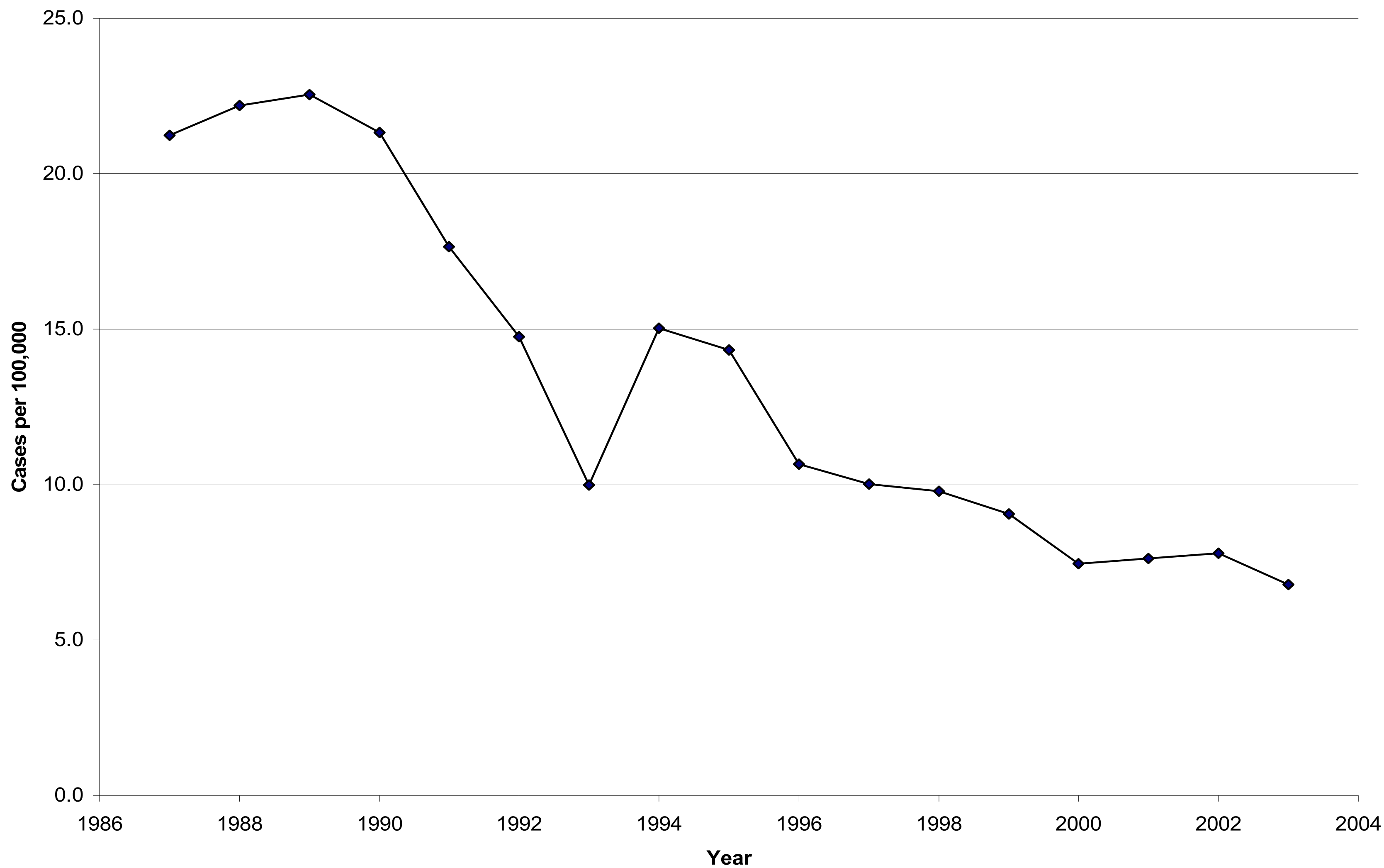
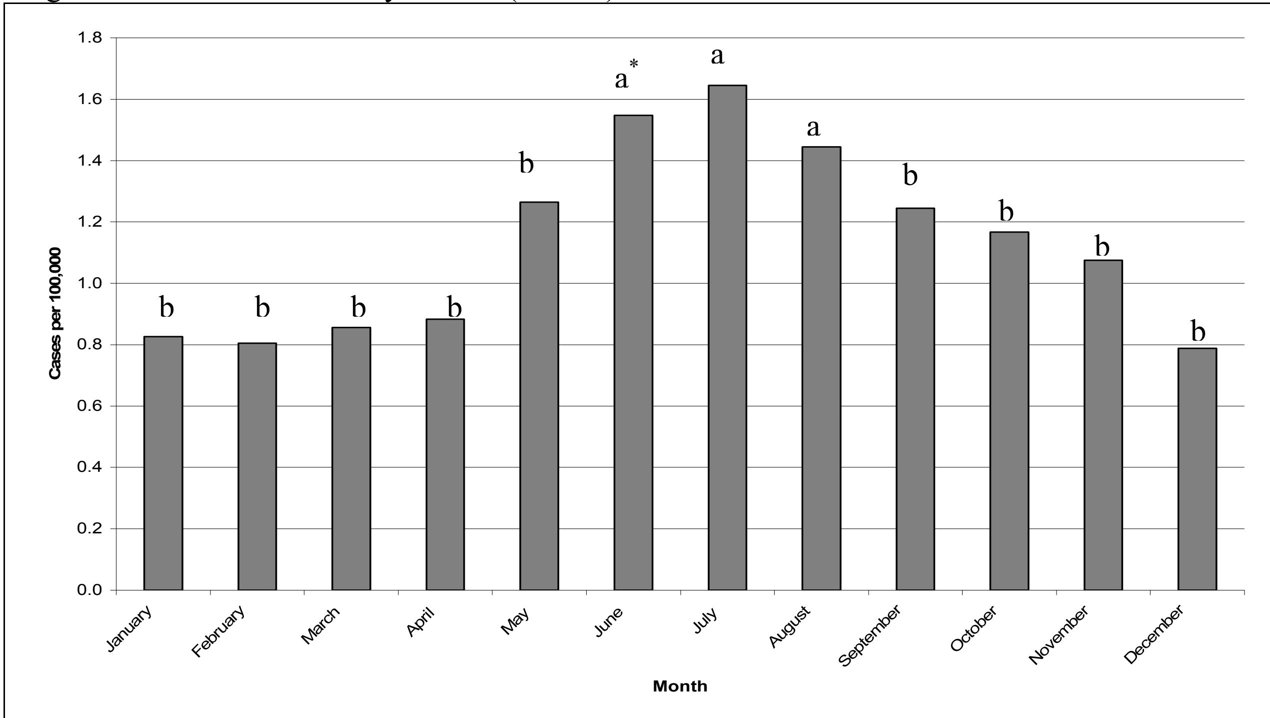
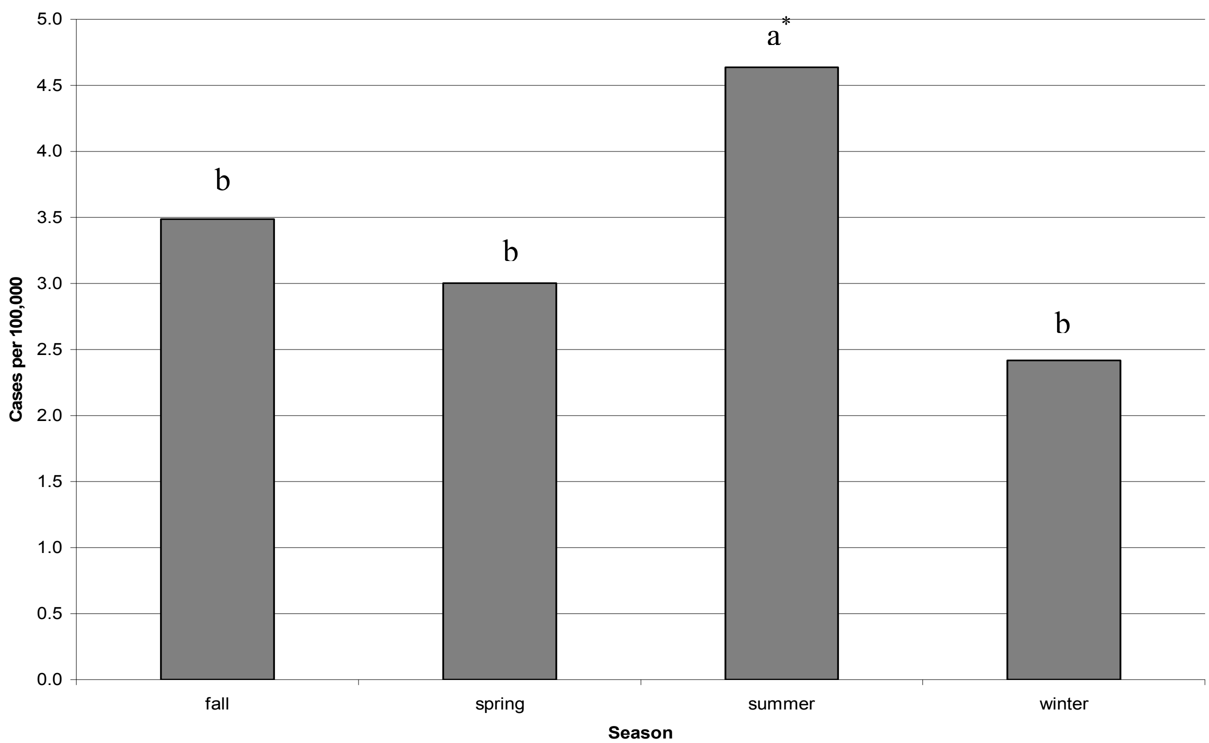


Figure 3a. Mean incidence by month. (N=204)



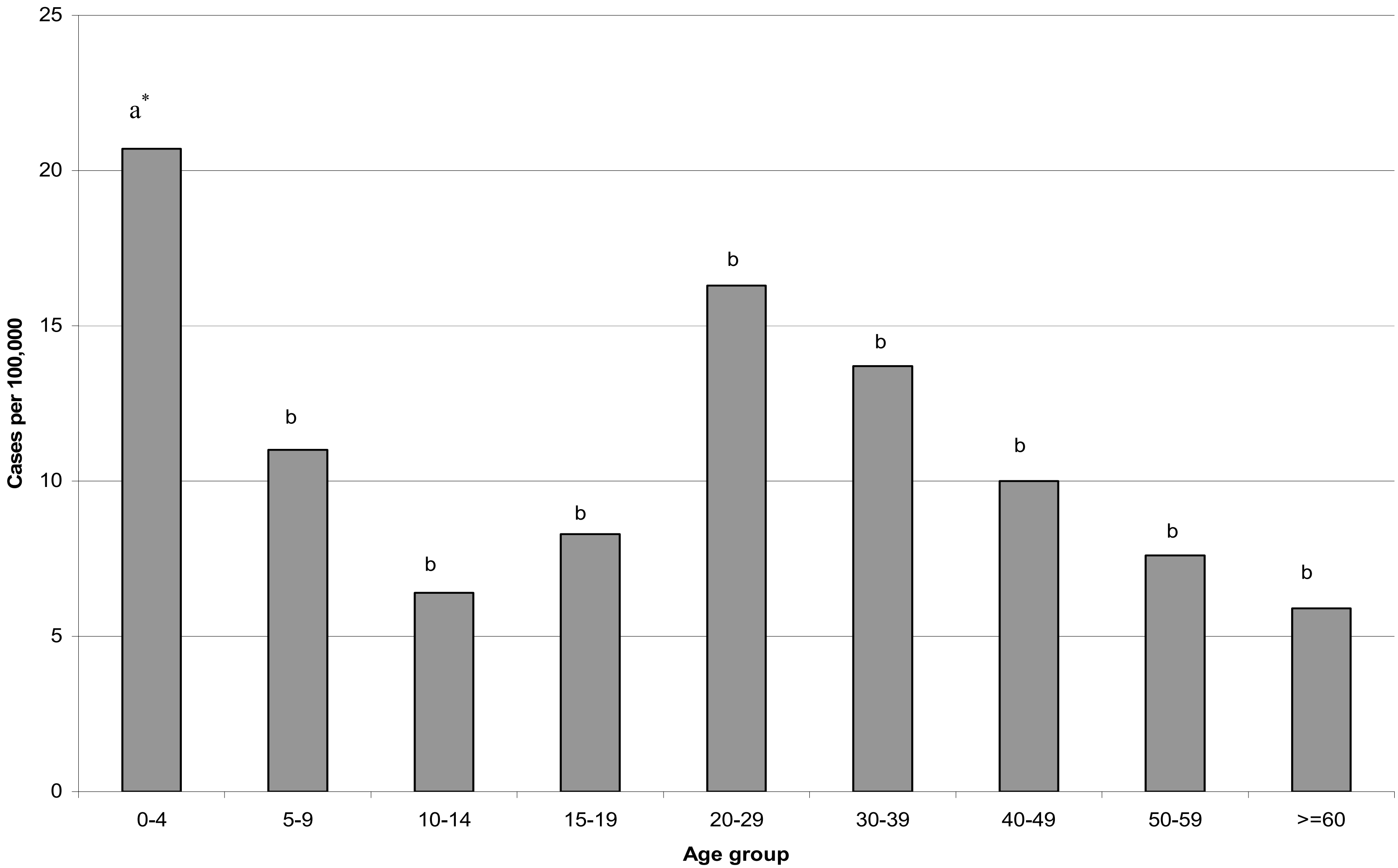
* Differing letters represent a significant difference in case rates.

Figure 3b. Mean incidence by season. (N=68)



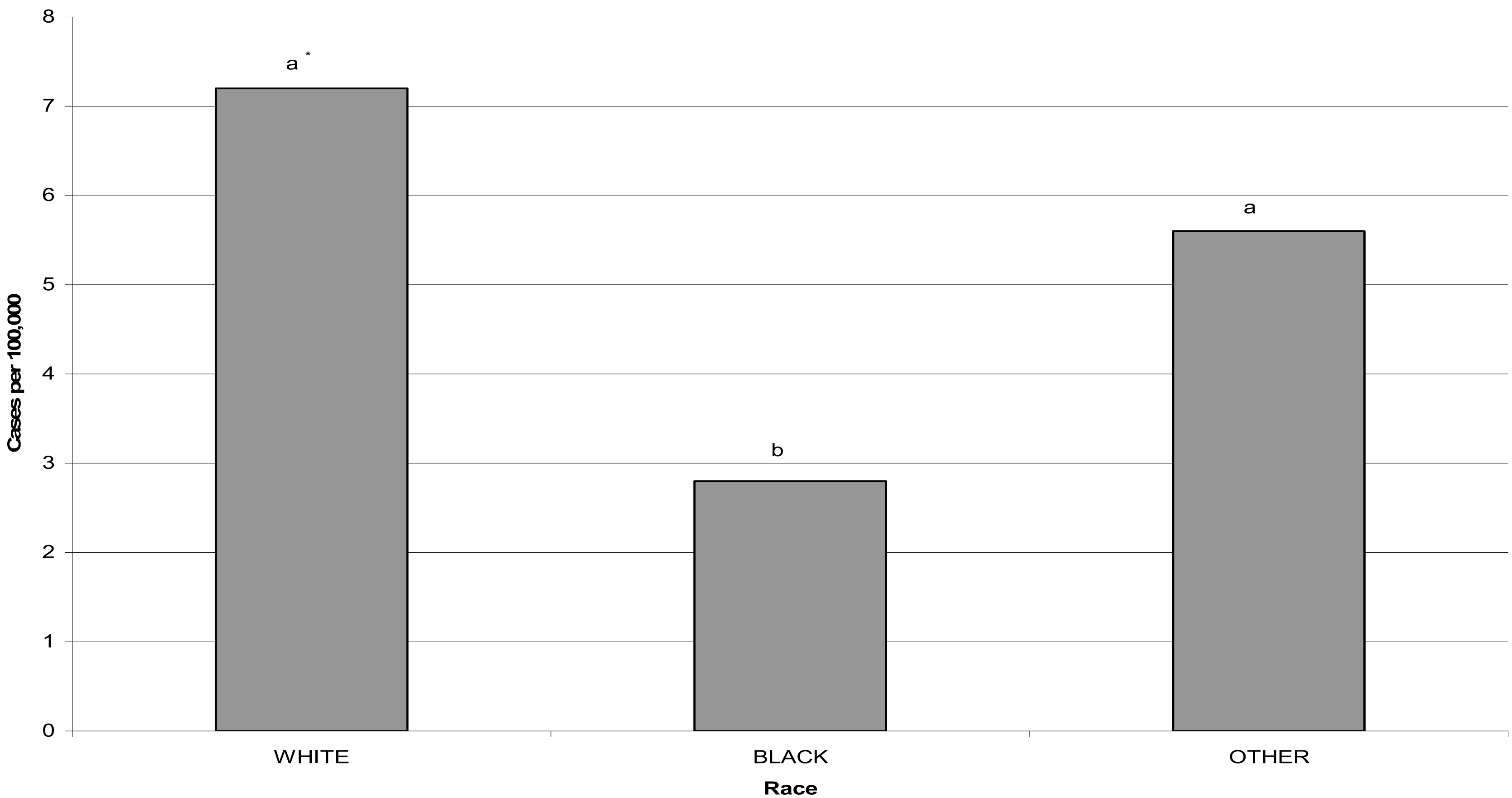
* Differing letters represent a significant difference in case rates.

Figure 4. Mean incidence (1992-2003) by age group



* Differing letters represent a significant difference in case rates.

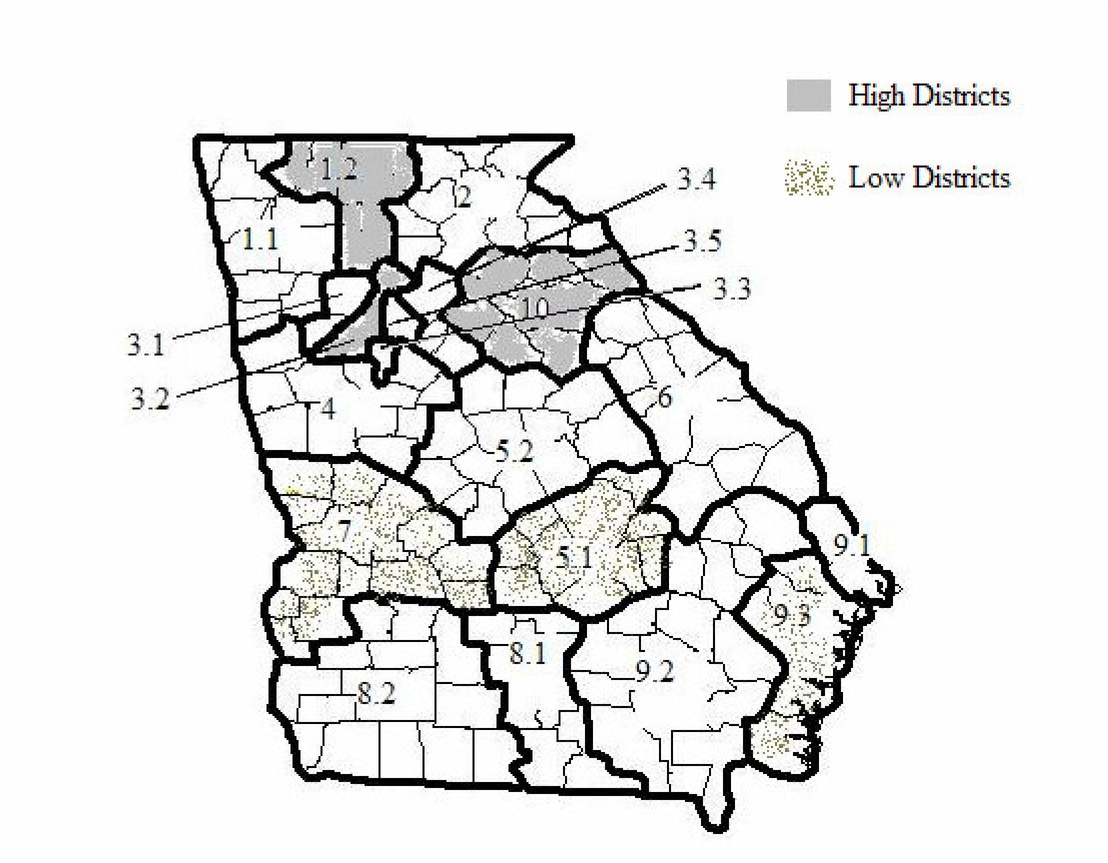
Figure 5. Mean annual incidence by race[1]



* Differing letters represent a significant difference in case rates.
1. Data collected from the Georgia's Division of Public Health reported the race as Black or African American, White, Asian, American Indian/Alaskan Native, or Multiracial. These groups were collapsed into three groups Black which included Black/African American reports, White which included White reports, and other which included Asian, American Indian/Alaskan Native, and Multiracial.

Figure 7. Counties consistently in the top (high) and bottom (low) quartiles for frequency as top (bottom) case rate counties for all months of study.

Figure 7. Health districts consistently in the high and low quartiles for case rates in Georgia.



CHAPTER 4

ENVIRONMENTAL FACTORS INFLUENCING THE INCIDENCE OF CAMPYLOBACTERIOSIS IN GEORGIA, USA, 1987-2003[2]

[2] Tiffiani Joy Miller Onifade, Erin Lipp, and Dana Cole. To be submitted to *Emerging Infectious Diseases*.

ABSTRACT

Campylobacter infection rates were examined in Georgia from 1987-2003 in conjunction with environmental factors (land-use, potable water source, sewage disposal, watershed impairment, and climatological factors (daily maximum and minimum temperatures, daily precipitation, and the El Niño-Southern Oscillation). Data were analysed on multiple scales including county for localized effects due to land-use and water resources, watersheds for impairment, and by river basin for climate related variables. Counties classified as 'ungrazed forests and woods' and 'swamplands' had the highest rates while the lowest were found in 'urban' counties (12.9, 11.8, and 5.06 annual cases per 100,000, respectively). While source of potable water and sewage disposal method both were significant factors in predicting rates in counties, they each explained less than 2% of the observed variability. There were no differences in case rates between watersheds classified as impaired by the US EPA because of high levels of fecal coliform bacteria. Significant, river basin differences in rates were seen between the Suwannee and Apalachicola having the highest basin rates (16.8 and 15.6 cases per 100,000, respectively) and the Ogeechee with the lowest rates (7.4 per 100,000). A time series model was developed for each basin to describe variability in observed data due to climatological factors. Time (because of the significant decline in rates over the period of record) and daily maximum temperature were the best predictors over all basins when adjusted for autocorrelation due to seasonal effects. These types of models may help to explain excess case rates in high rate counties which do not fit demographic trends, as described earlier.

INTRODUCTION

The gram-negative bacterium, *Campylobacter* has been recognized as the leading cause of diarrheal illness in the United States and worldwide, causing more cases than *Shigella* spp. and *Salmonella* combined (USDA, 2003, Altekruse et al., 1999). *Campylobacter* spp. are commonly associated with poultry, and other livestock, and it is thought that consumption of poultry is a major risk factor for campylobacteriosis (Kapperud et al., 1992). Campylobacters have also been transmitted by the water route (Kussin et al. 2005), which may be related to contamination from animal reservoirs (including poultry and cattle) especially in rural areas.

In U.S. an estimated 1% of the population is infected, with at least 21 reported cases per 100,000 people per year. In many regions of the world cases are on the rise (Coker et al., 2002). In the U.S., case rates have declined since the beginning of coordinated surveillance in 1996 (Samuel et al., 2004); however, distinct seasonal trends continue to cause a high burden of disease in summer months. Given the high prevalence of campylobacteriois (Oberhelman and Taylor, 2000, Coker et al., 2002, Lindback and Svensson, 2001, Samuel et al., 2002) and the potential for the infection to lead to more serious illnesses (Guillain-Barré Syndrome (1 in 1,000 cases) (CDC 2004), which costs the United States up to 1.8 billion dollars annually (Buzby et al., 1997)), it is important to identify and understand factors that influence the incidence of the disease both spatially and temporally (between years and seasons).

In analyses of campylobacteriosis in developed nations (e.g., U.S. and U.K.) consistent demographic trends in disease incidence have been observed, most notably a peak in cases among young children (<5 years old) and males (Samuel et al, 2004, Louis et al. 2005). Additionally, a distinct seasonal pattern with cases peaking in the summer months has been noted world-wide. While this seasonal trend is often attributed to food preparation issues related to picnics and eating outside of the home (Miller et al. 2004, Coker et al. 2002, Louis et al., 2005), this does not explain why the same pattern among cultures with different summertime customs. Others have suggested environmental factors may drive this pattern, including higher loading of the bacteria in livestock and increased transmission among poultry flocks by flies (Rosef and Kapperud, 1983, Hald et al., 2004, Nichols, 2005).

Demographic analyses in Georgia for case data collected between 1987 and 2003 revealed that counties with a high population density, young populations (<5 and 20-29 year age groups), and largely white populations were positively correlated with case rates; however, in this study several counties with among the highest case rates historically (up to 40.6 cases per 100,000) did not follow this trend (Chapter 2). These high incidence counties were all located in rural areas of southern GA with population densities of < 69.6 per mi^2. This disparity in population density is particularly interesting given that in a nation-wide study of campylobacteriosis in the U.K., Louis et al. (2005) found that case rates were negatively correlated with population density and positively correlated with agricultural land use. Louis et al. (2005), and others, have demonstrated that both environmental and weather related factors influence contamination of surface waters with enteric pathogens and disease patterns (Ashbolt, 2004, Kambole, 2003, Lipp et al., 2002, Patz, 2001). Given the agrarian nature of the 'anomalous' high case rate counties in Georgia (GASS, 2004) and the potential for environmental transmission to explain these rates, we hypothesized that non-demographic factors including environmental and weather-related variables may be important influences in disease incidence. Here we evaluate the role of land-use, water resources, weather and climate variability (El Niño-Southern Oscillation events) on a campylobacteriosis patterns in Georgia over a 17 year period (1987 – 2003).

METHODS

In order to capture multiple scales of influence on rates of campylobacteriosis, data were analyzed at county, watershed and river basin levels. Data were obtained for each of the 159 counties and aggregated into 53 watersheds (defined by USGS eight digit HUC codes) and nine river basins for analysis (Table 1). Geographic analyses were conducted at the county level to examine local-level land use factors that may contribute to campylobacteriosis rates, and at the watershed and water basin level to evaluate the role of regional impacts and climate factors that may be associated with regional trends in reported campylobacteriosis.

Campylobacteriosis Rates

Records of all culture confirmed *Campylobacter* cases in Georgia from 1987 to 2003 were provided by the Georgia Division of Public Health, Notifiable Diseases Section. All culture confirmed cases of campylobacteriosis in Georgia must be reported to either the local health department or regional health district, or the State Division of Public Health within one week of diagnosis. Variables that were extracted from the State database include county and city of residence, date of collection of specimen, date of culture confirmation, age, race, and gender. In instances where there was a missing identifier, the case was excluded from the calculation of incidence for that variable. Due to database errors, age data for *Campylobacter* cases were unavailable for years prior to 1992. Population estimates were obtained from both the US Census (http://www.census.gov/popest/datasets.html) and The Real Estate Center at Texas A&M University (TAMU) (http://recenter.tamu.edu/data/popc/popcs13.html). For *Campylobacter* rates among demographic variables such as age-group, race and gender, the US Census estimates were used, but this information was only available for the years of 1990-2003. For population-level county rates, population estimates were obtained from the Real Estate Center at TAMU for the entire time period of study (1987-2003). Monthly county incidence rates were calculated by dividing the number of cases reported in a county in the study month by the number of people in that demographic group in the county and multiplying by 100,000 to give the number infected per 100,000 people per month.

County-level Geographic Analyses

Land-use data were derived from the USGS land use map of Georgia (Hitt, 1991; Fig. 1). Counties were assigned to a major land-use category based upon the classification that accounted for the greatest proportion of the county's land area. The possible classifications of land-use were 1) cropland with pasture, woodland, and forest, 2) woodland and forest with some cropland and pasture, 3) forest and woodland mostly grazed, 4) forest and woodland mostly ungrazed, 5) swamp, 6) marshland, 7) urban areas, and 8) open water.

Information on source of drinking water (public or non-public) and type of waste water disposal (centralized sewer or on-site disposal, i.e., septic system or cess pit) for households in each county was obtained from the US Census Bureau (records were only available for 1990). The percent of homes using non-public water sources and percent using septic systems within each county were determined.

Statistical associations between monthly county case rates and land-use classification were assessed using Analysis of Variance (ANOVA) and post hoc Least Significant Difference (LSD) analyses were performed (SAS v.8). All associations were considered significant at $p \leq 0.05$. The GLM model (SAS v.8) was used to analyze the value of county percent of homes using non-public water sources and percent using septic systems to predict incidence rates.

Seasonal and Monthly Analysis

For the state, an ANOVA was performed to comparing case rates and month of the year. At the basin level of analysis, an autocorrelation procedure using month and incidence were performed for each of the basins with monthly lags incorporated to determine the seasonal patterns.

Watershed and Water Basin Geographic Analyses

Counties were assigned to watersheds (defined by USGS eight digit hydrologic unit codes (HUC)) based on the location of the county center using geographic information software (ARCGIS version 9.1). Each of the 53 watersheds were subsequently grouped into 9 river basins (Middle Tennassee- Hiwassee, Coosa-Tallapoosa, Savannah, Apalachicola (consisting of Apalachicola, Flint, and Chattahoochee), Altamaha, Ogeechee, Ochlocknee, Suwanee, and Satilla-St. Marys) (Table 1). Basins with less than 4 watersheds in them were excluded from analysis due to insufficient data. Watersheds were classified as impaired if any water body with in the watershed was impaired with high levels of fecal coliform bacteria as cited by the EPA (EPA, 1996, EPA, 1998, EPA, 2000, EPA, 2002).

Regional Water Quality Impairment. Information on impaired watersheds in Georgia (high levels of fecal coliform bacteria) was obtained from the Environmental Protection Agency (EPA) for 1996, 1998, 2000, and 2002 (EPA, 1996, EPA, 1998, EPA, 2000, EPA, 2002). The relationship between impaired watersheds and watershed case rates was analyzed using ANOVA (SAS v. 8) analysis and a post hoc LSD test was performed.

Meteorological and Climatological Factors. Daily precipitation, maximum daily temperature, and minimum daily temperature data were obtained from the National Climate Data Center (NCDC) for all weather stations in Georgia for 1987 – 2003. Data were available from

230 stations state-wide with an average of 4 stations per watershed, ranging from 1 to 16 stations per watershed. There were an average of 25 stations per basin, ranging from 1 to 218 stations per basin (Table 1). Data from all stations within an individual watershed or basin were compiled. Precipitation data were analyzed as the number of excess-precipitation days, which were determined by counting the number of days in a month with precipitation above the monthly mean for each watershed or basin. Monthly average daily maximum and minimum temperatures were calculated using the daily reported maximum and minimum air temperatures for all stations within a basin. These values were used in conjunction with the number of monthly precipitation-excess days in a General Linear Model (GLM) model (SAS v.8) to predict county incidence rates.

Climate variability was assessed using El Niño-Southern Oscillation events. Monthly sea surface temperature anomalies (SSTA) from the eastern equatorial Pacific (Niño Region 3.4; 5° N - 5° S and 170-120° W) were used as a proxy for an ENSO signal. Monthly data were obtained for 1987-2003 from the National Oceanic and Atmospheric Administration's (NOAA) National Weather Service Climate Prediction Center. Monthly SSTAs were converted to discrete categories for analysis by dividing the SSTA by 0.5, giving categories of half degree deviations in sea surface temperature.

Time series analysis (PROC AUTOREG) was used to evaluate the potential relationships between monthly campylobacteriosis rates within a water basin and meteorological and climate variables over time (study month). Given that case rates were count data and zero counts were frequently recorded for study counties, the *Campylobacter* rates were transformed using the Freeman Tukey Square Root Transformation (transformed rate = $(100{,}000)^{1/2}$ $\{[C/N]^{1/2} + [(C+1)/N]^{1/2}\}$ where C is the number of *Campylobacter* cases and N is the population) to accommodate model assumptions (Cressie, 1993). Basin-level variability in *Campylobacter* rates was evaluated for significant autocorrelation, and backward elimination of autocorrelation parameters was used to identify statistically significant autocorrelation functions to be retained in climate models of basin-wide monthly *Campylobacter* rates. Univariate associations between meteorological and climate variables (e.g., days of excess precipitation in study month, average maximum temperature, deviation of sea surface temperature) and monthly *Campylobacter* rates were evaluated, and variables were included in a multivariable model if $p \leq 0.10$. Lags of up to 3 months were evaluated for rainfall and sea surface anomaly variables in the univariate and bivariate models. Variables were retained in a multivariable model when $p \leq 0.05$. Model fit was assessed using the adjusted R^2 when all significant variables were included in the model.

RESULTS

Campylobacteriosis Rates

Between 1987 and 2003, the average annual incidence of culture confirmed *Campylobacter* infection in Georgia (statewide) was 13.4 ± 5.7 cases per 100,000 people with 16,119 reported cases and an average of 948 cases each year (Table 2). There were significant differences between basins with the highest rates in the Suwanee (16.8 per 100,000) and Apalachicola (15.6 per 100,000) basins and the lowest in the Ogeechee basin (7.4 per 100,000). Throughout Georgia, annual incidence declined through the period of record, with an average of 1.1 fewer cases per 100,000 people per year and an overall 68% decline in rates. This decline was not linear; data show a steep drop of 11.3 cases per 100,000 people between 1990 and 1993 (46.8% decrease), a small peak from 1993 to 1996, and a steady decline of 3.9 cases per 100,000 people from 1996 to 2003 (63.7% decrease). All basins showed declines over the period of study with Apalachicola showing the largest decline (80.6%) and Middle Tennessee showing the smallest decline (20.5%).

The mean annual case rate state-wide was significantly higher for males than for females, with 12.7 and 10.3 cases per 100,000, respectively. This pattern was observed for all basins. State-wide there were also significant differences across age groups. Mean annual case rates (N=12; 1990 – 2003, only) for children under 5 were significantly higher than any other group (Table 2). This group was followed by those aged 20-29. The lowest rates were seen in the >60 and 10-14 age groups. By basin, bimodal distributions were seen, the pattern varied between basins. In several basins (Coosa-Tallapoosa, Ochlockonee, Satilla-St Marys, and Suwanee) the highest rates were noted for the 0-4 and 5-9 age groups while other basins showed high rates in the 0-4 and 20-29 age groups. Case rates were significantly higher in young children (<5 years old) in the Suwanee and Satilla-St. Mary's basins where mean annual rates were 38.7 per 100,000 ($p<0.0001$), nearly double the state-wide average of 20.7 per 100,000.

County-Level Geographic Analyses

At the county level, land use, potable water source and method of wastewater disposal were evaluated to determine their relationship to incidence of campylobacteriosis. There were significant differences in land use categories with respect to incidence rates ($p=0.0021$). Counties categorized as either 'forest and woods, mostly ungrazed' or 'swamplands' had the highest annual incidence rates (12.9 and 11.8 cases per 100,000 people, respectively) while 'urban' counties had the lowest incidence rates (5.1 cases per 100,000 people). There was a small, but significant, inverse relationship between percentage of homes without municipal water and county incidence rates ($r^2=0.016$, $p<0.0001$). Likewise, counties with a higher percentage of homes with on-site waste disposal systems (septic systems and cess pits) corresponded weakly with lower incidence rates (r^2=0.012, p<0.0001).

Watershed and River Basin Geographic Analyses

Watersheds were evaluated for the relationship between impairment due to high levels of fecal coliform bacteria and incidence of disease. For the years analyzed, incidence of *Campylobacter* infection in those watersheds identified as impaired (~40/53 per year) were the same as in watersheds without high levels of fecal coliform bacteria.

Seasonality. State-wide between 1987 and 2003, case rates peaked in the summer months. Mean rates in June, July and August were significantly greater than those reported in other months (Fig. 2). Basin case rates exhibited a second, lower peak in the late fall, but this was not statistically significant. The results of analysis of significant seasonal autocorrelation of case rates varied among the different basins. All water basins exhibited significant autocorrelation between case rates reported within one month of each other. Only Altamaha, Suwannee, and Ogeechee basins exhibited significant short-term autocorrelation within a season (2 and 3 month lags). However, all basins except Satilla-St. Mary's and Ogeechee exhibited autocorrelation of case rates at a longer interannual interval of 10 to 12 months.

Case rates in all basins were evaluated for responses to ENSO (SSTA index), mean daily maximum temperature, mean daily minimum temperature, mean daily precipitation, and days with precipitation above the monthly precipitation mean (excess-precipitation days) over the 17 year period of record. In all basins, time (months) was a significant predictor of variability in case rates, reflecting the declining rate over the period of study. In the Apalachicola basin—the basin exhibiting the greatest decline over the study period—time was associated with nearly 60% of the case rate variability. The Satilla-St. Mary's basin exhibited the least change in case rates over time, with only 5.2% of the variability associated with this variable (Table 3). The daily maximum temperature was also significantly associated with case rates in all basins except Apalachicola in univariate analysis, explaining from 2.7% of the variability in case rates in the Ogeechee to 17.9% of the variability in case rates in the Altamaha basin. Precipitation measures were only significant in three of the basins with univariate analysis. Total monthly precipitation was a significant predictor of rates in the Ogeechee, Satilla-St. Mary's and Savannah basins but only explained 1.8 – 5.4% of the total variability. However, the number of excess precipitation days in a month was a significant predictor in the Altamaha, Satilla-St.Mary's, Savannah and Suwanee basins and explained 1.5 – 8.0% of the variability in univariate analysis. Half degree changes in SSTA (ENSO), monthly precipitation, and the interaction between half-degree SSTA changes (ENSO) measured two months previously and monthly precipitation also explained 6.9% and 3.1% of variability in basin case rates in the Apalachicola and Coosa-Tallapoosa basins, respectively.

In all basins, average maximum daily temperature and time were the most significant predictors of incidence using the autocorrelated adjusted data and produced the best fitting models predicting incidence. During the period over which climate data were available, average maximum daily temperature explained 90.1%, 87.8%, and 86.5% of the variation in incidence in the Savannah, Satilla, and Suwanee basins, respectively (Fig. 3). Time series models of Apalachicola, Altamaha, Ogeechee, and Coosa-Tallapoosa basins were most predictive when both average maximum daily temperature and time (study month) were included, and explained 72.3%, 58.1%, 33.7%, and 26.5% of the variation in case rates in those basins, respectively (Fig. 3).

DISCUSSION

During the 17 year period of analysis (1987-2003), rates of *Campylobacter* infection in Georgia averaged an annual 13.4 cases per 100,000 people and varied across the state from 16.8 cases per 100,000 people in Suwanee to 7.4 in Ogeechee. Between 1996 and 2003, the national (U.S) average was 21 cases per 100,000 people. During this period the incidence rate in Georgia declined from 21.2 to 6.8 cases per 100,000 people, a 68% decrease (average annual decrease of 5.4%). Nationally, a smaller decline in rates has been observed since 1996 (23% through 2000) with similar declines across all races, age groups, and genders (Samuel, 2004). The rate of decline observed among the different basins in Georgia varied, but the largest decline (80.8%) was seen in one of the high rate basins, Apalachicola. The declines observed across the United States and Georgia are significant due to the fact that around the world in both developed and developing countries the incidence of campylobacteriosis has risen substantially over the past 20 years (Coker et al. 2002). Possible explanations for this disparity have been suggested, including improvements in the meat processing and poultry industries in the U.S. associated with Hazard Analysis and Critical Control Points/ Pathogen Reduction (HACCP/PR) rule implementations (Buchanan and Whiting, 1998). However, these rules were implemented in 1997 and do not explain the significant decline noted throughout Georgia early in the period of study (prior to 1993).

Counties in Georgia with consistently high rates have been identified (Chapter 3) including Clinch, Lanier, and Ware in the Suwanee basin, Appling, Charlton, and Pierce in the Satilla – St. Mary's basin, Ben Hill in the Altamaha basin, Oglethorpe in the Savannah basin, and Schley in the Apalachicola basin (Table 1). None of these counties followed demographic trends noted for the rest of state, that is these high rate counties had a low population density and tended to trend toward the older age groups whereas the larger pattern suggested that high density counties with young populations had higher rates. These observations combined with recent studies associating *Campylobacter* infection rates with climate and agricultural land use (Louis et al., 2005; Kovats, 2005; Patrick, 2004) have made it evident that previous research using only demographic variables have not adequately explained the variation in *Campylobacter* infection rates in the U.S. and Georgia. This study examined possible environmental factors to explain trends in the Georgia *Campylobacter* infection rates.

Major environmental influences include land-use, potable water source, method of sewage disposal, watershed impairment, and climatological factors (daily maximum and minimum temperatures, daily precipitation/days above the monthly mean, and ENSO). These factors are greatly tied to water quality and can affect large areas. In order to examine these factors, the scale of effect had to be considered. The data were first examined on the county level to ascertain the relationship between land-use, potable water source, and method of sewage disposal to rates of *Campylobacter* infection. These counties were then aggregated into watersheds to examine the relationship of impairment of the watershed to incidence of *Campylobacter* infection. For the larger scale climatological factors, daily maximum and minimum temperatures, daily precipitation/days above the monthly mean, and ENSO, the watersheds were aggregated into the river drainage basins for proper analysis.

County. It has previously been shown that land use has a great effect on the local environment and human health (urban areas allowing for more runoff; forestlands allowing the least) (Interlandi and Crockett, 2003, Sherestha, 2003). The source of run-off can in turn affect the types and amounts of pathogens found in the waterways with agricultural and farmlands often associated with fecal pathogens (Atwill, 1995, Mallin et al., 2000, Graczyk et al., 2000, Crowther et al., 2002, Stanley and Jones, 2003, Ferguson et al., 2003, Kelsey et al., 2004). Indeed, Potter et al. (2002) has found an association between high concentrations poultry/farmland and high rates of campylobacteriosis (Potter et al., 2002). In this study we found that counties categorized as ‘forest and woods mostly ungrazed’ and ‘swamplands’ had the highest incidence rates while ‘urban’ counties had the lowest incidence rates, suggesting that rural areas may be more prone to high rates of infection. However, this presents a disparity between these findings and our demographic analyses that revealed that counties with higher population densities (presumably more urban) had higher rates (Chapter 3). This may be explained by the way that county land areas were assigned. The classification of counties was performed by examining the map for the major land-use type in that county (fig. 1), which does not measure population density rather it assigns a land-use category based on spatial aggregation and percentage of land-use type. In fact, only two counties were classified as urban. Despite these differences, the trends noted here for land-use suggest that areas with few population centers (or making up a small percentage of the county land area) and more agrarian or ‘natural’ lands had higher disease burden, which is consistent with other reports (e.g., Louis et al. 2005)

Statistically significant relationships were noted between the density of non-municipal potable water source and on-site sewage disposal and rates, which indicated that these factors were predictors of lower case rates. However, only 1.2% to 1.6% of the variability in the case data could be explained by either of these variables, suggesting that they are of low value in studying the epidemiology of this disease.

Watersheds. The majority of diarrheal disease, worldwide, is attributed to unsafe drinking water (WHO, 2003) where it is believed that pathogens from fecal mater are transmitted to humans (Atwill, 1995). *Campylobacter* have been readily found in natural waters (Lucey et al., 2000, Jones, 2001) and transmission to humans from water is known from outbreaks and sporadic cases (CDC, 1991, Barwick et al., 2000, Clark et al., 2003). In this study it was expected that watersheds that were found to be impaired with fecal coliform bacteria would have a higher incidence of campylobacteriosis; however, this was not observed. Watersheds with no impairment had similar rates to those with impairment. These results suggest that fecal coliform bactera may be a poor indicator of water contamination with specific enteric pathogens such as *Campylobacter,* or that hydrologic and climate factors may be stronger drivers of waterborne disease than microbial impairment alone.

Basin. The basin level analysis allowed for examination of large scale factors, such as climate, on disease rates. It has been shown that variation in precipitation affects the local environment and human health in that extreme changes in precipitation are known to be associated with decreased water quality (Leeming et al., 1998, Lipp et al. 2001, Interlandi and Crockett, 2003) and increased gastrointestinal disease (Curreno et al., 2001, Lipp et al, 2002), including campylobacteriosis (Louis et al., 2005). Temperature has also been shown to have a great effect on campylobacter survivability such that lower temperatures are favorable (Buswell, 1998); however, published studies have found that higher temperatures and hours of sunshine are significantly associated with the campylobacteriosis incidence (Kovats, 2005; Louis, 2005; Patrick, 2004). Both high temperature and the number of hours of sunlight in the summer help to explain the consistent seasonality of this disease; but still do not provide a mechanism for the trend. These associations are consistent with our findings. Time series models that included precipitation and either maximum daily temperature or minimum daily temperature ($R>0.7$) explained a significant percentage of the variability in incidence of campylobacteriosis by basin, when adjusted for seasonal effects. Maximum daily temperature alone was best able model those basins for which weather data were only available beginning in 1997 (Savannah and Suwanee basins) and in 1999 (Satilla basin). For basins with complete weather data (1987 – 2003), increasing average maximum daily temperature and short-term (seasonal) and longer-term (annual) temporal associations gave the best models, with these variables accounting for the most variation in rates in the Apalachicola basin model with 72.3% of the total variation explained. It is important to note that this is also one of the basins with the highest case rates. Only Suwanee had higher rates, and increasing maximum daily temperature alone explained 86.5% of the variation in *Campylobacter* case rates during the short period of time for which climate data were available.

It has been shown that ENSO events have effects on the environment and public health due in part to their effect on local and regional weather patterns (Schmidt et al., 2001, El-Askary, 2004), which impacts water quality (Lipp et al., 2001, Schmidt et al., 2001) and waterborne disease (Lipp et al., 2002, Patz, 2002). While local ENSO effects have not been studied in detail for Georgia, regional analyses show that precipitation is significantly affected by ENSO such that El Niño and La Niña events result in higher and lower precipitation, respectively. ENSO events can be modeled using a SSTA proxy, where higher SSTA are indicative of an El Niño state and lower SSTA of a La Niña state. Univariate models using 0.5 degree changes in SSTA were significant predictors of disease incidence in the Coosa-Tallapoosa and Apalochicola basins at 2-months lags. However, the strong decreasing trend in case rates over the study period combined with incomplete knowledge of the increments of change in SSTA and precipitation that may be associated with local-level changes in case rates prevented adequate analysis of the potential role that this large scale climate driver may play in human campylobacteriosis.

CONCLUSIONS

In Chapter 3 we presented results that demonstrated demographic patterns associated with high case rates were high population density, young populations (<5 and 20-29 year age groups), and largely white populations; however, in the counties with the most frequent high case rates over time this trend was not observed. These high incidence counties were all located in rural areas of southern GA with population densities of < 69.6 per mi^2. We hypothesized that other factors were influencing the distribution of rates in Georgia, particularly in these regions.

Here the environmental variables land use, source of potable water, sewage disposal method, watershed impairment, and climatological factors were evaluated for their role in case rates in Georgia. Declining rates across the state over time was often among the best predictors of case rates in time series analyses. It is of note, however, that some river basins exhibited only small changes over time, indicating that much of the decline in state-wide rates may be due to only a few areas (basins). While precipitation and ENSO events had some influence on certain basins, temperature (maximum daily temperature) was the most important environmental predictor of basin-wide variability in case rates.

The counties of interest, which had high rates despite a low population density, included Clinch, Ware and Lanier, all located in the Suwanne basin. While differing from the demographics of the state, the trends in case rates in this watershed better correspond to previous research that suggest that rural and agricultural areas are more prone to high incidence of campylobacteriosis (e.g., Kovats, 2005; Louis et al., 2005; Patrick, 2004). Furthermore, the primary role of temperature in explaining the case rate variability is also consistent with reports from other areas (Kovats, 2005; Louis et al., 2005; Patrick, 2004). Therefore, it seems that in Georgia, environmental factors may be the best predictors of disease in some rural areas whereas demographics may play a greater role in highly metropolitan areas. These observations are difficult to interpret, however, because of the incompatibilities between the various units of analyses and the lack of understanding of the natural history of campylobacteriosis among these different demographic and geographic units of analysis. This study highlights the poorly understood ecology of this disease and suggests that there are multiple risk factors of disease at the individual level that are modified by large scale and regional environmental impacts on pathogen presence. This information on the difference between urban and rural centers is important in attempts to prevent and understand this disease and suggests that different strategies may be needed.

REFERENCES

Altekruse, S.F., Stern, N.J., Fields, P.I., Swerdlow, D.L., 1999. *Campylobacter Jejuni*—An Emerging Foodborne Pathogen. Emerging Infectious diseases. 5:28-35.

Ashbolt, N.J., 2004. Microbial contamination of drinking water and disease outcomes in developing regions. Toxicology. 198(1-3):229-238.

Atwill, E.R., 1995, Microbial Pathogens Excreted by livestock and Potentially Transmitted to Humans through Water. Veterinary Medicine Teaching and Research Center, University of California Davis.

Barwick, R., Levy, D., Craun, G., Beach, M., Calderon, R., 2000. Surveillance for waterborne disease outbreaks. MMWR. 49(SS04):1-35.

Buchanan, R.L., Whiting, R.C., 1998. Risk Assessment: A Means for Linking HACCP Plans and Public Health. Journal of Food Prot. 61:1531-1534.

Buswell, C.M., Herlihy, Y.M., Lawrence, L.M., McGuiggan, J.T.M., Marsh, P.D., Keevil, C.W., Leach, S.A., 1998. Extended Survival and Persistence of Campylobacter spp. in Water and Aquatic Biofilms and their Detection by Immunoflourescent-Antibody and –rRNA Staining. Applied and Environmental Microbiology. 64, 733-741.

Buzby, J.C., Roberts, T., 1997. Estimated Annual Cost of *Campylobacter*-Associated Guillain-Barré Syndrome. USDA/ERS report, Washington DC.

CDC (Center for Disease Control), 1991. *Campylobacter* enteritis—New Zeland, 1990, MMWR. 40(7):116-117,123.

CDC, 2004. *Campylobacter* Infections. Http://www.cdc.gov/ncidid/dbmd/diseaseinfo/campylobacter_t.htm. [online]

Coker, A.O., Isokpehi, R.D., Thomas, B.N., Amisu, K.O., Obi, C.L., 2002. Human Campylobacteriosis in Developing Countries. Emerging Infectious Diseases. 8(3):237-243.

Cressie, N., 1993. Statistics for spatial data. Wiley-Interscience, New York, N.Y.

Crowther, J., Kay, D., Wyer, M.D., 2002. Faecal-indicator concentrations in waters draining lowland pastoral catchments in the UK: relationships with land use and farming practices. Water Research. 36 (7), 1725-1734.

Curreno, F., Patz, J., Rose, J., Late, S., 2001. The association Between Extreme Precipitation and Waterborne Disease Outbreaks in the United States, 1948-1994. American Journal of Public Health. 91(8):1194-1197.

EL-Askary, H., Sarkar, S., Chiu, L., Kafatos, M., El-Ghazawi, T., 2004. Rain gauge derived precipitation variability over Virginia and its relation with the El Nino southern oscillation. Advances in Space Research 33 (3), 338-342.

Environmental protection agency (EPA), 1996. List of Impaired Waters. The National Water Quality Inventory Report to Congress.

EPA, 1998. List of Impaired Waters. The National Water Quality Inventory Report to Congress.

EPA, 2000. List of Impaired Waters. The National Water Quality Inventory Report to Congress.

EPA, 2002. List of Impaired Waters. The National Water Quality Inventory Report to Congress.

Ferguson, C., de Roda Husman, A.M., Altavilla, N., Deere, D., Ashbolt, N., 2003. Fate and Transport of Surface Water Pathogens in Watersheds. Critical Reviews in Environmental Science and Technology. 33 (3), 299-361.

GASS (Georgia Agricultural Statistics Service), 2004, Number of Farms and Land in Farms. Georgia Farm Report. 4(3):3.

Graczyk, T., Evans, B., Shiff, C., Karreman, H., Patz, J., 2000. Environmental and Geographical Factors Contributing to Watershed Contamination with *Cryptosporidium parvum* Oocysts. Academic Press, Environmental Research Section A. 82:263-271.

Hariharan, H., Murphy, G.A, Kempp, I., 2004. *Campylobacter jejuni*: Public health Hazards and potential control methods in poultry: a review. Vet Med. 49(11):441-446.

Hitt, K.J., 1991. WSGSWR Landuse Digital map file (GA) of major land uses in the United States. USGS, Reston, Va.

Interlandi, S.J., Crockett, C.S., 2003. Recent water quality trends in the Schuylkill River, Pennsylvania, USA: a preliminary assessment of the relative influences of climate, river discharge and suburban development. Water Research. 37 (8), 1737-1748.

Jones, K., 2001. Campylobacters in water, sewage and the Environment. Journal of Applied Microbiology. 90,68S-79s.

Kambole, M.S., 2003. Managing the water quality of Kafue River. Physics and Chemistry of the Earth. 28, 1105-1109.

Kapperud, G., Skjerve, E., Bean, N., Ostroff, S., Lassen, J., 1992. Risk factors for sporadic *Campylobacter* infections: result of case-control study in southeastern Norway. J Clin Microbiol. 30(12):3117-3121.

Keener, K.M., Bashor, M.P., Curtis, P.A., Sheldon, B.W., Kathariou, S., 2004. Comprehensive Review of *Campylobacter* and Poultry Processing. Comprehensive Reviews in Food Science and Food Safety. 3:105-116.

Kelsey, H., Porter, D., Scott, G., Neet, M., White, D., 2004. Using geographic information systems and regression analysis to evaluate relationships between land use and fecal coliform bacterial pollution. Journal of experimental marine biology and ecology. 298:197-209.

Kistemann, T., Claben, T., Koch, C., Dangendorf, F., Fischeder, R., Gebel, J., Vacata, V., Exner, M., 2002, Microbial load of Drinking Water Reservoir Tributaries during extreme Rainfall and Runoff. Applied and Environmental Microbiology. 68, 2188-2197.

Kussin, M., Nuortin, J., Hannien, L., Koskela, M., Jussila, V., Kela, E., Miettien, I., Ruutu, P., 2005. A large outbreak of campylobacteriosis associated with municipal water supply in Finland. Epidemiol Infect. 133(4):593-601.

Kovats RS, Charron D, Cowden J, D'Souza RM, Ebi KL, Edwards SJ, Gauci C, Gerner-Smidt P, Hajat S, Hales S, Hernández Pezzi G, Kriz B, Kutsar K, McKeown P, Mellou K, Menne B, O'Brien S, van Pelt W, Schmid H (2005) Climate variability and *campylobacter* infections: an international study**.** International Journal of Biometeorology, 49(4):207-214.

Leeming, R., Bate, N., Hewlett, R., Nichols, P.D., 1998. Discriminating faecal pollution: a case study of stormwater entering Port Phillip Bay, Australia. Water Science and Technology. 38 (10), 15-22.

Lindback, J., Svensson, A., 2001. *Campylobacter* infections in Sweden-A statistical analysis of temporal and spatial distributions of notified sporadic campylobacter infections. Mathematical Statistics Stockholm University, Research report 2001:4. ISSN 1650-0377.

Lipp, E.K., Schmidt, N., Luther, M.E., Rose, J.B., 2001, Determining the effects of El Nino-Southern Oscillation events on Coastal Water Quality. Estuaries. 24. 491-497.

Lipp, E.K., Huq, A., Colwell, R.R., 2002. Effects of Global Infectious Disease: the Cholera Model. Clinical Microbiology Reviews. 15, 757-770.

Louis, V., Gillespie, I., O’Brien, S., Russek-Cohen, E., Pearson, A., Colwell, R., 2005. Temperature-Driven *Campylobacter* Seasonality in England and Wales. Applied and Environmental Microbiology. 71(1): 85–92.

Lucey, B., Crowley, D., Moloney, P., Cryan, B., Daley, M., O'Halloran, F., Threlfall, E.J., Fanning, S., 2000. *Campylobacter* spp. of human and Animal Origin. Emerging Infectious Diseases. 6(1)

Mallin, M., Williams, K., Esham, C., Lowe, P., 2000. Effect of Human development on bacteriological water quality in coastal watersheds. Ecological Applications. 10(4):1047-1056.

Miller, G., Dunn, G., Smith-Palmer, A., Ogden, I., Strachan, N., 2004. Human camoylobacteriosis in Scotland: seasonality, reagional trends and bursts of infection. Epidemiology Infection. 132:585-593.

Nichols, G., 2005. Fly Transmission of *Campylobacter*. EID. http://www.cdc.gov/ncidod/EID/vol11no03/04-0460.htm.

Oberhelman RA, Taylor DN. *Campylobacter* infections in developing countries. In: Nachamkin I, Blaser MJ, editors. *Campylobacter*, 2nd edition. Washington: American Society for Microbiology; 2000. p.139-53.

Patrick, M., Christiansen, L., Waino, M., Ethelburg, S., Madsen, H., Wegener, H., 2004. Effects of climate on incidence of *Campylobacter* spp. in humans and prevalence in broiler flocks in Denmark. App Environ microbiol. 70(12):7474-80.

Patz, J.A., 2001. Public Health Risk Assessment Linked to Climatic and Ecological Change. Human and Ecological Risk Assessment. 7 (5), 1317-1327.

Patz, J., 2002. A human disease indicatior for the effects of recent global climate change. PNAS. 99(20): 12506-12508.

Potter, R., Kaneene, J., Gardiner, J., 2002. A comparison of *Campylobacter jejuni* enteritis incidence rates in high and low poultry density counties: Michigan 1992-1999. Vector Borne Zoonitic Dis. 2(3):137-143.

Rosef, O., Kapperrud, G., 1983. House Flies (*Musca domestica*) as Possible Vectors of *Campylobacter fetus* subsp. *Jejuni*. Applied and Environmental Microbiology. Feb:381-383.

Samuel, M. Reilly, K., Shallow, S., Marcus, R., Segler, S., McGivern, T., Kassenborg, H., Hollinger, K., Vose, D., Bartholomew, M., Kennedy, M., Vugia, D., 2000. Burden of *Campylobacter* Infection in United States and Declining Trend in California, FoodNet 1996-1998. 2nd International Conference on emerging Infectious Diseases, Atlanta, GA, July.

Samuel, M.C., Vugia, D.J., Shallow, S., Marcus, R.,Segler, S., McGivern, T., Kassenborg,H., Reilly, K., Kennedy, M., Angulo, F., Tauxe, R.V., 2004. Epidemiology of Sporadic *Campylobacter* Infection in the United States and Declining Trend in Incidence, Food Net 1996-1999. CID, 38, S165-S174.

Schmidt, N., Lipp, E.K., Rose, J. B., Luther,M. E., 2001. Enso Influences on Seasonal Rainfall and River discharge in Florida. American Meterological Society. 14, 615-628.

Shrestha, M.N., 2003. Spatially Distributed Hydrological Modelling considering Land-use changes using Remote Sensing and GIS. Map Asia Conference 2003. GIS development.net, 1-8.

Stanley, K., Jones, K., 2003. Cattle and Sheep Farms as Reservoirs of *Campylobacter.* Journal of Applied Microbiology. 94:104s-113s.

USDA (US_Food_and _Drug_Administration), 2003, posting date. Foodborne Pathogenic Microorganisms and Natural Toxins Handbook http://vm.cfsan.fda.gov/~mow/chap4.html [Online]

Van Gilder, T., Vugia, D., Fiorentino, T., Segler, S., Carter, M., Smith, K., Morse, D., Cassidy, M., Angulo, F., 1999. Decline in Salmonella and *Campylobacter* but not E. coli O157 isolation rates in FoodNet sites: Farm, food, or fluctuation? 37th Annual Meeting of the Infectious Disease Society of America, Philadelphia, PA, November.

WHO (World Health Organization), 2003. Quantifying selected major risks to health. The world health report 2002. World health Organization. Geneva. (Chapter 4)

Table 1. Waterbasins with corresponding watersheds, counties, and number of weather stations in that basin.

Basin	Watersheds	Counties	Number of Weather Stations
Altamaha	Altamaha River, Little Ocmulgee River, Lower Ocmulgee River, Lower Oconee River, Ohoopee River, Upper Ocmulgee River, Upper Oconee River	LONG, MONTGOMERY, WAYNE, BLECKLEY, DODGE, WHEELER, BEN HILL, HOUSTON, PEACH, PULASKI, TELFAIR, TWIGGS, WILCOX, BALDWIN, HANCOCK, LAURENS, WILKINSON, JOHNSON, TATTNALL, TOOMBS, TREUTLEN, BIBB, BUTTS, DEKALB, GWINNETT, HENRY, JONES, LAMAR, MONROE, NEWTON, ROCKDALE, WALTON, BARROW, CLARKE, GREENE, JACKSON, JASPER, MORGAN, OCONEE, PUTNAM	192
Apalachicola	Apalachicola River, Ichawaynochaway Creek, Kinchafoonee-Muckalee Creeks, Lower Chattahoochee, Lower Flint, Middle Chattahoochee - Lake Harding, Middle Chattahoochee - Walter F. George Reservoir, Middle Flint - Lake Blackshear, Spring Creek, Upper Chattahoochee River, Upper Flint	CALHOUN, RANDOLPH, TERRELL, LEE, SUMTER, WEBSTER, CLAY, BAKER, DECATUR, DOUGHERTY, MITCHELL, COBB, DOUGLAS, FULTON, HARRIS, HEARD, TROUP, CHATTOOGA, MUSCOGEE, QUITMAN, STEWART, CRISP, DOOLY, MARION, SCHLEY, EARLY, MILLER, SEMINOLE, FORSYTH, HABERSHAM, HALL, LUMPKIN, WHITE, CLAYTON, COWETA, CRAWFORD, FAYETTE, MACON, MERIWETHER, PIKE, SPALDING, TALBOT, TAYLOR, UPSON	212
Coosa-Talapoosa	Conasauga River, Coosawattee River, Etowah River, Oostanaula River, Upper Coosa River, Upper Tallapoosa River	MURRAY, WHITFIELD, GILMER, GORDON, BARTOW, CHEROKEE, DAWSON, PAULDING, PICKENS, CHATTAHOOCHEE, FLOYD, POLK, WALKER, CARROLL, HARALSON, FANNIN	89
Middle Tennesee	Hiawassee River, Middle Tennessee - Chickamauga Creek	TOWNS, UNION, CATOOSA, DADE	7

Ochlockonee	Apalachee Bay-St. Marks, Lower Ochlockonee, Upper Ochlockonee	GRADY	1
Ogeechee	Canoochee River, Lower Ogeechee River, Ogeechee River Coastal, Upper Ogeechee River	BRYAN, CANDLER, EMANUEL, EVANS, BULLOCH, CHATHAM, LIBERTY ,MCINTOSH, GLASCOCK, JEFFERSON, JENKINS, WARREN, WASHINGTON	41
Satilla-St. Marys	Cumberland-St. Simons, Little Satilla River, Satilla River, St. Marys River	APPLING, ATKINSON, BACON, BRANTLEY, CAMDEN, COFFEE, JEFF DAVIS, PIERCE, CHARLTON, GLYNN	47
Savannah	Brier Creek, Broad River, Lower Savannah River, Middle Savannah River, Seneca River, Tugaloo River, Upper Savannah River	BURKE, BANKS, FRANKLIN, MADISON, OGLETHORPE, MCDUFFIE, EFFINGHAM, SCREVEN, COLUMBIA, RICHMOND, TALLIFERRO, RABUN, STEPHENS, ELBERT, HART, LINCOLN, WILKES	54
Suwannee	Aucilla River, Little, Upper Suwannee River, Withlacoochee River	IRWIN, LANIER, LOWNDES, TURNER, THOMAS, TIFT, CLINCH, ECHOLS, WARE, BERRIEN, BROOKS, COLQUITT, COOK, WORTH	41

Table 2. Mean annual incidence of campylobacteriosis by basin for the total population and by gender and age group.

Basin	Mean Incidence (1987-2003)	Percent Decline	Incidence by Gender (1990-2003)		Incidence by Age Group (1992-2003)								
			male	female	0-4	5-9	10-14	15-19	20-29	30-39	40-49	50-59	≥60
Altamaha	11.5	68.4%	10.8	8.8	16.4	7.3	4.9	6.6	14.3	10.6	7.8	6.3	5.5
Apalachicola	15.6	80.8%	13.1	10.5	15.6	8.6	5.6	5.8	12.8	11.5	8.1	6.9	6.7
Coosa- Talapoosa	11.4	39.8%	13.0	9.9	25.2	15.3	6.1	9.3	13.8	10.4	8.5	7.7	5.9
Middle Tennesee	12.8	20.0%	12.8	11.2	23.3	14.4	5.2	11.2	17.3	10.3	13.9	8.1	9.3
Ochlockonee	12.7	31.4%	11.6	6.2	19.8	15.4	4.7	9.8	0.0	10.4	5.0	0.0	14.7
Ogeechee	7.4	72.6%	6.1	6.0	7.6	4.3	3.6	3.2	6.4	5.2	5.6	4.1	5.3
Satilla-St. Marys	13.4	44.4%	14.8	11.8	38.7	16.3	5.7	12.7	10.4	8.8	4.7	8.9	8.2
Savannah	12.3	42.6%	12.8	10.2	16.5	8.5	5.1	7.6	13.5	12.4	8.6	8.9	8.4
Suwannee	16.8	49.6%	19.0	16.1	38.7	18.9	11.9	13.6	15.6	12.9	10.7	8.9	8.4
Georgia	13.4	68.0%	12.7	10.3	20.7	11.0	6.4	8.3	16.3	13.7	10.0	7.6	5.9

Table 3. Proportion of variability (R^2) explained by variables significantly associated ($p \le 0.10$) with campylobacteriosis in univariate analysis (no adjustment for autocorrelation).

	Time	PPT	Days over mean	Tmax	ENSO*PPT interaction (ENSO Lag)
Altamaha	37.9		1.5	17.9	
Apalachicola	59.7				6.9 (2 months)
Coosa-Tallapoosa	11.5			9.9	3.1 (2 months)
Ogeechee	30.0	1.8		2.7	
Satilla-St. Mary's	5.2	5.4	8.0	13.3	
Savannah	33.5	5.1	7.4	15.5	
Suwanee	30.6		1.9	11.5	

Figure 1. Landuse categories.

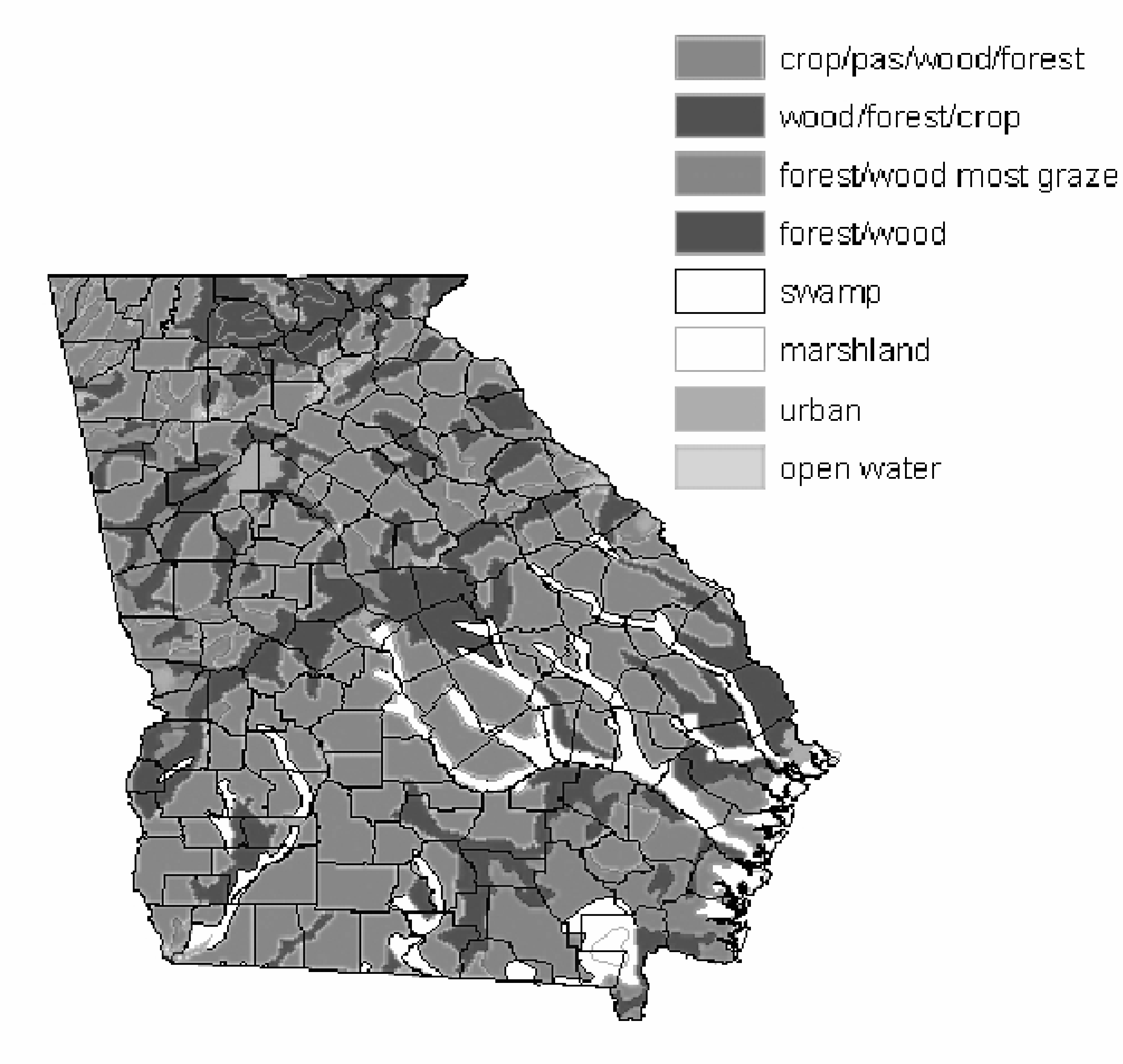


Figure 2. Monthly incidence of campylobacteriosis (1987 – 2003) for the state of Georgia, USA.

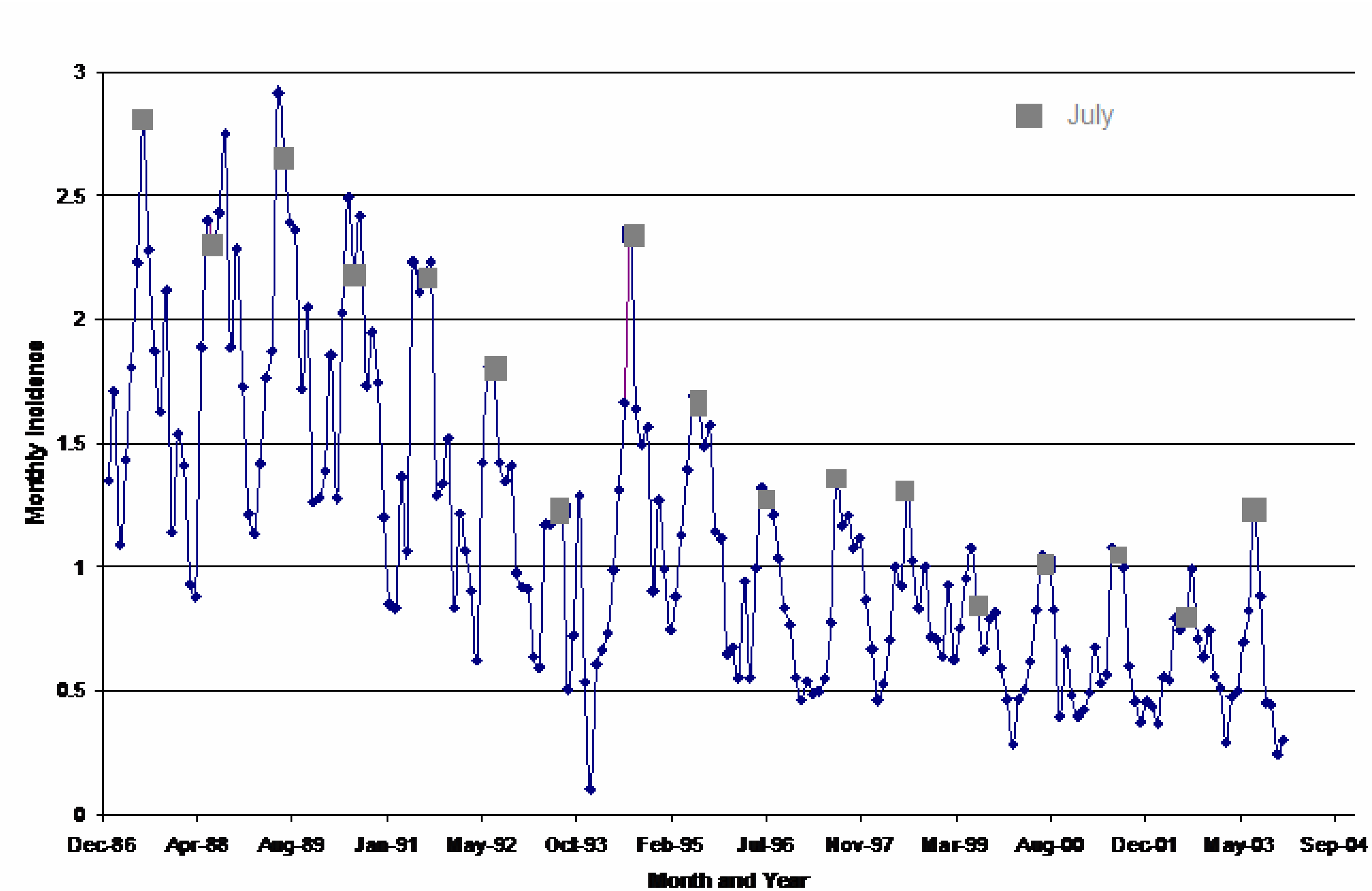
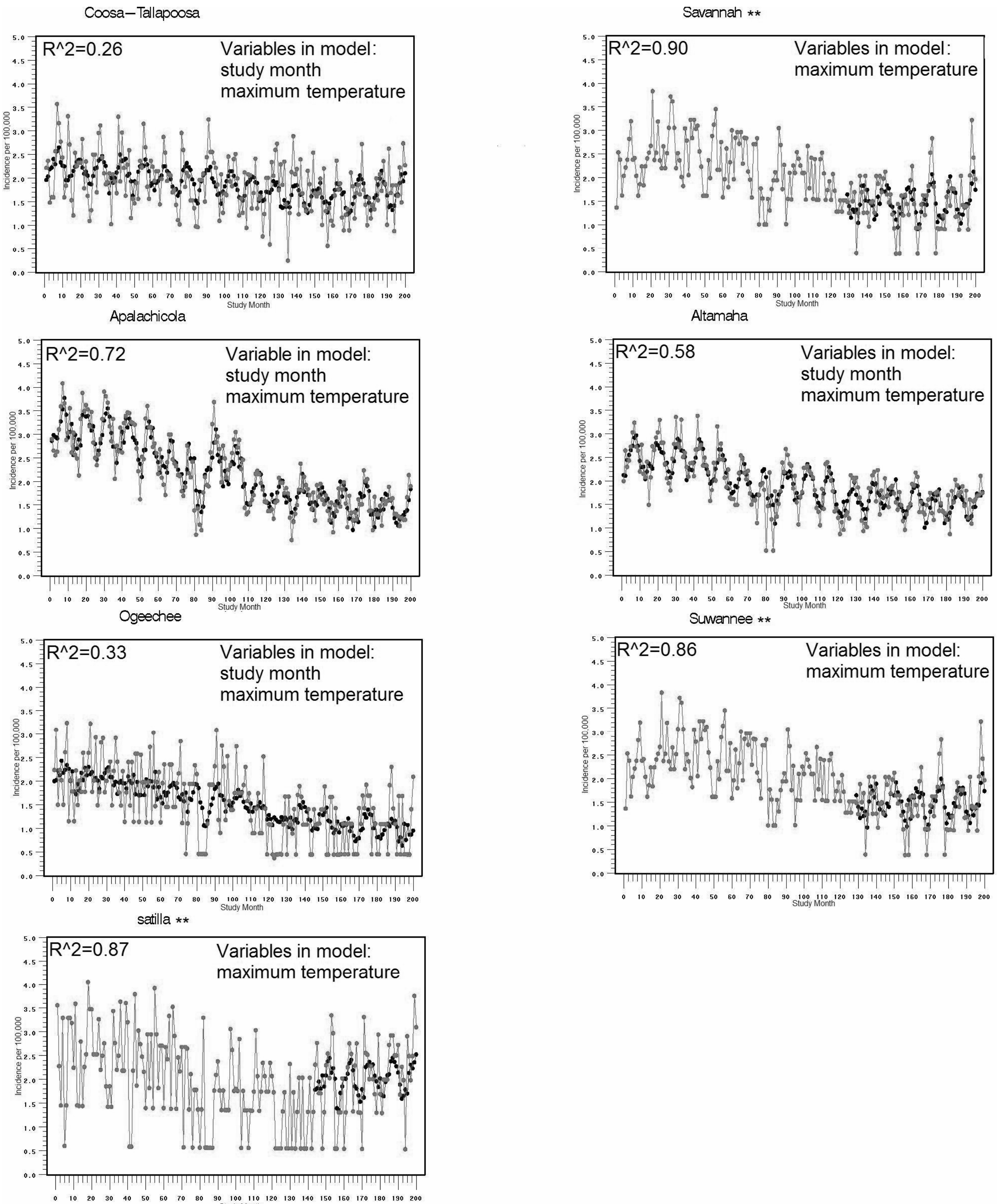
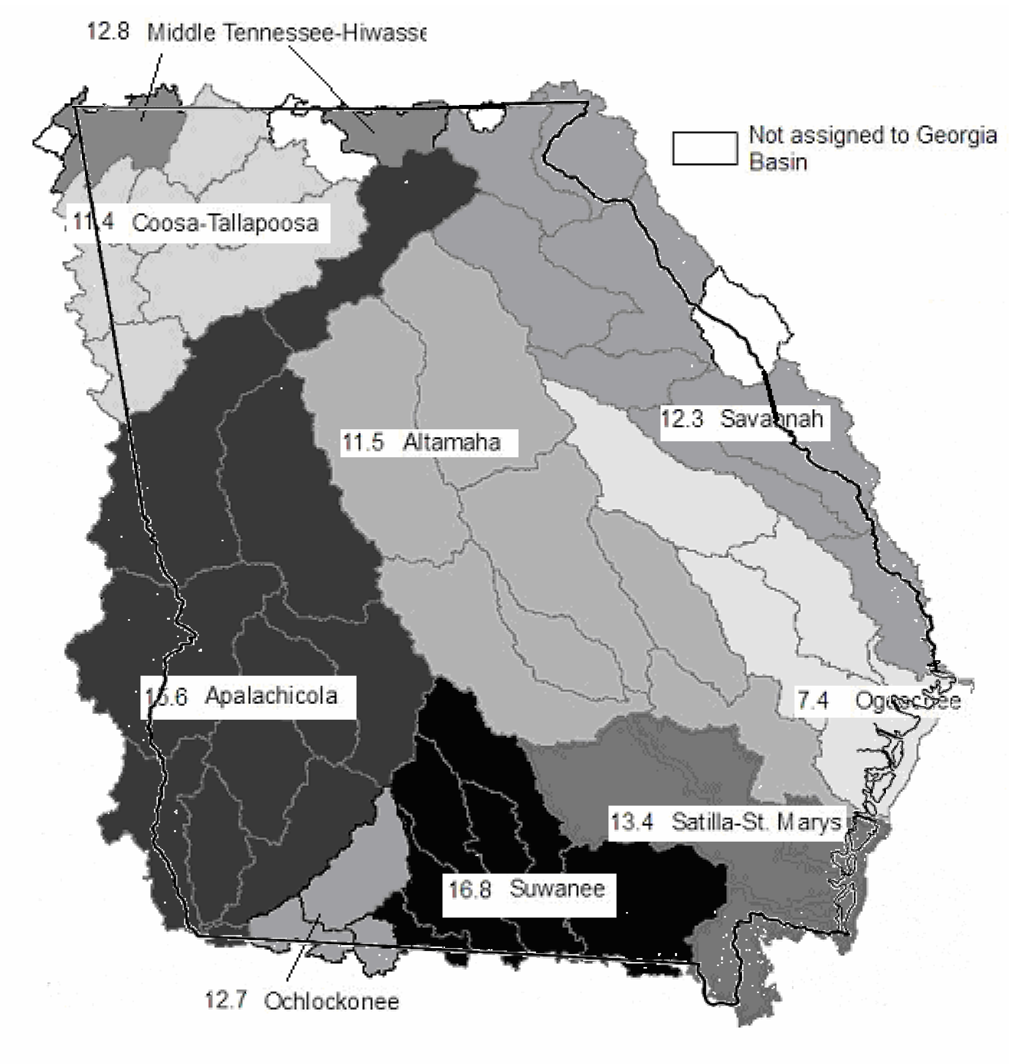


Figure 3. Basin predicted (gray line) and observed rates (black line) (per 100,000) over time (study month, beginning January 1987 through December 2003).



** Precipitation data only available for a portion of the evaluation period. Rates shown are tukey transformed. Predictive models of rates include adjustments for seasonal and interannual variation.

Figure 4. Incidence within Georgia's river basins (cases per 100,000).



CHAPTER 5

CONCLUSIONS

Published literature has shown the relationship of climate to health and disease. Large climatic events (e.g., ENSO) affect global and local weather patterns resulting in increased precipitation and runoff. Based on the type of land use, this runoff can be great and can contain pathogens such as *Campylobacter*. This pathogen is able to persist in natural waters, where humans may be exposed. The source of the drinking water may also be a key factor in the transmission of the disease. The goal of the research, presented in this thesis, was to describe the trends and relate land use, weather, and other environmental factors with changes in Georgia *Campylobacter* case rates with the long term aim of linking key environmental drivers with climate change and variability (i.e., ENSO).

Most studies of campylobacteriosis in the U.S. to date have relied on Food Net data (that only represents a very small portion of the US population --5.4% in 1996 and 9.5% in 1999--and is only available from 1996) to describe and identify trends in campylobacteriosis. With these data, extrapolations have been made to describe many observed trends, particularly the decline in incidence. This decline has been noted from 1996-2003 and has been attributed to improvements in the poultry industry. In this study we found that the rate of the major decline in rates in Georgia occurred prior to implementation of HACCP changes in the poultry industry made in 1997 and the decline in disease rates in Georgia actually slowed from 1996 through 2003. This study is important because it allowed for the examination of trends prior to Food Net surveillance. The other trends identified in this study included geographic variation in rates by county, and basin, a bimodal distribution of rates by age with the highest rates in the 0-4 and 20-

29 year age groups, males having higher rates than females, and blacks having significantly lower rates than whites. These findings provided another source of discrepancy, because the counties that consistently had the highest rates did not follow these trends. This suggested that there were other factors influencing the incidence of campylobacteriosis in Georgia.

The evaluation of environmental factors demonstrated that there was a significant influence of these variables on *Campylobacter* infection rates in Georgia, with temperature having the largest influence. Of the states participating in Food Net surveillance Georgia reports the fewest cases of campylobacteriosis, yet has the highest amount of hospitalizations from the disease. Consequently, the burden of this disease on the health and economics of this state is great. In efforts to decrease the incidence of campylobacteriosis it is important to understand the the complex ecology of the disease and examine the potential role of non-foodborne routes of infection in order to finds new methods of prevention. This research provides some evidence of a waterborne route of infection. Given these findings, it could be of particular importance in public health to use these factors in formulating predictive models and prevent future disease.