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Connecticut Primary Care Physicians and Chronic Lyme Disease

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This is to certify that the doctoral dissertation by

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has been found to be complete and satisfactory in all respects,
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2019

Abstract

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MA, Central Connecticut State University, 2006

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Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

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Abstract

The prevalence of chronic Lyme disease (CLD) remains relatively unknown in Connecticut because there is not an agreement on what CLD is and how it should be diagnosed in addition to which pathological agent causes CLD. The aim of this quantitative study was to assess whether there were significant differences between two groups of primary care physicians (PCP) working in Connecticut from two different points in time regarding their knowledge in the diagnosis, treatment, and management of CLD. A knowledge, attitude, and practice model was used as the underlying theoretical framework for this study. A random cross-sectional survey was mailed out to the 1,726 PCPs found in the list of certified medical doctors in Connecticut of 2015. One hundred and forty-five PCPs responses (11.9% response rate) were received and compared to responses from previous data (a 2010 study) of 285 PCPs (39.1% response rate) from the list of certified medical doctors in 2006. The PCP estimated mean number of patients diagnosed and treated for CLD was not significantly different between 2006 and 2015. However, a significantly higher number of PCPs in 2015 reported knowing Lyme disease (LD) symptoms but not feeling comfortable diagnosing LD ($\chi^2 = 536.83$, $p < 0.001$), and significantly more PCPs in 2015 reported knowing LD symptoms and feeling comfortable diagnosing CLD ($\chi^2 = 265.41$, $p < 0.001$). This study can promote social change by encouraging Connecticut PCPs to recognize CLD as a diagnosis to enable the development of registries and case-control assessments. The findings of this study may also inspire future studies.

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Dedication

I dedicate my dissertation work to FBI Agent Samuel Hicks, an exceptional young man whose life was cut short. Tragically, Special Agent Hicks died when he was 33 years old. He was memorialized by former FBI Director Robert S. Mueller, III, who stated, “Though our hearts ache, we trust that Sam awaits us in a better place. And until we meet again, may we all find joy in the example of a life lived to the fullest.” Although I never had the opportunity to meet Special Agent Hicks in person, I became a great admirer of him after reading his biography. Special Agent Hicks and I have shared interests, such as science, connections with people from Jordan, and love for our nation.

Sometimes, people think about how their lives may have been changed if they had made different choices. If I had the opportunity to live a second life, I would like to live a humble and meaningful life like FBI Special Agent Hicks. He was a science teacher, police officer, forensic scientist, and FBI agent. There are few people so committed to bravery, fidelity, and integrity as those citizens who choose to serve others by keeping the nation safe. His biography has inspired me to become a forensic microbial scientist.

It is an honor for me to finish my doctoral degree and to continue the work of FBI Special Agent Samuel Hicks. I think that his primary goals were to love and serve the United States of America where anyone—especially the young—can dream about pursuing any career they want under the Constitution.

Acknowledgments

I would like to acknowledge my committee members as well as all the professors I had at Walden University for getting me to this point in my path of higher education. I must give special recognition to Dr. Nancy Rea, Dr. Root, and Jen Rothamel for their continuous support during difficult times I had while working on the completion of this dissertation. At the same time, I want to thank other educators (from CCSU, UFL, and COSC) who believed in me to come to Walden University. Your faith in me will never be forgotten because you all inspired me to put higher education to benefit our society and this great nation above all things. Additionally, I want give thanks with the bottom of my heart to my family members and friends for their strong support during good and challenging times in this path of learning. During these nine years of educating myself at Walden, I had to say goodbye to two special people in my life who were pillars of hope and humility for me: my mother, and with all respects to Dr. Jack Miller, former president of Central Connecticut State University. Also, I want to give thanks the CT Law enforcement agencies (Greenwich Police Department, New Britain Police Department, and the New Haven FBI) for wishing me all the time the best of luck during my journey here at Walden University. I also have to give many thanks to Dr. Johnson, Dr. Cartter, Dr. Grady, and Dr. Stafford for helping me when I requested information from them to advance my research. Lastly and above all, I want to give special recognition to the Lord, who taught to stand firm and to believe all things can be possible.

"Success is not final, failure is not fatal: it is the courage to continue that counts."

—Winston Churchill.

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Chapter 1: Introduction to the Study

Introduction

In this study, I used knowledge from epidemiology, microbiology, and public health to investigate chronic Lyme disease (CLD) also known as post treatment Lyme disease syndrome (PTLDS), a probable but unreported new health condition that affects humans (Centers for Disease Control and Prevention [CDC], 2019a; Johnson, Shapiro, & Mankoff, 2018). I describe how frequently primary care physicians (PCPs) diagnosed and treated Lyme disease (LD) and CLD/PTLDS in Connecticut; however, there has been no agreement on what CLD/PTLDS is, how it should be diagnosed, and certainty regarding the pathological agent that causes CLD. There is speculation that CLD/PTLDS may be a health condition disseminated through the bites of vector-borne pathogens, and many researchers associate CLD/PTLDS with LD (Van Hout, 2018).

Therefore, this study was conducted as a validation of the previous research done on the same topic by Johnson and Feder (2010), who were pioneers investigating CLD/PTLDS in Connecticut among PCPs. Johnson and Feder found the differences in the knowledge, attitudes, and practices (KAP) of physicians who diagnosed and treated CLD/PTLDS, who were undecided on CLD, and who did not believe that CLD/PTLDS existed in the last 3 years. Johnson and Feder found that a few physicians (less than 3%) diagnosed patients with CLD/PTLDS, and 49% of physicians did not treat their patients with CLD/PTLDS because they believed that it did not exist. Data from Johnson and Feder's study (PCP survey responses from 2006) were compared to data in this current study (PCP survey responses in 2015).

I aimed to collect data and use descriptive and analytical epidemiological knowledge to examine CLD/PTLDS, a potential new health challenge, as well as study how PCPs diagnose and treat patients for CLD/PTLDS. This research is a quantitative cross-sectional study on how frequently Connecticut PCPs have diagnosed and treated patients for LD and CLD/PTLDS in the last 3 years. Results were compared to the 2006 distributions of PCP found in the historical population published in 2010 from a study on the same topic. Chapter 1 continues with presenting the problem, background, purpose, research question, theory, and rationale for the selection of the theory frame design, concise definitions, assumptions, limitations, potential contributions, and a study summary.

Background

CLD/PTLDS is a health challenge (Ali, Vitulano, Lee, Weiss, & Colson, 2014; Cameron, 2010; Johnson & Feder, 2010, Johnson, Wilcox, Mankoff, & Stricker, 2014). However, physicians and other health professionals have not developed a protocol to diagnose and treat CLD/PTLDS. Numerous physicians do not believe that CLD/PTLDS is a real illness affecting humans because no one has found valid evidence-based medical knowledge about the causal agent and databases collected to confirm or corroborate CLD/PTLDS as a new disease (Baker, 2008; Cameron, 2010; Feder et al., 2007; Johnson & Feder, 2010; Lantos, 2011; Lantos, 2015a; Wormser & Shapiro, 2009). Despite the lack of primary evidence (e.g., origin, mode of transmission, prevalence, incidence rates, and risk factors) to identify a possible new or emergent infectious illness, epidemiology can be used as a deductive science to gather new insights when the pathogen is unknown

to the medical community. It is also advantageous to compare past and present cases when investigating a disease that affects the members of a community, which is further supported by PCPs' knowledge that can provide insights for epidemiological and evidence-based medical investigations.

Various scientists have contributed to the origin of evidence-based medicine without being aware they used the field principles of epidemiology. With such epidemiological applications as data collection and the use of statistical analysis, they were able to contribute to the cure for many infectious diseases in the past. For example, Hippocrates (the prescription of a form of aspirin and the introduction of how the environment may be a risk factor for diseases), Edward Jenner (the vaccination of Smallpox), Ignaz Semmelweis (prevention of the transmission of puerperal fever), Joseph Lister (the use of antiseptic), Robert Koch (germ theory), and Alexander Fleming (the discovery of penicillin) made profound contributions in the field of medicine (Gaynes, 2017; Hajar 2015).

Some new advances in epidemiology include clinical epidemiology (Mullan, 1984; Young, Naude, Brodovcky, & Esterhuizen, 2017), foundations for microbiomics (Foxman & Martin, 2015), molecular epidemiology (Carroll et al., 2015), primary care epidemiology (Hannaford, Smith, & Elliott 2006), and public health informatics (Friede, Blum, & Mc Donald, 1995). Because of these epidemiological advances and the use of electronic primary care records, surveillance, and public health informatics, medical doctors and other health practitioners (e.g., epidemiologists) can help prevent, eliminate, and control diseases. For example, Koch had applied data collection and surveillance

practices with his discovery of *Mycobacterium tuberculosis* in 1882, which has the major symptoms of a fever, severe coughing, and chest pain (Fogel, 2015). Koch observed how patients with tuberculosis had similar symptoms, and with microscopic laboratory techniques was able to recognize the bacteria that caused their symptoms. Koch's discovery established the importance of case definitions in preventing diseases (Cambau & Drancourt, 2014). Additionally, Koch's work set the precedent for evaluating diseases with epidemiological applications, creating follow-up for effective treatment techniques, and using laboratory techniques as support for clinical diagnoses (Cambau & Drancourt, 2014). However, there are not always methods for data collection and surveillance because there are no accepted case definitions, international classification of disease (ICD) codes, or clear guidelines for diagnosis and treatment, which is the case for CLD/PTLDS.

Though not all health conditions are recognized, the CDC has a surveillance system—the standardization of the list of reportable diseases across the United States and territories (CDC, 1990a). Additionally, after the 1990s, the developed guidelines for surveillance by telecommunications systems required public health agencies to relay reportable diseases to the CDC. Consequently, standardized case definitions for reportable diseases were needed (CDC, 1990a, 1990b). Once a disease's case definition is established and reported, term standardization enables epidemiologists to calculate incidence, prevalence, and risk factors affecting humans and animals. The case definition process begins after a new disease is found and aids in the collection of epidemiological information. Therefore, epidemiologists focus on determining and monitoring the

distribution and determinants of diseases within susceptible populations via public health surveillance (Choi, 2012; Kuller, 2016). Moreover, after case definition usage is established, researchers can track incidence rates and monitor temporal or long-term trends in disease occurrence. Epidemiologists also examine factors such as whether the disease is seasonal, acute or chronic, and infectious or noninfectious. The Council of State and Territorial Epidemiologists in the United States (CDC, 1990a, 1997) started to use case definitions to classify and survey diseases in 1990:

- Confirmed case: a case that is classified as confirmed for reporting purposes.
- Probable case: a case that is classified as probable for reporting purposes.
- Laboratory-confirmed case: a case that is confirmed by one or more of the laboratory methods listed in the case definition under "Laboratory criteria for diagnosis." Although other laboratory methods may be used in clinical diagnosis, only those listed are accepted for laboratory confirmation for reporting purposes.
- Clinically compatible case: a clinical syndrome generally compatible with the disease, but no specific clinical criteria need to be met unless they are noted in the case classification.
- Supportive laboratory results: specified laboratory results consistent with the diagnosis but not meeting the criteria for laboratory confirmation.
- Epidemiologically linked case: a case in which the patient has/has had contact with one or more persons who have/had the disease, and transmission of the agent by the usual modes of transmission is plausible. A case may be

considered epidemiologically linked to a laboratory-confirmed case if at least one case in the chain of transmission is laboratory confirmed.

- Meets the clinical case definition: meets precisely the clinical case definition. Although in clinical practice the diagnosis may be made with the use of other criteria, for reporting purposes the stated criteria must be met. (Wharton, Vogt, & Buehler, 1990).

In the field of public health (i.e., epidemiology) the number of individual illness cases is significant, and the data enable epidemiologists to calculate incidence rates. This information is vital for health practitioners, such as PCPs and local health directors, to monitor diseases in their communities. Most disease investigations are initiated once the incidence exceeds expected occurrence levels for the specific condition and time. In some cases, there is a well-organized system for collecting data from ill community members, which is the case for CLD/PTLDS. It is frequently not reported by local health departments because it is a health condition without a standardized case definition and unknown etiological origin. Therefore, PCPs may have no easy way to share CLD/PTLDS patient information with health agencies such as the Connecticut Department of Health (CT DPH). Further, access to data from epidemiological research is limited to public health officers, which results in a lack of disease prevention and control efforts (Bach et al., 2017; Choi, 2012; Kuller, 2016). Thus, understanding the importance of public health data collection and surveillance will help analyze quantitative information, which may lead to health policies to reduce mortality and morbidity (Wetterhall, Pappaioanou, Thacker, Eaker, & Churchill, 1992).

Defining and Diagnosing Chronic Lyme Disease

In the United States, LD is a major disease caused by *B. burgdorferi* and *B. mayonii* (Dolan et al., 2017). LD is transmitted to humans through the bites of infected blacklegged ticks (Citera, Freeman, & Horowitz, 2017; Moore et al., 2016). The CDC estimates that there are more than 300,000 LD cases in the United States annually (Rebman et al., 2017). The most common symptom is the erythema migrans (EM) rash (Nadelman et al., 2012). However, not all patients who contract LD develop this red rash (Citera et al., 2017). Table 1 presents the basis for different diagnoses, and Table 2 presents the ICD codes for Lyme Disease.

Table 1

Categories for Diagnosis

Patient Category	Basis for Diagnosis
Undisputed Lyme disease	Diagnosed on appropriate clinical grounds in early disease or by reference laboratory testing in disseminated Lyme disease.
Post-Treatment Chronic Lyme syndrome	Diagnosed as above but failing to experience complete symptom resolution after standard antibiotic therapy.
Alternatively, diagnosed chronic Lyme syndrome	Diagnosed on clinical grounds supported only by alternative tests, the validity of which is questioned by major reference laboratories and the CDC.
Seronegative Lyme disease	Diagnosed on purely clinical grounds (a controversial category outside of early disease).

Note. Information from Patrick et al. (2016).

Table 2

ICD-10 Codes for Lyme Disease

Diagnosis Code	Description	Category
A69.2	LD	Other spirochetal (A69)
A69.20	LD, unspecified	Other spirochetal (A69)
A69.21	Meningitis due to LD	Other spirochetal (A69). Meningitis in LD · Meningitis (basal) (basic) (brain) (cerebral) (cervical) (congestive) (diffuse) (hemorrhagic) (infantile) (membranous) (metastatic) (nonspecific) (pontine) (progressive) (simple) (spinal) (subacute) (sympathetic) (toxic)
A69.22	Other neurologic disorders in LD	Other spirochetal (A69). Cranial neuritis · Meningoencephalitis · Polyneuropathy · Cranial neuritis due to LD · Lyme cranial neuritis · Lyme meningoencephalitis · Lyme polyneuropathy · Meningoencephalitis due to LD
A69.23	Arthritis due to LD	Other spirochetal (A69). Lyme arthritis · Arthritis, arthritic (acute) (chronic) (nonpyogenic) (subacute) M19.90 due to or associated with LD
A69.29	Other condition associated with LD	Other spirochetal (A69). Lyme myopericarditis · Myocarditis (with arteriosclerosis) (chronic) (fibroid) (interstitial) (old) (progressive)

Note. Information from http://www.icd10data.com/ICD10CM/Codes/A00-B99/A65-A69/A69-/A69.20. CLD/PTLDS does not have an ICD code so patients can be diagnosed and have their health insurance paying such medical process like in the case here with LD.

In 2019, the International Lyme and Associated Diseases Society (ILADS) defined CLD (also known as PTLDS) as "an ongoing infection with any of the pathogenic bacteria in the *Borrelia burgdorferi* sensu *lato* group that is poorly understood and often mischaracterized." Associated with this definition in 2018, the International Lyme and Associated Diseases Society recognized that symptoms of fibromyalgia, chronic fatigue syndrome, and depression were often misdiagnosed in patients with CLD/PTLDS (ILADS, 2018, p. 8). Other symptoms for CLD/PTLDS include peripheral neuropathy, motor neuron disease, neuropsychiatric presentations, cardiac presentations with electrical conduction delays and dilated cardiomyopathy, and musculoskeletal problems (ILADS, 2004).

Many health organizations, including the CDC (2019) and the National Institute of Allergy and Infectious Diseases (2019), do not accept the term *CLD*/*PTLDS* as a standard medical diagnosis. These health organizations prefer the term *PTLDS*. PTLDS is a known disease related to LD in patients who previously had EM or recurring symptoms (CDC, 2019a; Horowitz & Freeman, 2018). The CDC defines PTLDS (also known as CLD) as a health condition in which patients treated for LD continue to have symptoms of fatigue, pain, or joint and muscle aches after two to four weeks (CDC, 2017c). However, the cause of PTLDS remains unknown (Marques, 2008). Consequently, an ICD-10 diagnosis code is designated for PTLDS and not for the term CLD alone because the International Lyme and Associated Diseases Society definition does not fit a diagnosis among PCPs. Therefore, the controversial health condition of CLD/PTLDS may never be reported or will be under- or mis-reported by the CDC, National Institute of

Health, Infectious Diseases Society of America, and International Lyme and Associated Diseases Society. Additionally, these health organizations do not agree on billing and legislation guidelines for appropriately treating LD patients (Naktin, 2017). Therefore, there are many gaps in the medical field regarding CLD/PTLDS.

There is also controversy surrounding the diagnosis of CLD/PTLDS (Lantos, 2015a; Maloney, 2016). The Infectious Diseases Society of America, ILADS, and the CDC have differing perspectives on the existence of CLD/PTLDS. Many medical doctors do not believe that CLD/PTLDS is a chronic form of LD, and epidemiologists are not sure of its origins. Researchers have not identified a biological agent that causes CLD/PTLDS, and there is no reliable laboratory test to detect it, which have impeded the empirical study of CLD/PTLDS (Lantos et al., 2015c; Maloney, 2016).

To address the lack of knowledge on CLD/PTLDS, Johnson and Feder (2010) conducted a study on physicians' KAP regarding CLD/PTLDS. They collected KAP data from a sample of 285 PCPs practicing in the state of Connecticut. Johnson and Feder found that less than 3% of the 285 PCPs in their study had diagnosed patients with CLD/PTLDS, 49.8% of the PCPs did not treat their patients for CLD/PTLDS because they did not believe the condition existed, and 48.1% of the PCPs reported being undecided as to whether CLD/PTLDS existed. However, little KAP knowledge of CLD/PTLDS has been obtained in the 10 years since Johnson and Feder's study, the only exception being a study by Ferrouillet, Milord, Lambert, Vibien, and Ravel (2015). Ferrouillet et al.'s (2015) study was similar in nature and scope to that of Johnson and Feder but was focused on both LD and CLD/PTLDS. Ferrouillet et al. found that there

were significant differences in the knowledge and practices of physicians regarding LD diagnosis and treatment. Additionally, Ferrouillet et al. discovered that physicians had diverse responses to the diagnosis, treatment, and management of LD and CLD/PTLDS. Ferrouillet et al.'s findings demonstrate the necessity of this research because they may be relevant in improving physician's knowledge toward the latest trends of CLD/PTLDS in Connecticut.

Another survey implemented in this study could address the informational gaps related to CLD/PTLDS to build on the data collected by previous researchers. A new study may help broaden the understanding of CLD/PTLDS in Connecticut. This study expands the fields of medicine and epidemiology by applying both nonparametric and parametric statistical analyses to gather evidence-based medical research when encountering a health challenge (Levman & Takahashi, 2016; Roy et al., 2009). Therefore, I conducted the same survey used by Johnson and Feder (2010) with a statistical application to allow for the assessment, measurement, and evaluation of whether awareness and treatment by PCPs have changed in Connecticut. All independent variables pertain to the two study groups of Connecticut PCPs (2006 vs. 2015). I employed Chi-square (χ^2) goodness-of-fit tests when the dependent variables were categorically coded and one-sample *t* tests when the dependent variables were ratio coded.

This study filled the gap by investigating the KAP of PCPs' positions on CLD/PTLDS in Connecticut. The CT DPH currently does not collect epidemiological information about CLD or PTLDS as distinctive from LD reporting, which is expected

from the Council of State and Territorial Epidemiologist's surveillance across the U.S. States and Territories. This study is therefore limited because I was unable to ask PCPs in Connecticut to utilize any of the ICD A69 subcodes to characterize the cases into specific CLD/PTLDS categories epidemiologically. Therefore, the ability to collect epidemiological data on CLD cases is limited in this study.

This study also contributes new knowledge to address gaps in communication among PCPS in Connecticut regarding the status of CLD in Connecticut by comparing two different PCP profiles (2006 vs. 2015). Lapses in communication between health professionals about a critical issue of concern can create poor awareness of the magnitude of the health problem, inefficiency in financing, and lack of adequate health policies to benefit the members of a community (Mallonee, Fowler, & Istre, 2006). Therefore, I aimed to assess, evaluate, and compare the differences in the KAP among PCPs who (a) diagnose and treat CLD/PTLDS, (b) are undecided about it, and (c) do not believe that it exists. These correlations were used to validate (yes or no) the outcomes found in Johnson and Feder's (2010) study.

After the position of PCPs is known regarding CLD/PTLDS, this study may have scientific merit if the data obtained can enhance the necessity for the creation of a baseline electronic system that will collect and document data from cases of CLD/PTLDS. The study may also lead to equal guidelines across medical doctors to use same standard care practices for diagnosing and treating CLD/PTLDS. As Moffett and Moore (2011) stated, a competent physician treats patient equally under similar circumstances. However, it is difficult to expect the same care from PCPs when they

diagnose and treat patients without standardized care and guidelines (Cameron et al., 2014, Infectious Diseases Society of America, 2006). When comparing the PCPs' responses from the previous study (Johnson & Feder, 2010) and this study, it was expected that the outcomes of the Chi-square (χ^2) goodness-of-fit and the one-sample *t* test will help PCPs to find new and constructive data that can be utilized to infer solutions to improve their medical practices and approaches to better serve LD and CLD/PTLDS patients. As Skela-Savič, Macrae, Lillo-Crespo, and Rooney (2017) stated in their study, "Healthcare improvement science is the generation of knowledge to cultivate change and deliver person-centered care that is safe, effective, efficient, equitable and timely. It improves patient outcomes, health system performance, and population health" (p. 1)

The results of the study have the potential to contribute to social change by presenting the position of PCPs regarding CLD/PTLDS in Connecticut as a new disease, which may encourage future research and validation of CLD/PTLDS as a diagnosis. This conflict around CLD/PTLDS may affect numerous patients who are or were severely sick with CLD in Connecticut. Patients with CLD have found no much medical support for their illness status (Ali et al., 2014; Johnson et al., 2014). Patients with CLD/PTLDS have felt neglected without any medical help and paid more money out of their pocket when they visited physicians in the state of Connecticut (Johnson et al., 2014). Patients with CLD/PTLDS also lost their jobs and are or were experiencing a higher degree of disability (Johnson et al., 2014).

Problem Statement

There was a need to conduct a validation study to assess, evaluate, and determine whether there are changes in Connecticut PCPs' knowledge about the diagnosis, treatment, and management approaches for CLD/PTLDS. LD could be associated with the pathology of CLD/PTLDS; however, that association is currently unproven. Although the pathological agent, transmission, and treatment of LD are well known, questions remain regarding the best medical treatment practices for CLD/PTLDS (Bernard et al., 2016; Delong, Blossom, Maloney, & Phillips, 2012). LD mimics other conditions, and patients are not always aware that they have contracted the disease (Marzec et al., 2017). There are few guidelines for the diagnosis, treatment, documentation, and management of CLD patients.

There is also gap in the knowledge regarding significant differences in the KAP of physicians on the diagnosis, treatment, and management of LD and CLD/PTLDS among physicians who diagnose and treat CLD/PTLDS, physicians who are undecided on CLD/PTLDS, and physicians who do not believe that CLD/PTLDS exits. Thus, I surveyed these physicians by using Chi-square test (χ^2) and *t* tests. The problem is current and significant to the discipline because new knowledge on this topic may contribute to social changes that will improve strategies in protocols needed for PCPs to deal with CLD/PTLDS patients.

Purpose of the Study

The purpose of this quantitative study with a nonexperimental cross-sectional comparative research design was to assess, exanimate, and determinate (for validity

purposes) whether there were significant differences between two groups of PCPs working in Connecticut regarding their KAP in the diagnosis, treatment, and management of LD and CLD/PTLDS. In this study, the CT DPH medical doctors/Doctor of Osteopathic Medicine (MD/DO) of 2015 was the independent variable for all study questions. The complete data set for the Connecticut PCPs group from the list of certified medical doctors in 2006 or CT DPH MD/DO of 2006 could not be obtained from Johnson and Feder (2010). Therefore, I used the data presented in their study, and this group of physicians is treated as a population with frequency and mean level data that was compared to the data obtained from the sample of physicians in this study.

The first research question acted as a validation check, and it was expected that the two groups would have similar frequencies of PCPs with general or family practice, internal medicine, pediatric, and other primary care specialties since the two cluster groups were withdrawn from the original lists of CT DPH MD/DO of 2006 and 2015. The dependent variable for the second research question is the knowledge of LD, measured categorically, and the dependent variable for the third research question was the knowledge of CLD/PTLDS, the categorical variable. For the fourth and fifth research questions, one-sample *t* tests were conducted to determine whether the two groups of PCPs significantly differ concerning the number of patients diagnosed with and treated for CLD/PTLDS, as well as the average course of antibiotic treatment for patients diagnosed with CLD/PTLDS, the respective dependent variables. This study allowed for a priori assumption and/or premise for the existence of CLD/PTLDS as defined by

International Lyme and Associated Diseases Society(Cameron et al., 2014; ILADS, 2004).

Research Questions and Hypotheses

Research Question 1: Are the frequency distributions of the 2015 sample of Connecticut PCPs across the four primary practice specialty areas (i.e., family medicine, internal medicine, pediatrics, other) significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

$H_0$1: The frequency distributions of the 2015 sample of Connecticut PCPs across the four primary practice specialty areas (i.e., family medicine, internal medicine, pediatrics, other) are not significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

H_a1: The frequency distributions of the 2015 sample of Connecticut PCPs across the four primary practice specialty areas (i.e., family medicine, internal medicine, pediatrics, other) are significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

Research Question 2: Are the frequency distributions of the 2015 sample of Connecticut PCPs across the two knowledge of LD categories (i.e., know symptoms of LD and feel comfortable diagnosing and treating LD vs. know LD but do not feel comfortable diagnosing and treating LD) significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

$H_0$2: The frequency distributions of the 2015 sample of Connecticut PCPs across the two knowledge of LD categories (know symptoms of LD and feel comfortable

diagnosing and treating LD versus know LD but do not feel comfortable diagnosing and treating LD) are not significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

H_a2: The frequency distributions of the 2015 sample of Connecticut PCPs across the two knowledge of LD categories (know symptoms of LD and feel comfortable diagnosing and treating LD versus know LD but do not feel comfortable diagnosing and treating LD) are significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

Research Question 3: Are the frequency distributions of the 2015 sample of Connecticut PCPs across the three knowledge of CLD/PTLDS categories (do not believe CLD exists, do not feel comfortable diagnosing and treating CLD/PTLDS, and feel comfortable diagnosing and treating CLD/PTLDS) significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

H_03: The frequency distributions of the 2015 sample of Connecticut PCPs across the three knowledge of CLD/PTLDS categories (do not believe CLD exists, do not feel comfortable diagnosing and treating CLD/PTLDS, and feel comfortable diagnosing and treating CLD/PTLDS) are not significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

H_a3: The frequency distributions of the 2015 sample of Connecticut PCPs across the three knowledge of CLD/PTLDS categories (do not believe CLD/PTLDS exists, do not feel comfortable diagnosing and treating CLD/PTLDS, and feel comfortable

diagnosing and treating CLD/PTLDS) are significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

Research Question 4: Is the estimated average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2015 sample of Connecticut PCPs significantly different from the average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

$H_0$4: The estimated average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2015 sample of Connecticut PCPs is not significantly different from the average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

H_a4: The estimated average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2015 sample of Connecticut PCPs is significantly different from the average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

Research Question 5: Is the estimated average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2015 sample of Connecticut PCPs significantly different from the average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

$H_0$5: The estimated average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2015 sample of Connecticut PCPs is not

significantly different from the average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCP

H_a5: The estimated average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2015 sample of Connecticut PCPs is significantly different from the average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCP.

The KAP survey used in this study was relevant to measure how many PCPs diagnose and treat CLD/PTLDS, are undecided on CLD/PTLDS, or do not believe that CLD/PTLDS exists. Abdullah et al. (2013) have established the reliability and validity for the KAP questionnaire. The Cronbach's alpha coefficients were 0.96 (knowledge), 0.63 (attitude), and 0.79 (practice). The alpha coefficients were acceptable (Nyunnally, 1978).

Theoretical Framework

In 1962, Rogers developed the diffusion of innovations theory (Chien-Yun, Wan-Fei, Yu- His, & Chia-Hung, 2012; Rogers, 2004). This innovations theory is a systematic research investigation tool that can be applied to support how new concepts or ideas are distributed and adopted by groups within society over time. Researchers in the modern medical field have utilized diffusion of innovation theory to promote an understanding of health challenges and to incorporate innovation adoptions into KAP for societal benefit (Agyeman et al., 2009; Chien-Yun et al., 2012; Launiala, 2009).

Examples of researchers who use the KAP theory to change physician behavior include AI-Dharrab, Mangoud, and Mohsen (1996) and Magri, Johnson, Herring, and Greenblatt (2002). Al-Dharrad et al. administered a KAP study to physicians and nurses to collect data on hypertension in Saudi Arabia. Magri et al. described a KAP questionnaire that was administered to New Hampshire PCPs to obtain insights into LD diagnoses. Recently, Awad and Aboud (2015), Chien-Yun et al. (2012), and Ferrouillet et al. (2015) also used a KAP survey to investigate health concerns.

In this study, I used the KAP model as the underlying theoretical framework in this cross-sectional epidemiological study as a quantitative research method (Launiala, 2009). The KAP model served as a standard for this study because I collected significant quantitative data to identify insights related to physician care for CLD/PTLDS patients based on medical knowledge and practices. These data were beneficial to prove or disprove this study's hypotheses.

There are currently many knowledge gaps regarding the underlying agents that may cause CLD/PTLDS in Connecticut residents. New information regarding what has been or needs to be performed to identify possible risk factors about the disease's origin in Connecticut is important to discover the etiological agent, determine the distinctive symptoms, and develop corroborative tests that yield an accurate diagnosis and treatment by PCPs. However, the application of the KAP model was not used to answer questions regarding the causative agent for CLD/PTLDS. Instead, the questionnaire focused on obtaining documentation regarding the KAP of Connecticut PCPs who treat CLD/PTLDS patients. PCPs (e.g., family/general, pediatrician, and internal medicine physicians) were

chosen because they are typically the first resource for patients (Eldein, Mansour, & Mohamed, 2013). The testable Research Questions and hypotheses were used to determine if there are methods to improve the doctor-patient relationship in potential CLD/PTLDS cases. This study's findings may be useful if CLD/PTLDS is identified as a distinct disease with a functional case definition in the future (Souri et al., 2017; Stricker & Fesler, 2018). The survey data may produce significant information on the medical care needs of CLD/PTLDS patients. Additionally, it is essential to determine whether there are significant differences in the duration of prophylaxis given to CLD/PTLDS patients. In this study, I applied the KAP model to test the hypotheses.

Nature of the Study

In this quantitative study, I employed a comparative cross-sectional research design to determine whether there were significant differences regarding LD and CLD/PTLDS KAP between the group of 285 Connecticut PCPs in Johnson and Feder's (2010) study and the 145 PCPs in this study. The comparison element of the study pertained to the differences in categorical and ratio-coded dependent variables between the two groups of PCPs. The study design was cross-sectional because the data were collected from PCPs.

This study's independent variable was the PCP groups—that is, those in Johnson and Feder's (2010) study and those in this study. This study had five dependent variables. The first three dependent variables were categorically coded. The first three dependent variables measured (a) the type of PCP (i.e., family/general practice, internal medicine, pediatrics, other), (b) knowledge levels of LD, and (c) knowledge levels of CLD/PTLDS.

The last two dependent variables were ratio coded and measured the estimated number of patients diagnosed with and treated for CLD within 3 years and the estimated average course of antibiotic treatment (in weeks) for patients with CLD(PTLDS).

As the researcher of this study, I made similar attempts to replicate Johnson and Feder's (2010) sampling and methodological (i.e., recruitment, data collection, measurement) procedures to make valid and appropriate comparisons between the data in this study and that reported in their study. The participant inclusion criteria were the same as those previously used. The criteria required that the physician (a) was certified to practice medicine in the state of Connecticut, (b) currently practiced medicine in the state of Connecticut, and (c) was a PCP with an identified PCP specialty (i.e., family medicine, internal medicine, pediatrics, and others that included emergency medicine).

I utilized Johnson and Feder's (2010) KAP survey and developed a survey packet that included a KAP survey, a letter of introduction outlining the purpose of the study, an informed consent form, and a stamped, addressed envelope for returning the questionnaire. In alignment with Johnson and Feder, the study packet was mailed to 33% of the PCPs whose work contact information was available from the CT DPH. Surveys were expected to be returned from an equivalent number of PCPs

SPSS 24.0 software was used to enter and analyze the survey data. However, because I was unable to obtain the entire data set used by Johnson and Feder (2010), it was treated as the population when compared to the sample obtained in this study. Sample-to-population comparisons require the use of specific statistical tests for

hypothesis testing, which included Chi-square (χ^2) goodness-of-fit tests and one-sample *t* tests.

There are differences between LD and CLD (Crowder et al., 2014). There are also differences between CLD, which is given the name PTLDS. However, I combined CLD and PTDS as CLD/PTLDS to be inclusive for the purpose of this investigation. Other definitions to clarify my use of terms are provided in this section.

Antibiotics: Antibiotics are classes of drugs prescribed to patients by a medical doctor with the purpose to kill or inhibit the growth of disease-causing microorganisms. Antibiotics (e.g., penicillin, streptomycin) must be given after a bacterial infection (Hamilton & Wenlock, 2016).

Bias: Bias is the presence of systematic errors in the study design, conduct, or analysis (Althubaiti, 2016).

Beliefs: Beliefs are traditional ideas that one can have regarding an issue. For example, a medical procedure can be informed by what people believe is the right choice of treatment (Launiala, 2009).

Chronic diseases: Chronic diseases are chronic illnesses classified as noncommunicable diseases or degenerative diseases characterized by an uncertain etiology, multiple risk factors, long latency period, prolonged time, and non-contagious origin with some degree of degeneration and disability (Fradgley, Paul, & Byrant, 2015).

Chronic Lyme disease (CLD): CLD is the occurrence of a constellation of persistent symptoms in patients with or without evidence of previous *Borrelia burgdorferi* infection (Ali et al. 2014; Johnson & Feder, 2010). Though there are varying

definitions for this term, CLD occurs when patients are diagnosed with and treated for LD and may continue to experience worsening symptoms after treatment is received. In other cases, there is no known etiologic agent or sign of the typical rash of LD or information about laboratory testing related to *Borrelia burgdorferi* or *B. mayonii* (Lantos, 2015a). In this study this term is used as CLD/PTLDS.

Erythema Migrans (EM): EM is a circular skin lesion that outwardly looks like a red patch (rash) with a central clearing and appears as a bullseye after a deer tick bite (Allen, Vin, Warner & Joshi, 2016; 2016; Torbahn et al., 2016).

Evidence-based medicine: Evidence-based medicine is the integration of the current best research using clinical expertise, pathophysiology knowledge, and patients to make the best medical decisions from observations and data obtained from clinical studies (Cameron et al., 2014).

Immunity: Immunity is protection against a disease. There are two types of immunity status: passive and active. The immunity protection status of a person is indicated by the presence of antibodies in the blood and can usually be determined by a laboratory test (Warrington, Watson, Kim, & Antonetti, 2011).

Infectious diseases: Infectious diseases are caused by pathogenic microorganisms (e.g., bacteria, viruses, parasites, or fungi) that can be transmitted directly or indirectly from one person to another (Nii-Trebi, 2017).

Lyme disease (LD): LD is the most common vector-borne infectious disease in the United States. It is caused by the spirochete *Borrelia burgdorferi* or *B. mayonii* (Dolan et al., 2017).

Multi-system infectious disease syndrome: Multi-system infectious disease syndrome is a term used mainly by Horowitz in treating patients for CLD (Horowitz & Freeman, 2018).

Primary care epidemiology: Primary care epidemiology represents applications and methods to collect the data of health problems encountered in a primary care diagnosis setting (e.g., etiology, prevention, and diagnosis to improve their management). (Mullan, 1984).

Physician: A physician is a certified medical doctor who is qualified to practice medicine and take care of people or patients (e.g., conduct examinations, prescribe medications, and order, perform, and interpret diagnostic tests; U.S. Labor Department, 2017).

Post-treatment Lyme disease syndrome (PTLDS): PTLDS is a term established by the CDC in 2006 (Maloney 2016; Lacout, El Hajjam, Marcy, & Perronne, 2018) to refer to a health condition in patients with LD who maintain symptoms for more than six months after the first presentation of LD. In some cases, PTLDS is recognized by other organizations and researchers as CLD. In this study this term will be apply as CLD/PTLDS. PTLDS is accepted by the CDC and the Infectious Diseases Society of America as a diagnostic term for patients whose symptoms persist after the typical 2 to 4 weeks of antibiotic treatment (Aucott, Rebman, Crowder, & Korte, 2013; Horowitz & Freeman, 2018).

Public health surveillance: Public health surveillance is the ongoing practice of conducting the systematic collection, analysis, interpretation, and dissemination of health data for planning, implementation, and evaluation (Choi, 2012, p. 1).

Risk factors: Risk factors are conditions or measurements associated with the probability of disease or death and not necessarily recognized by people or patients (Willadsen et al., 2016).

Surveillance: Surveillance within a medical domain refers to the continuous methodical and systematic collection, analysis, and interpretation of health data essential for the planning, implementation, and evaluation of public health practice. It is thoroughly integrated with the timely dissemination of these data to those who need to know (Adokiya, Awoonor-Williams, Beiersmann & Müller, 2015).

Zoonotic diseases: Zoonotic diseases are infectious diseases that can be transmitted from animals to humans or vice versa (Scoth, Mattocks, Rabinowitz, & Brandt, 2013).

Zoonotic infection agents: Zoonotic infection agents are viruses, bacteria, fungi, and parasites that cause zoonotic diseases (Walter-Toews, 2017).

Assumptions

One of the main assumptions pertained to the use of CLD/PTLDS. For this study, a priori existence of CLD/PTLDS as defined and diagnosed by the International Lyme and Associated Diseases Society was accepted (Cameron et al., 2014), although the International Lyme and Associated Diseases Society (2004) definition of CLD/PTLDS contained no link to the etiologic agent of LD (e.g., through documentation of serologic

evidence; Johnson & Feder, 2010). The International Lyme and Associated Diseases Society asserts that a bacterium causes LD and can persist in patients after the traditional 28-day antibiotic treatment (Cameron et al., 2014; Johnson & Feder, 2010; Marzec et al., 2017; Stricker & Johnson, 2008). They (ILADS) supported two main reasons why the CLD/PTLDS term is preferred among health care providers as (a) patients with CLD/PTLDS suffer from inclusive constitutional symptoms as musculoskeletal, and neuropsychiatric symptoms, and (b) patients had used a multiples treatment (i.e., medicines and long courses of intravenous antibiotics).

I also assumed that the growth or reduction of the population of PCPs (family physician, pediatrician, and internal medicine physicians) in Connecticut drastically changed over time in the last 10 years but stays stable within less than 20% of variation (Appendix C). In addition, I assumed that the external validity and the internal validity in this study have limitations because the results were not representative for all medical doctors in Connecticut that were listed in the CT DPH MD/DO of 2015 (i.e., all PCPs) when comparing it with the CT DPH MD/DO of 2006 (Appendix E). However, I assumed that PCPs survey responses in this study (2015) would be a representative of the PCPs distribution (or responses) of 2006 because I followed the same sampling frame that Johnson and Feder (2010) used. Additionally, I assumed that the data obtained from this study could not be generalized to medical doctors working in other states in the United States.

Despite these assumptions, I assumed that the study was appropriate to evaluate the KAP of PCPs in regard to LD and CLD/PTLDS. I also assumed that the results of this

study have a proper level of construct validity because I used the same survey, same sample frame, and same protocols as Johnson and Feder (2010). The only variations were the length of the invitation to participate or cover letter. Previous researchers used just one short paragraph, whereas I used a whole page to comply with the Walden Institutional Review Board (IRB). I also added two other questions at the end of the questionnaire used in this study (Appendix A).

Scope and Delimitations

I sought information that can be used to help to resolve current disagreements between PCPs and patients with CLD/PTLDS in Connecticut. Having a consensus among PCPs about CLD/PTLDS may bring benefits to their medical practice and patients. The data were from PCPs working in Connecticut in 2006 and 2015. The purpose of the study was to identify whether there were significant differences after 10 years on the position of PCPs on the KAP concerning the diagnosis and treatment of CLD/PTLDS in Connecticut and to validate the results of Johnson and Feder's (2010) study. Johnson and Feder limited questions on LD and CLD/PTLDS to 3 years before the survey's distribution, and I followed the same procedure despite potential concerns for recall bias (Althubaiti, 2016).

This study had volunteer participation drawn from randomly selected certified Connecticut PCPs to answer a mail survey related to LD and CLD/PTLDS. Many PCPs in Connecticut may have differing positions in attentiveness to CLD/PTLDS as to how they diagnose and treat patients with LD and CLD/PTLDS. To make this study as objective as possible, I defined CLD/PTLDS in the survey cover letter, which was mailed

with the survey as "the persistence (more than six months) of *Borrelia burgdorferi* infection, despite multiple standard courses of antibiotics." The term *LD* was not defined in the cover letter or survey because this was not the focus of this study. Another reason why I did not define LD is because I wanted to compare the outcomes published by Johnson and Feder (2010) with the same questions (including one two questions about LD in the survey) plus two more questions at the end to be in compliance with the Walden IRB requirements for consent. Thus, I assumed that all study PCPs were considering the same clinical definition of CLD/PTLDS when completing the survey.

The sample size for this study included randomly selected participants with available mailing addresses. For this quantitative KAP survey, the subjects were medical doctors from the active list of the Connecticut State Health Department Certified Medical Doctors/Surgeons in 2015 (CT DPH, 2015). The exact number of CT DPH PCPs of 2015 who took part is discussed in Chapter 3. The CT DPH MD/DO of 2015 was made up with the names of physicians, their work or practice addresses, medical license numbers, the expiration of their medical license numbers, and their specialty.

The study was limited to PCPs working in Connecticut. Therefore, the criteria for this target population included medical doctors who actively practiced medicine in 2015, were licensed by the state of Connecticut, and practiced as pediatricians, family doctors, or internal medicine doctors. PCPs' names were collected from the certified list of physicians working in the following categories in 2015: family doctors or general medicine, pediatrics, and internal medicine. A purposeful selection (nonrandom) identified the participants for this study within the three categories because it was the best

method to find a representative volunteer sample of Connecticut physicians whose practices were most likely to diagnose CLD/PTLDS or related conditions. Computer randomization was used to eliminate selection bias and to obtain the correct number of necessary participants. The variables studied were drawn from a population of health care practitioners that worked as medical doctors. Johnson and Feder (2010) studied a similar population in 2006 and selected participants using random selection. The investigative period lasted no longer than 2 months and involved a one-time mailed survey. Thus, it was essential to obtain the correct mailing addresses from the list of selected participants.

The exclusion criteria were medical doctors with a specialization in categories other than the study's specified groups of family or general physicians, pediatricians, and internal medicine physicians. However, emergency physicians were accepted in this study because the previous study also included them in the statistical analysis (Johnson & Feder, 2010). Emergency physicians have a crucial role when dealing with prospective LD patients since in some occasions many of them may show up at the hospital emergency room looking for someone to remove ticks found on themselves or with EM manifestations (Applegren & Kraus, 2017). Additionally, physicians have the best intentions to help patients with the diagnosis and treatment of LD from the exposures of ticks on individuals or with the rash to eliminate LD complications especially if such patients may be living in geographical areas of endemic of *Ixodes scapularis* ticks (Applegren & Kraus (2017).

Limitations

The study was limited because I could not control all potentially confounding factors if there were present in this cross-sectional research. Confounding variables or confounders are often defined as the variables correlate (positively or negatively) with both the dependent variable and the independent variable (Pourhoseingholi, Baghestani, & Vahedi, 2012). Therefore, confounding factors can cause a false relation between an exposure and an outcome, especially in clinical trials. Even though this study was not a clinical trial, there is a study design limitation because the associations of exposure and outcomes are simultaneously evaluated or measured. It is impossible to assess any temporal relationships between exposures and outcomes in cross-sectional studies (Carlson, 2009; Salem, 2015). Without longitudinal data, it is not possible to establish an exact cause and effect relationship (Salem, 2015). However, cross-sectional studies are less expensive than longitudinal studies.

The design of this study may have also produced selection bias because cross-sectional studies rely on one-time responses and no other personal risks, behaviors, or confounders. Another critical consideration is selection bias if proper randomization is not achieved. A nonresponse from selected participants may produce bias because the survey's population was reduced (Thorpe et al., 2008).

Another important limitation is recall bias, which occurs when there are differing levels of accuracy from the point from the informant (Althubaiti, 2016). Recall bias in epidemiological and medical research may be due to difficulty in remembering previous significant details related to the participant's disease when responding to self-reporting

surveys (Althubaiti, 2016). The recall period in this study was 3 years ago. Thus, this period may cause less reliable recalled information given by the PCPs who participated in this study. The study design in the questions used in the survey was 3 years ago because it was stated in the survey used by the previous researchers (Johnson & Feder, 2010).

Self-selection is another form of bias that occurs when a complex decision is made quickly by the respondents. In this study, a few survey responses stated indicated that the PCPs had participated in the previous survey. In PCPs' responses, there were a large number of PCPs who did not believe in CLD/PTLDS as well others who stated they believe in CLD as a new disease.

Other limitations pertained to the method of data collection. One of the disadvantages of mailed surveys is that correct addresses are required for each participant in addition to resources to cover delivery costs (Edwards, 2010). Consequently, an individual other than the intended respondent may answer the survey. Participants answering the questions in a retrospective survey may find that recalling previous actions or past details related to their disease is challenging. The day and season period when the survey was mailed out may also have caused limitations (PRA, n.d.). Another disadvantage was that the cover letter was a whole page, which may have affected the response rate. Medical doctors do not have much free time to read while serving their patients; they work long hours, and the surveys were mailed at their workplaces (Pedrazza, Berlanda, Trifiletti, & Bressan,2016).

Social desirability bias may also occur in administering questionnaires or surveys when the data or responses to questions are affected by social desirability, approval, or

the inability to be guaranteed anonymity or confidentiality (Althubaiti, 2016). The survey responses of the instrument used in this study were to be answered without the name of the PCPs participants to eliminate social desirability by using a previously conducted survey for data collection of this study (Althubaiti, 2016). It is essential to avoid social desirability bias when constructing a data collection method (Althubaiti, 2016). Social desirability bias should not have affected this study because the survey was random and was to be answered anonymously.

Another limitation of this study was the inability to corroborate the medical data reported from the CT DPH and the CDC because there is not an approved case definition for CLD (PTLDS). At this time, there is the confusion about how to employ the term CLD/PTLDS. Consequently, there was a lack of known published reported surveillance data on the term CDL or PTLDS. PTLDS is a term appropriate to be used to identify patients afflicted with CLD (CDC, 2019a) for reasons that are explained in detail in Chapter 2. Therefore, in this study both terms were considered similar as CLD/PTLDS to be in accordance with the CDC, even residents in Connecticut preferred the term CLD (Johnson & Feder, 2010).

Significance

Researchers from several scientific disciplines are currently investigating CLD/PTLDS, which may lead to discoveries and knowledge about it and the health controversy surrounding it. One of the primary areas of study in this research is the potential close relationship between CLD/PTLDS and documented cases of LD in Connecticut. LD can be a serious health problem if unrecognized and untreated (Ljøstad

& Mygland, 2013). However, although there is a potential relationship with CLD/PTLDS and LD, there is also a potential that CLD/PTLDS occurs without clinical or diagnostic evidence of *B. burgdorferi* infection. Therefore, some researchers think that it is inappropriate to use the term *CLD*, which implies a *B. burgdorferi's* etiology (National Institute of Allergy and Infectious Diseases, 2019).

This study may enable future researchers to identify a possible link between LD and CLD/PTLDS. This may inform Connecticut residents about the severe health implications that may affect them if a relationship between LD and CLD/PTLDS is found. The number of LD cases in Connecticut has increased over the last 30 years. The CT DPH has reported 2,108 confirmed and 810 probable cases of LD since 2013 (Garnett, Connally, Stafford, & Carter, 2011). Therefore, there is a need to determine whether there is a relationship between misdiagnosis (or failure to receive an early diagnosis and management) of LD and the presumed onset of CLD/PTLDS. The prevention of CLD/PTLDS onset will protect patients from neurological complications, central nervous system effects, and other complications such as arthritis (Bratton, Whiteside, Hovan, Engle & Edwards, 2008). The results of this study may provide physicians with knowledge for diagnosing, managing, and treating patients with LD and CLD/PTLDS so that patients will not be misdiagnosed, poorly maintained, or undertreated. This study may provide significant insights on this complex health issue because it addresses information gaps (besides the intents of validation of the previous research) about CLD/PTLDS as a potential persistent and contemporary public health concern and how to avoid disability and morbidity. Additionally, many patients have

become frustrated when they did not receive an accurate diagnosis and treatment for an illness that they believed was CLD/PTLDS (Lantos, 2015a).

The potential benefits of this study also include increasing the awareness of CLD/PTLDS within the Connecticut health professional community and to improve the diagnosis barriers (e.g., lack of case definition, ICD-10 code, standardized medical guidelines, better practices) that PCPs face when working with CLD/PTLDS patients. This is significant because the doctor–patient relationship is the core of care in collecting data, diagnosing, and helping patients heal (Dorr Goold & Lipkin, 1999, p. 27). This study may result in benefits and social changes that will improve communication between PCPs, public health organizations (e.g., CDC, World Health Organization, Council of State and Territorial Epidemiologists, CT DPH, Connecticut Medical School), professional medical societies, and people with presumed cases of LD and CLD/PTLDS. It is essential that these public health organizations see the need to collect more information and to create a database for surveillance purposes to document what is happening to potential CLD/PTLDS patients.

The study may also advance current medical knowledge and show whether a belief in CLD/PTLDS affects a physician's KAP regarding the diagnosis, treatment, and management of LD (within the context of the survey) and CLD/PTLDS. This study may advance medical practices by providing an opportunity for PCPs to reach a consensus of what they should do to help CLD/PTLDS patients. The study may also contribute positive and constructive ideas for social change within the health care field by

influencing PCP outcomes. Additionally, the findings of this study may encourage changes in the protocol presently used by PCPs to help CLD/PTLDS patients.

Summary

CLD/PTLDS is a new health condition without a case definition (CDC, 2019a), so it has not been defined, classified, or accepted as a reportable disease in Connecticut. It is common practice in Connecticut for all certified physicians who examine or treat patients' reportable infectious diseases to report to the director of the DPH on any notifiable mandated infections encountered. Researchers agree that CLD/PTLDS has not garnered sufficient attention from health care professionals and that many people who stated that they had CLD/PTLDS did so because of conflicting information as well as because of the lack of a case definition for CLD/PTLDS (Henry & Carr, 2012; Johnson & Feder, 2010; Lantos, 2015a; Stricker & Johnson, 2008; Stricker & Fesler, 2018).

This study was conducted to acquire new evidence-based knowledge to help the medical community (particularly PCPs) determine whether there is a need to create better practices to evaluate, diagnose, and treat potential CLD/PTLDS patients. The findings of this study may also encourage PCPs to develop a case definition for CLD/PTLDS. Additionally, if CLD/PTLDS is considered a distinct condition, a new surveillance system could be used for chronic Lyme spectrum illness prevention. The study could advance knowledge in the discipline by exploring the differences in KAP of two PCPs distributions (2006 vs. 2015) in Connecticut.

Chapter 2 provides the literature review regarding the latest findings related to CLD/PTLDS and why it is not currently a reportable disease. Chapter 3 describes the

primary methodology used in this quantitative study. Chapter 4 contains the results and includes statistical data analyses with corresponding figures and tables. Finally, Chapter 5 provides information about the public health implications, recommendations, and concluding remarks about the KAPs on treating CLD/PTLDS patients in Connecticut.

Chapter 2: Literature Review

Introduction

The prevalence of CLD/PTLDS remains relatively unknown in Connecticut. Furthermore, there is currently a significant division between two professional medical societies, the Infectious Diseases Society of America and the International Lyme and Associated Diseases Society, about the guidelines for the diagnosis and treatment of CLD/PTLDS (Davidsson, 2018; Feder et al., 2007; Johnson & Feder, 2010). The diagnosis and treatment of CLD/PTLDS is now one of the most debated medical health challenges in Connecticut and the rest of the United States (Feder et al., 2007; Lantos, 2015a). The controversy centers on whether CLD/PTLDS is a separate illness (Feder et al., 2007; Johnson & Feder, 2010, Lantos, 2015a). The argument is caused by the lack of information about the etiological agent, as well as a lack of reliable clinical testing, no ICD code, and no standardized clinical guidelines for treatment. Medical doctors, especially PCPs, may have different KAPs on the most appropriate treatment for CLD/PTLDS (Johnson & Feder, 2010). A significant point of conflict among medical doctors is over the practice of long-term treatment with IV therapy.

Another part of the debate is the many stories from CLD/PTLDS patients who had positive and negative outcomes after receiving IV treatments with antibiotics such as individuals afflicted with CLD/PTLDS who have contributed testimonials via social media (e.g., Facebook, YouTube, blogs). An example on YouTube is the story of Monica Amore (Amore, 2009). In Monica Amore's testimonial, she reported the success of long-term IV antibiotic therapies, and she has been healthy and recovered. However, there are

also negative stories about the adverse effects of long-term IV antibiotic therapy for individuals diagnosed with CLD/PTLDS. In 2000, Patel, Grogg, Edwards, Wright, and Schwenk (2000) presented a testimonial from a 30-year-old female who was diagnosed with CLD/PTLDS. The woman received 27 months of IV treatments with cefotaxime and died from septic thrombus infection that was not caused by CLD/PTLDS but rather from a secondary infection from IV Groshong catheters that caused a fatal infection with *Candida parapsilosis* (Patel et al., 2000).

To address these issues regarding the diagnosis and treatment of CLD, I conducted this study to compare a sample of PCPs to those in a seminal study published in 2010. In this chapter, I introduce for the consideration of the literature reviews these subtopics as *literature search strategy, theoretical foundation, problems with the case definition of chronic lyme disease, controversy with the diagnosis of chronic Lyme disease, controversy with bacteria and chronic Lyme disease diagnosis, relationship between Lyme disease and Chronic Lyme disease , disagreement on treatment for Lyme disease and Chronic Lyme disease, persistence of Borrelia burgdorferi after antibiotic treatment, diagnosis, treatment, and management of Lyme Disease, Chronic Lyme disease , diagnosis, treatment, and management of Post-Treatment Lyme Disease Syndrome*. The chapter ends with a summary and conclusion.

Literature Search Strategy

The literature for this study was discovered with ProQuest Dissertations and Theses, EBSCOHost, Google, Google Scholar, the Walden University Library, the University of Connecticut's Lyman Medical Library, and YouTube. Sources included in the literature review were primarily published from 2006 to 2018. Search terms included *knowledge, attitudes, and practices of physicians*; *Lyme disease*; *chronic Lyme, treatment, and management of LD and CLD/PTLDS*; *physicians who are undecided on CLD/PTLDS*; *physicians who do not believe that chronic LD exists*; and *knowledge, attitudes, and practices (KAP) theory*. Statistical applications of SPPS used in public health research were identified for this section of the literature review.

Additionally, the literature search was undertaken to collect information regarding CLD and PTLDS, and CDL/PTLDS. The literature review included research on the definitions of CLD and PTLDS; controversial issues regarding diagnosis; variability of treatment for CLD or PTLDS; associations between LD and CLD; the persistence of the *B. burgdorferi* after treatment with antibiotics; available clinical testing for CLD/PTLDS and LD; problems for primary, family, and general care physicians, including pediatricians and internal medicine physicians reporting on CLD/PTLDS; the latest CLD/PTLDS research; research gaps for CLD/PTLDS; the relationship between biofilms and CLD/PTLDS; and a review of research methods, including surveys, conducted on the same or related subjects outside of Connecticut.

Theoretical Foundation

Public health researchers have used the diffusion of innovations theory to ground their research for adopting innovative procedures (e.g., taking antibiotics or medications, accepting treatment for diseases like diabetes, etc.), which may lead to concrete, desired changes in societal behavior for improving wellness in a community (Abdullah, Aziz, Harum, & Burhanuddin, 2013; AL-Dharrab, Mangoud, & Mohsen,1996; Lien & Jiang, 2016; Zhang et al., 2015). In addition to the diffusion of innovations theory, I used the KAP approach to understand PCPs' KAP when they treat LD and CLD/PTLDS. The diffusion of innovations theory can be applied to research assessing participants' KAP in public health settings (Launiala, 2009). KAP can also be applied when examining physician behavior to improve health status (Awad & Aboud, 2015; Chien-Yun et al., 2012; Fauman, 2006).

The KAP approach was the most appropriate method to examine the difference in the KAP of PCPs concerning LD and CLD/PTLDS. This approach was informed by the research questions and helped identify the research design decisions (i.e., the method of inquiry, data collection, and analysis). Thus, for this study, the KAP approach was used (see Figure 1) to test the research questions and hypotheses.

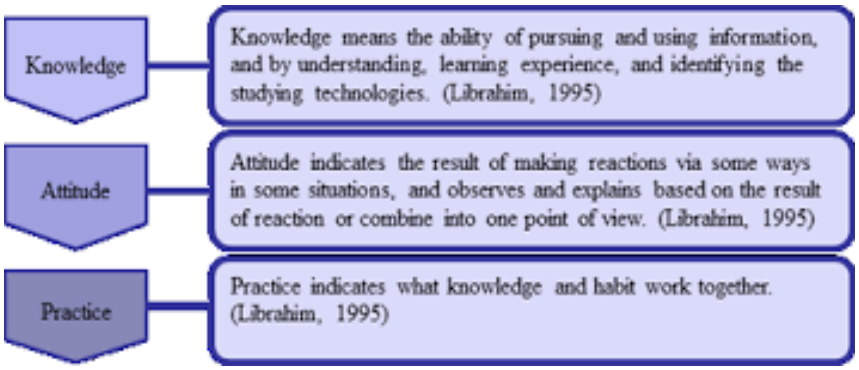


Figure 1. The knowledge, attitude, and practice (KAP) diagram. Adapted from "A study on Modification of Knowledge, Attitude, and Practice on Vocational High School Electronic Courses Integrated with Nanotechnology Concept," by Chien-Yun et al., 2012, *International Journal of Thermal & Environmental Engineering, 4*, p. 74.

Problems with the Case Definition of Chronic Lyme Disease

PCPs are required to have a comprehensive knowledge of toxicology, pathology, and clinical sciences to diagnose and treat patients following the laws and ethics of the state in which they practice medicine (Grudniewicz et al., 2015). This study was focused on the applications used in epidemiology with inductive and deductive applications to gather new insights about CLD/PTLDS as a possible new health issue affecting residents in Connecticut. The International Epidemiological Association (2017) defined epidemiology as the "study of the occurrence and distribution of health-related events, states, and processes in specified populations, including the study of the determinants influencing such processes, and the application of this knowledge to control relevant health problems." This epidemiology definition emphasizes big data, genealogy, and personalized medical therapies (Kuller, 2016).

The initial step in conducting an epidemiological investigation on contagious diseases or chronic diseases is to formulate a case definition . This initial step helps identify the disease's potential infectious agent or the risk factors, leading to a definite diagnosis by a certified medical doctor or laboratory staff. A case definition identifies the risk factors and may allow disease trends to be documented in most cases with electronic reporting records or geographic information systems of ill patients. Once a disease has a case definition, it can be reported to local, state, and federal agencies (Coggn, Martyn, & Evanoff, 2005).

The next step requires physicians to diagnose and report details about the results of physical and pathological examinations, diagnostic tests, and treatments administered to patients (Rajkomar & Dhaliwal, 2011). A correct diagnosis helps health care professionals identify the source, mode of transmission, and cause of the investigated disease (Rajkomar & Dhaliwal, 2011). Without a case definition, professionals cannot perform an effective analysis of the data obtained from the current or previously afflicted members of the community.

Although CLD does not have an approved case definition, the CDC recognizes PTLDS as a health condition (Borchers, Keen, Huntley, & Gershwin, 2015). Borchers et al. (2015) described PLDS as a health condition found in patients treated with antibiotics who continue to have persistent symptoms from a previous LD infection. The Infectious Diseases Society of America accepts this definition of PLDS (also known as PTLDS). Other researchers have defined CLD/PTLDS as a persistent infection caused by *B. burgdorferi* that may or may not have laboratory or clinical evidence and that requires a

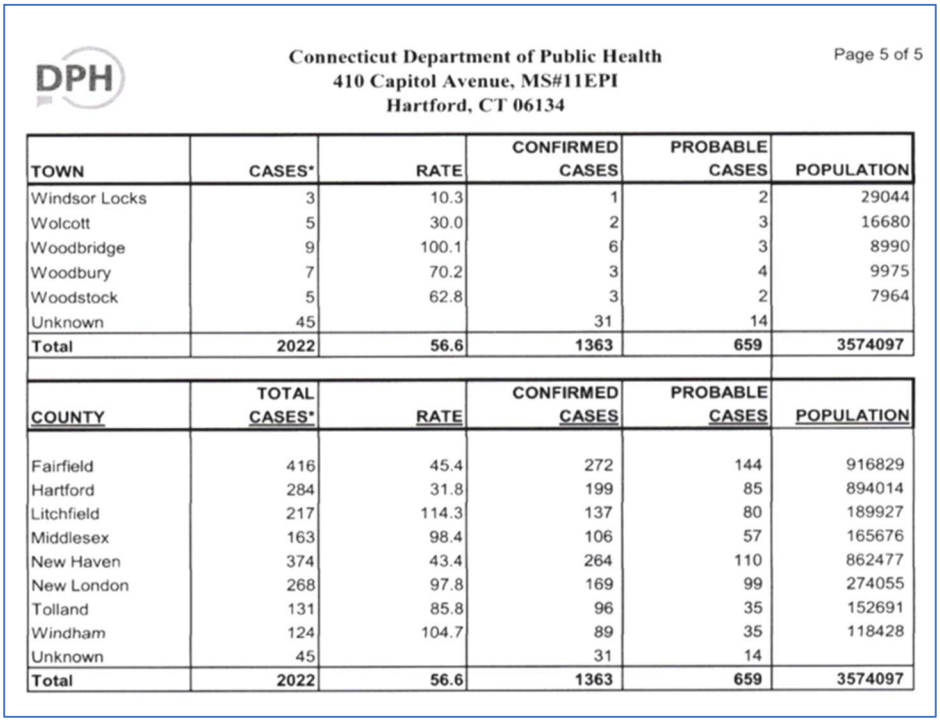
more extended treatment period that uses intravenous and/or oral therapies (Johnson & Feder, 2010). For example, Lantos et al. (2015b) described CLD/PTLDS as a health condition present in some patients with prolonged, medically unexplained physical symptoms and/or uncorroborated alternative medical diagnoses. Lantos and Wormser (2014) and Chan et al. (2013) also found that a small group of individuals who thought that they had CLD/PTLDS were also treated for coinfections, such as with *Babesia, Anaplasma* and *Bartonella.* However, there is still an issue with defining CLD without clinical laboratory evidence (Klempner et al., 2012).

There are many definitions of CLD/PTLDS, which reflects the issue of whether it is a health condition or a disease and whether it deserves a new classification. For instance, Ścieszka et al. (2015) suggested that PTLDS and PLDS are interchangeable terms. Most people living in Connecticut are familiar with the terms CLD or PTLDS (Feder et al., 2007; Johnson et al., 2014). Moreover, before the CDC, researchers have rejected the CLD term and preferred the term *tick-associated poly-organic syndrome* (Borchers et al., 2015; Clarissou et al., 2008). Regardless, ILADS (2004, 2005) defines CLD as a blend of recurrent symptoms with debilitating subjective physical manifestations that include extreme fatigue, arthralgia, myalgia, vague memory and poor concentration, strong headaches, and irritability. However, the Infectious Diseases Society of America (2017) does not acknowledge CLD term alone and has rejected this definition (Johnson et al., 2014; Johnson & Feder, 2010; Johnson & Stricker, 2010). Despite disagreements, one suggestion for a case definition for CLD is that it must meet the following criteria: (a) the illness is present for at least a year, (b) there are persistent

and significant neurologic involvements or active arthritic manifestations, and (c) patients must still be infected with the *B. burgdorferi* bacteria following antibiotic treatment (Burrascamo, 2008).

In Connecticut, CLD/PTLDS is currently a health condition without an acceptable epidemiological case definition. CLD/PTLDS is not accepted, recognized, or reported in the United States. Further, CLD/PTLDS patients in Connecticut and across the nation struggle to obtain treatment for the disease, mainly due to a lack of acceptance by the medical community. Therefore, evidence-based medical knowledge may yield scientific information on the possible relationship between CLD/PTLDS and LD, which could affect Connecticut residents.

Though there is no official definition to report cases of CLD/PTLDS, the latest statistics from the CT DPH in 2017 show a decrease in the number of cases reported and documented in the state (see Figure 2). Additionally, the latest statistics from the CT DPH (2018) show a total of 1,363 confirmed cases and an overall incidence rate of 56.6 cases per 1,000,000. Most of the reported cases were from New Haven County.



DPH

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TOWN	CASES*	RATE	CONFIRMED CASES	PROBABLE CASES	POPULATION
Windsor Locks	3	10.3	1	2	29044
Wolcott	5	30.0	2	3	16680
Woodbridge	9	100.1	6	3	8990
Woodbury	7	70.2	3	4	9975
Woodstock	5	62.8	3	2	7964
Unknown	45		31	14	
Total	**2022**	**56.6**	**1363**	**659**	**3574097**

COUNTY	TOTAL CASES*	RATE	CONFIRMED CASES	PROBABLE CASES	POPULATION
Fairfield	416	45.4	272	144	916829
Hartford	284	31.8	199	85	894014
Litchfield	217	114.3	137	80	189927
Middlesex	163	98.4	106	57	165676
New Haven	374	43.4	264	110	862477
New London	268	97.8	169	99	274055
Tolland	131	85.8	96	35	152691
Windham	124	104.7	89	35	118428
Unknown	45		31	14	
Total	**2022**	**56.6**	**1363**	**659**	**3574097**

Figure 2. Lyme disease cases and rates (per 100,000) by count. From "Lyme Disease Statistics," by CT DPH, 2018 (https://portal.ct.gov/-/media/Departments-and-Agencies/DPH/dph/infectious_diseases/lyme/stats/CTLDStats2017.pdf?la=en)

In addition to the cases of CLD in Connecticut, the ILADS (2004) estimated the prevalence of CLD/PTLDS to be between 34% and 64% of studied cases in 1994 for patients who were seen by a physician and thought they might have LD. It is suggested that 10% to 20% of patients who underwent 2 to 4 weeks of treatment for LD had persistent symptoms with or without the presence of *B. burgdorferi* (Adrion et al., 2015, Maloney, 2016). However, the limited amount of scientific data on the topic has resulted in differing physician opinions about the duration or the therapeutic window to treat CLD/PTLDS patients (Feder et al., 2007; Lantos et al., 2015b; Ścieszka et al., 2015). But De Long, Hsu, and Kotsoris (2019) estimated that in 2020, the prevalence of

CLD/PTLDS in the United States will be higher than in 2016, with as many as 1,944,189 (95% CI: 1,619,988- 2,304,147) CLD/PTLDS cases. As indicated by this prevalence rate, CLD/PTLDS is a concern not just for Connecticut, but the United States as a whole.

Controversy with the Diagnosis of Chronic Lyme Disease

A group of scientists and health professionals have suggested that CLD/PTLDS occurs due to inappropriate antibiotic treatment of the LD-causing bacteria (ILADS, 2004, 2015). These health care professionals believe that the most efficient method to treat and cure CLD/PTLDS is the use of long-term antibiotics (Cameron et 2014; ILADS, 2004, 2015). Most physicians who belong to the health professional group support extended antibiotic treatment if needed by CLD/PTLDS patients (ILADS, 2004, 2015). However, another group of scientists and health professionals consider CLD/PTLDS to be multiple spectrum diseases that result from unknown causes and are unrelated to the persistence of *B. burgdorferi* (Baker, 2012; Infectious Diseases Society of America, 2017; Marques, 2008). These professionals do not recommend long-term antibiotic treatment for potential CLD/PTLDS patients (Infectious Diseases Society of America, 2006, 2015, 2017, 2019). These different perspectives and treatment approaches indicate the need for a resolution to assist those with CLD/PTLDS such as identifying a pathogen that causes CLD/PTLDS.

One of the reasons CLD/PTLDS is a controversial diagnosis is the absence of an identified pathogen or other noninfectious agents that can show causation (Ali et al., 2014; Auwaerter et al., 2011; Feder et al., 2007; Marques, 2008; Wormser, 2007). If the pathogen or other noninfectious agents that cause CLD/PTLDS are unknown, it is

impossible to determine which laboratory tools should be used to identify unknown agents, particularly if they are biological in origin. Additionally, the lack of standardized diagnostic criteria within the medical community makes it challenging for physicians to provide treatment and manage CLD/PTLDS (Feder et al., 2007; Lantos, 2011; Ljostad & Mygland, 2012; Stricker & Johnson, 2008). Another challenge associated with CLD/PTLDS is the lack of information about the role of the autoimmune system (residual or persisting antigens) and toxins produced in CL/PTLDS patients (Miklossy, 2012; Miller, 2016).

Controversy with Bacteria and Chronic Lyme Disease Diagnosis

When a bacteria diagnosis is needed, a patient's blood sample is the standard for obtaining and examining bacteria culture samples (direct cultures or indirect plus serum analysis; Villa et al., 2017). Gold standard testing in microbiology is derived from Koch's work, which documented the protocols necessary to isolate pathogens and relate the pathogens to a specific disease or to prove their microbial etiology or infectious origin in outbreak cases (Mortimer, 2003). Koch's protocols are the contemporary basis for direct pathogen identification from cultures using microscopic and xenodiagnostic techniques (Fredricks & Relman, 1996; Hess, 2017; Mortimer, 2003). Koch's Postulates include the following: (a) the bacterial agent must be present with every case of the disease, (b) the microorganism must be isolated from a host source and grown purely by means of laboratory in vitro techniques, (c) the same grown microorganism must be confirmed as the symptom-causing agent when it was introduced into a healthy susceptible host, and

(d) the same pathogen should be recovered again from the infected host (Fredricks & Relman, 1996; Hess, 2017; Mortimer, 2003).

Other serology and immunology testing used to identify bacteria, parasites, viruses, and diseases include agglutination methods, precipitation methods, electrophoresis methods, labeling techniques in immunoassays and complement fixation, and fluorescent antibodies (Villa et al., 2017). Measuring the levels of antibodies is possible when identifying the bacteria that is resulting in the illness; the identification of these antibodies is often used to prescribe the proper antibiotic treatment. Other identification methods for disease-causing parasites in humans include using blood smears and serology testing. Parasites are sensitive to antibiotics, and viral infections require more complex methods than bacterial infections to be identified by DNA or RNA cultures. Viral infections cannot be eliminated or cured with antibiotics.

A related issue is that PCPs need to have confidence in laboratory test results because they are clinically relevant to giving the correct and precise diagnoses and treatments to patients (Infectious Diseases Society of America, 2017). There is currently no corroborating evidence regarding the relationship between bacterial infections and CLD/PTLDS. Some scientists support the notion that two possible central pathways lead to CLD/PTLDS in patients: (a) the persistent presence of bacteria following traditional antibiotic treatment for LD or (b) late or delayed treatment of LD and other tickborne infections. Due to the debate surrounding CLD/PTLDS, most physicians in the United States, as well as Connecticut are divided as to whether CLD/PTLDS is a new disease

distinct from other conditions or if it is related to *B. burgdorferi,* which results in LD (Johnson & Feder, 2010).

Relationship Between Lyme Disease and Chronic Lyme Disease

LD is a tickborne disease that was discovered in 1977 in Connecticut when a group of children and several adults suffered from swollen joints (Berndtson, 2013; Johnson & Feder, 2010; Herrington et al., 1977). *B. burgdorferi* is a spirochete that causes LD (Johnson & Feder, 2010; Owen, 2006) and was discovered by William Burdgdorferi (Berndtson, 2013; Johnson et al., 1984; Tilly, Rosa, & Stewart, 2008). In 1977, LD became the most reported vector-borne disease in the United States (Johnson & Feder, 2010; Magriet al., 2002; Hickling & Stromdahl, 2012). In 2010, there were more than 30,158 reported cases of contracted LD in the United States (Overstreet, 2013). However, LD is more prevalent in the Northeastern region of the United States (Overstreet, 2013). LD was classified as a reportable disease in Connecticut in 1991, according to the CDC (Bratton et al., 2008). In 2017, the age groups most affected by LD in Connecticut were those who were older than 60 and younger than 10 (see Figure 3). Unlike CLD/PTLDS, LD has a known etiological agent, and its early diagnosis followed by antibiotic treatment is effective.

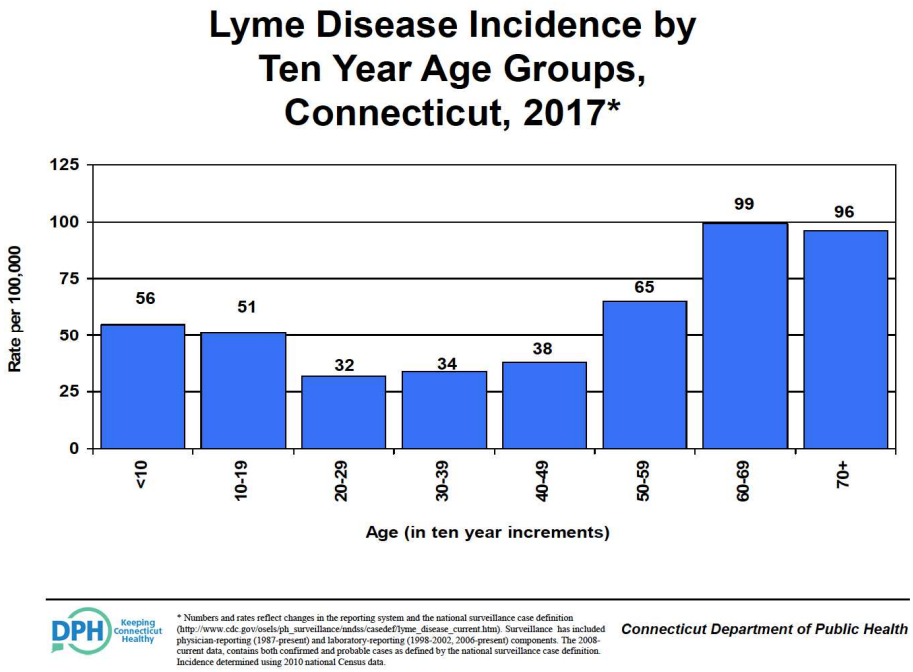

Figure 3. Lyme disease incidence rates by age group, 2017. From "Lyme Disease Incidence by Ten Year Age Groups, Connecticut, 2017*" by CT DPH, year 2017 (https://portal.ct.gov/-/media/Departments-and-agencies/DPH/dph/infectious_diseases/lyme/stats/LD-Incidence-Ten-Year-Age-Group-2017.pdf?la=en)

Researchers who argue for the existence of CLD/PTLDS believe that CLD/PTLDS patients are infected with the same bacterium that causes LD (Auwaerter, 2007). However, as cases of CLD /PTLDS continue to emerge in Connecticut (Johnson et al., 2014) even after antibiotic treatment, physicians believe that the bacteria remain active (Branda et al., 2018). This belief suggests that the traditional regimen of two to four weeks of oral antibiotics (typically doxycycline or amoxicillin) is ineffective in eliminating the bacteria (Ljostag & Mygland, 2013). Other researchers believe that it is

possible to contract CLD/PTLDS without a visible tick bite or without having presented the EM rash—a hallmark indicator of LD.

Biofilm Formation and *Borrelia burgdorferi*

Biofilms are produced by bacteria responsible for infections such as periodontitis, chronic otitis, endocarditis, and lung and gastrointestinal infections (Stricker & Johnson, 2011). According to Barthold (2014), *B. burgdorferi* does not form a biofilm as it grows in the collagenous connective tissue. However, other researchers have discovered that CLD/PTLDS is related to the formation of biofilms in humans after an infection with *B. burgdorferi* at the "persister stage" (Sapi et al., 2012; Stricker & Johnson, 2011). Sapi et al. (2016) suggested that *B. burgdorferi* may initiate a biofilm response due to the presence of motile spirochetes that transform into cystic, granular, or "cell-wall-deficient" forms when it encounters various unfavorable environmental conditions. Sapi et al. (2012) hypothesized that *B. burgdorferi* can form a biofilm during in vitro and in vivo studies. Moreover, Theophilus et al. (2015) indicated the possible presence of antibiotic-resistant *B. burgdorferi* persister cells. Theophilus et al. (2015) claimed that biofilms explain the LD relapse after antibiotic treatments. There is no effective treatment for biofilms (Stricker & Johnson, 2011).

Disagreement on Treatment for Lyme Disease and Chronic Lyme Disease

There is no universal agreement within the medical community on how to treat CLD/PTLDS (Maloney, 2016). Numerous questions were raised by Barbour (2015) and other health professionals concerning the treatment practices for LD and CLD/PTLDS, including (a) the effectiveness of shorter or longer periods of antibiotic treatment, (b)

whether one antibiotic is more effective than a combination of two medicines delivered simultaneously, (c) whether patients without typical symptoms or a confirmed bacterial agent present should be treated, and (d) whether conventional methods are better to treat people with LD or CLD/PTLDS than unconventional methods of modern medicine. Although CLD/PTLDS is assumed to be a bacterial infection-based disease, there is no conclusive evidence regarding its origin. The ingestion or inhalation of pathogens, as well as trauma, needle sticks, arthropod bites, or sexual transmission are all bacterial infection routes. The most common hypothesis for CLD/PTLDS transmission is that it is related to an arthropod bite, which is typical for in medically important diseases with rare or unknown cures (e.g., malaria) (Duron & Hurst, 2013).

The most commonly documented treatment practices for patients with CLD/PTLDS are related to persistent symptoms of the LD bacteria. Some researchers and health professionals assert that LD and other tick-borne coinfections may be connected to the etiological agent(s) of CLD/PTLDS (Cameron, 2010; ILADS, 2015). Most known bacterial diseases are cured with the use of antibiotics; however, it is also essential to take steps to prevent antibiotic resistance (Foxman & Martin, 2015).

Antibiotics (antibacterial or bactericidal agents) are selective toxicity chemical substances produced by microorganisms or plants with the ability to kill or inhibit another type of organism. There are antibiotics that kill the bacteria (i.e., bactericidal) and those that inhibit bacterial growth but do not kill bacteria (i.e., antibacterial) (Davies & Davies, 2010). Antibiotics that kill bacteria use the following mechanisms of action: (a) inhibition of bacterial cell wall synthesis (i.e., cephalosporin, carbapenems,

monobactams, vancomycin, cyclosserine, and bacitracin), (b) inhibition of protein synthesis (i.e., aminoglycosides, tetracyclines, chloramphenicol, erythromycin, clindamycin, and linezolid),(c) inhibition of nucleic acid synthesis (i.e., sulfonamides and trimethoprim), (d) inhibition of the DNA synthesis of quinolones and flucytosine, and (e) inhibition of mRNA synthesis (i.e., rifampin) (Davies & Davies , 2010).

Certain antibiotics act as agents that alter cell membrane function (e.g., polymyxins) (Brown, & Dawson, 2017), whereas other antibiotics have a mechanism for altering fungal cell membranes (Ost et al., 2016). The latter include amphotericin B, nystatin, and azoles (Serhan, Stack, Perrone, & Morton, 2014). In 1928, Alexander Fleming discovered penicillin, one of the most common antibiotics (Davies & Davies, 2010).

Penicillin is bactericidal but only kills when the infected cells grow; this occurs through inhibiting the peptidoglycan biosynthesis for the bacteria's cell walls. Penicillin has been an effective treatment for Gram-positive bacteria and some spirochetes (e.g., syphilis), as well as some Gram-negative bacteria (Zaffiri, Gardner, & Toledo-Pereyra, 2012). Penicillin has also been used to treat patients with LD (Wormser et all., 2000; Wormser et al., 2006). The traditional treatment for LD at the early stages, however, is with oral antibiotics, such as doxycycline (100 mg twice per day), cefuroxime (500 mg three times per day), or amoxicillin (500 mg twice per day) for a period of 21 days in patients who exhibit EM (Wright et al., 2012; Gasmi et al., 2017). Physicians who treat those with late-stage LD prefer to use ceftriaxone (2 g intravenously per day) and

penicillin G (Wright et al., 2012). Some researchers have stated that doxycycline cannot be used as an effective oral antibiotic to cure late-stage LD (ILADS, 2004).

The preferred antibiotic to treat LD in children and pregnant women is amoxicillin (Wormser et al., 2006), although intravenous ceftriaxone or penicillin have been found to be most satisfactory in treating patients in the late stages (ILADS, 2004). Patients treated with proper antibiotics in the early stages usually recover rapidly and completely. Antibiotics commonly used in oral treatment include doxycycline, amoxicillin, cefuroxime axetil, azithromycin, and penicillin (Torbahn et al., 2016). Patients with certain neurological or cardiac illnesses may require intravenous treatment with antibiotics, including ceftriaxone or penicillin (Barbour, 2015; Burrascano, 2008; Cameron, 2009; ILADS, 2014; Wills et al. 2016).

Studies suggest that the presence of the bacteria that causes LD may persist after treatment (Cameron, 2009; Wills et al., 2016). Gene mutation is a potential explanation for why the *B. burgdorferi* strain is resistant to certain antibiotics (Barbour, 2015). For example, it can change its morphology (i.e., pleomorphic) depending on surrounding environmental conditions, as does *B. burgdorferi sensu lato,* which creates complications for the development of an effective vaccine (Meriläinen et al. 2015). There is controversy regarding the safety levels and protocol of antibiotic use against tickborne diseases, including LD and CLD/PTLDS (Barbour, 2015).

Researchers and patients advocate for extended antibiotic use for CLD/PTLDS patients (Wright et al., 2012). These supporters believe that the prolonged symptoms of late LD, CLD/PTLDS are related to autoimmune responses triggered by an association

with *B. burgdorferi* and reactions with human leukocyte antigen haplotypes (Wright et al., 2012). Researchers and patients who advocate for extended antibiotic use for people with CLD/PTLDS also advocate for prolonged antibiotic use in late stage LD patients; these people are often members of ILADS (2004; 2015). However, the American Academy of Neurology, the American Academy of Pediatrics, the College of Rheumatology, and the Infectious Diseases Society of America do not support the use of prolonged antibiotic treatment (Wright et al., 2012). Questions remain regarding the safe lengths of time that humans should receive prolonged antibiotics for LD, CLD/ PTLDS (Cameron, 2006, 2010; Delong et al., 2012; Klempner et al., 2001; Klempner et al., 2013, Krupp et al., 2003; Stricker, 2007).

The National Institute of Allergy and Infectious Diseases (2019), as part of the National Institute of Health, sponsored four placebo-controlled clinical studies to evaluate the effectiveness of prolonged antibiotic treatment following standard recommended treatment regimens in patients with persistent symptoms related to those caused by *B. burgdorferi* (National Institute of Allergy and Infectious Diseases, 2019) The National Institute of Health (2019) showed that prolonged antibiotic treatment in these patients was not more beneficial than the short-term therapy given to patients by most U.S. doctors. According to Klempner et al. (2013), the findings suggest that there is no justification for the medical community to treat patients with extended periods of antibiotics administered by intravenous routes (Klempner et al., 2013).

Persistence of *Borrelia burgdorferi* after Antibiotic Treatment

LD is the most common arthropod vector-borne disease in the United States and is transmitted to humans through the bite of an infected *I. scapularis* tick (Stricker & Fesler, 2018, Wright et al., 2012). However, not all *I. scapularis* ticks carry *B. burgdorferi.* The CDC (2017b) issued a press release on the discovery of another type of bacteria, *Borrelia mayonii*, which causes LD. *I. scapularis* acquires the infected spirochete through blood contact with small mammals, particularly *Peromyscus leucopus,* a white-footed mouse (Bratton et al., 2008; Tracy & Baumgarth, 2017; Vuong et al., 2017). The spirochete grows in the tick's midgut and is transmitted to humans through the tick's salivary glands (Patton et al., 2011; Talwani, & Gilliam, 2012; Tabbasam, Malik, Asghar, Paracha, & Nazir, 2016; Wright et al., 2012).

Infected individuals commonly have early flu-like symptoms, such as headache, muscle and joint pains, fever, and malaise (Torbahn et al., 2016); therefore, it is helpful if they are aware of a previous bite. In other cases, the best tool that physicians and health professionals have at their disposal to diagnose LD is an early visual sign of the EM rash (Gasmi et al., 2017; Lantos et al., 2015c; Wright et al., 2012). This EM rash is not visible or present in all individuals infected with *B. burgdorferi* (Allen et al., 2016). Furthermore, EM is not easy for all physicians and health professionals to identify if the patient has multiple skin rashes (Kemperman, Bakken, & Kravitz, 2008).

The recognition of EM by physicians and other health care professionals is essential, as there are no certified clinical serology tests that identify the spirochete in patients' blood or the antibodies produced when *B. burgdorferi* is present during the first

two weeks of infection (Gasmi, 2017; Kemperman et al., 2008). It is possible to perform additional testing for LD between the third and sixth week after a *B. burgdorferi* infection. Testing would include an enzyme-linked immunoassay (ELISA) to show positive cases and a Western blot to corroborate these cases (Aguero-Rosefield, Wang, Schwartz & Worsmer, 2005; Dessau, Bangsdborg, Ejlertsen, Skarphedinsson, &, Schonheyder, 2010; Ogden et al., 2017).

B. burgdorferi persists in patients with continuous LD or PLTDS, which others may argue is a CLD/PTLDS symptom (Cameron, 2010). There are key aspects to consider when conducting clinical or epidemiological investigations regarding the persistence of *B. burgdorferi* and its relationship to late LD and CLD/PTLDS. It is necessary to assess the following: (a) the history of tick exposure, (b) the history of living in or having traveled to an endemic area for ticks, and (c) the history of the presence of the EM rash (Fallon et al., 2008).

There are concerns regarding the persistent presence of *B. burgdorferi* after early and late-stage treatment (Berndtson, 2013; Cameron, 2010; ILADS, 2014; Middelveen et al., 2018). Scientists have found that *B. burgdorferi* can evade the immune system in mammals making its eradication difficult in later stages (Barbour, 2012; Norris, 2014). Some patients have alluded to this reason for why they became sick; this assertion is also consistent with the opinion of CLD/PTLDS (Allen et al., 2016; Berndtson, 2013). *B. burgdorferi* possesses unique properties related to its virulence genes and outer bacterial membrane protein, making its eradication more difficult than other known spirochete infections (Tilly et al., 2008).

Several studies on laboratory animals (e.g., mice, dogs, and monkeys) document the persistence of *B. burgdorferi* after antibiotic treatment (National Institute of Health, 2015). Some of these studies on laboratory animals found the presence of its DNA after antibiotic treatment. However, this presence of its DNA cannot indicate a genetic product of an active bacterial infection (Feder et al., 2007; Tabbasam et al., 2016).

Embers et al. (2012) used toxicological techniques of xenodiagnoses and indirect fluorescent antibody staining to test the hypothesis that the spirochete in animal tissue persists after antibiotic treatment. Embers et al. (2012) performed two experiments using xenodiagnoses. The results of those two xenodiagnoses studies show the presence of debris or DNA material from *B. burgdorferi*. Although this DNA material was found, and pieces of the spirochete were hidden in the tissue, it is not entirely certain whether the same DNA material was viable, attenuated, or dormant (Lyer et al., 2013). Additionally, *B. burgdorferi* was found to integrate unique properties into its bacterial loci to create genetic changes that interfere with antibiotic treatment effectiveness (Lyer et al., 2013).

Molecular biology studies can be used to help researchers understand certain behavioral aspects of *B. burgdorferi* when an antibiotics regimen is used to eradicate the infection. These molecular biology studies shine a light on LD patients under treatment, the effectiveness of late treatment, and the possible relationship between CLD/ PTLDS. In conclusion, a significant debate continues on the existence of *B. burgdorferi* and its ability to cause chronic symptoms in untreated or undertreated patients, whether at the early or late stages of LD (Stricker & Johnson, 2013).

Clinical Testing to Diagnose Infections of Lyme Disease and Its Relationship to Testing for Chronic Lyme Disease

Although CLD/PTLDS has no known etiological agent, testing may be challenging and may not be specific, nor is there a diagnostic for it (CDC, 2019). Many PCPs may diagnose and treat a late LD infection (ILADS, 2014, Lantos, 2015a). LD has signs and symptoms that are less specific than other bacterial infections; thus, it is inevitably difficult to diagnose. Laboratory testing is recommended only for patients who notice the typical symptoms of LD (Gasmi et al., 2017). To understand the complexity and irregularity of testing for LD, it is essential to discuss its etiological agent, *B. burgdorferi* (Burrascano, 2008; Hyde, 2017; Wormser et al., 2006).

B. burgdorferi is a motile (Sultan et al., 2013, 2015) spirochete with the following attributes: irregular, loosely coiled, helical, weakly Gram-negative, size range from 0.20 to 0.30 μm in diameter, and 10 to 40 μm in length (Aberer & Duray, 1991; Marquez, 2015; Meriläinen et al. 2015). This spirochete has complex nutritional demands and is very challenging to cultivate in vitro using Barbour-Stoener Kelly (BSK) medium (Aberer & Duray, 1991; Marques, 2008; Sultan et al., 2015). Isolation of *B. burgdorferi* from the EM rash is possible, but there is less opportunity for isolation in late-stage LD infections (Moore et al., 2016).

Not all people exposed to the spirochete will develop an infection or present with the typical EM rash (Gasmi et al., 2017). Therefore, people may be unaware of a *B. burgdorferi* infection in the early stages. The longer an infection with LD continues, the more difficult it is to find the most suitable clinical and serology tests to facilitate its

diagnosis. Consequently, there is a need to have well-trained medical and laboratory staff in areas where LD persists until new medical advances can corroborate the etiological agents for CLD/PTLDS.

The microscopic examination of blood or tissues from patients with LD is not recommended because *B. burgdorferi* is rarely found in clinical specimens (Wormser et al., 2006). Culturing is not a common practice for clinical samples obtained from patients because *B. burgdorferi* is difficult to isolate and observe under a microscope and because it has a low growth process (Marques, 2008; Sultan et al., 2015). *B. burgdorferi* is also difficult to grow in vitro (Marques, 2018), as it requires special media or nutrients. Molecular diagnostic techniques for the diagnosis of LD, such as the use of nucleic acid amplification techniques for DNA or RNA, have lower sensitivity than the culture techniques for special properties, such as the motility of *B. burgdorferi* (Eshoo et al., 2012; Marques, 2015; Sultan et al., 2015). Unlike other bacterial infections where pathogen detection is performed directly or indirectly from a culture, LD diagnosis is not determined using the direct presence of the bacteria (Marquez, 2015).

LD has three distinct stages of pathogenic development on a patient after a positive tick bite *(*Applegren & Kraus, 2017*)*. The first stage or early stage is described mainly as the recognition of symptoms as fever, headache, fatigue, pain in the joins and the present of the EM (Nadelman et al, 2012). The second stage is described as when *B. burgdorferi* spreads throughout the whole body of the sick person. At this second stage, patients may exhibit symptoms like arthritis, meningitis, myocarditis, from weeks to months from the initial infection (Applegren & Kraus, 2017). In the third stage of LD,

patients have chronic symptoms as chronic arthritis, neurologic defects, or skin lesions (Applegren & Kraus, 2017).

In the early stage of LD infection, the bacteria hide (move) into the inner cells (inside the cell membrane) of the human host (Eshoo et al., 2012; Porcella & Schwan, 2001). This movement causes the bacteria not to be free in the bloodstream as many other infections (i.e., syphilis). Thus, a direct blood test to identify the infection by morphology of *B. burgdorferi* is not applicable at early stages and late stages of LD where the bacteria has moved to the organs of the central nervous systems (Applegren & Kraus, 2017). The early stage of LD diagnosis is based on the presence of antibodies found in the serum of samples from patients during the early stages of infection (Borchers et al., 2015; Burrascano, 2008).

However, if the serology testing of antibodies is conducted early when the EM rash is present or immediately after the tick bite, the results may have very low sensitivity and may occasionally be reported as negative (see Figure 4). Lantos et al. (2015c) also discussed the validity of serology testing in low-prevalence regions where the prevalence of ticks and LD is low and in which health professional may have a greater difficulty in making an accurate LD diagnosis.

Sensitivity/specificity of commercial two tier testing for convalescent/late stage Lyme disease in the US*			
Study/Year	**Patients/Controls**	**Sensitivity**	**Specificity**
Schmitz (1993)	25/28	66%	100%
Engstrom (1995)	55/159[†]	55%	96%
Ledue (1996)	41/53	44%	100%
Tilton (1997)	23/23	45%	100%
Trevejo (1999)	74/38	29%	100%
Bacon (2003)	106/559	67%	99%
Binnicker (2008)	35/5	49%	100%
Steere (2008)	76/86[††]	18%	99%
TOTAL	435/951	46%	99%
*Limited to studies from the US that included negative controls; [†]Non-commercial ELISA and Western blot; [††]Non-commercial ELISA			

Figure 4. Sensitivity/specificity of commercial two-tier testing for convalescent/late state Lyme disease in the United States. Adapted from "Two-Tiered Lab Tests Miss More Than 50% Of The Cases Of Lyme Disease," by L. Johnson, n.d. (https://www.lymedisease.org/lyme-basics/resources/two-tiered-lab-tests-miss-50-percent-of-lyme/)

Due to these difficulties, Connecticut physicians cannot diagnose early LD based on laboratory testing of patient blood samples. Clinical testing used in most of the United States and Connecticut is based on the presence of the EM rash and immunological and DNA applications. Some of these clinical tests are based on elevated sedimentation, elevated IgM levels, and mildly elevated hepatic transaminase (SGPT/ALT) levels.

Common immunological assays used after two weeks of LD infection include indirect fluorescent antibody staining, staining methods, and the enzyme-linked immunosorbent assay (ELISA), as well as western blot for corroboration (Aguero-

Rosenfeld et al., 2005; Liu et al., 2016). The most common tests used to diagnose LD are the indirect immunofluorescence assay and enzyme-linked immunosorbent assay (Liu et al., 2016). ELISA is the most sensitive test for most stages of LD because it uses purified or recombinant antigens. Serology testing is weak and unreliable for testing the early stages due to problems with sensitivity, cross-reaction activity from bacteria other than those being screened, and the need to create a single method to detect infection (Liu et al., 2016).

The ELISA test kit, also called the C6 peptide test (Chan et al., 2013; Wright et al., 2012), has been used since 2000, but the sensitivity is higher (60%) in patients and may still yield false positives. This ELISA test kit has better sensitivity than the two-tier ELISA test, although it was not tested in children (Chan et al., 2013; Lipsett et al., 2015). Lloyd and Hawkins (2018) reported that the C6 peptide test had a different sensitivity of 66.7% to 75%. Lloyd and Hawkins (2018) suggested that the reason for the variation may be due to the ribosomal spacer type (RST) genotype.

The ELISA test has been used as a screening assay, as it has a specificity rating of 90%-100% (Ljøstad & Mygland, 2013). The infection must be older than two weeks to measure the level of antibodies raised against the pathogens. Health care practitioners recommend that people test for IgM antibodies after the second week of exposure, as they may last up to four weeks post infection (Gasmi et al., 2017). Western blot is used to confirm a positive ELISA reaction (CDC, 1995, 2005; Ogden et al., 2017).

Antigenic heterogeneity *B. burgdorferi* and other species affect the test's sensitivity (Bonin, 2016; Branda, Linskey, Kim, & Steere, 2011). The variability of

ELISA and Western blot kits to test for LD depends on the infection's stage and the species of *Borrelia*. Various types of ELISA have been validated and approved by the FDA and accepted by the CDC (CDC, 1995; CDC, 2005).

This form of antibody testing uses blood serum samples from people presumed to have LD; however, it is not as sensitive as other serum commercial kits that are currently used for other diseases (e.g., syphilis). A commercial kit with two-tier testing often includes two steps: an EIA or immunofluorescent assay indirect fluorescent antibody staining that is followed by supplemental IgM and IgG immunoblots or western blot that use antibodies for LD. These antibodies depend on the manufacturer and location due to the geographic variability of the *Borrelia* species (Bonin, 2016; Branda et al., 2011; Gasmi et al., 2017; Wormser et al., 2013). However, in the United States, two-tier testing for LD according to the CDC's established criteria has a sensitivity close to or higher than 68% with a specificity of 99.5% (Wormser et al., 2013).

Branda et al. (2011) examined an alternative two-tiered strategy. The purpose of Branda et al.'s (2011) study was to investigate the sensitivity of the three testing strategies. Branda et al. (2011) randomly selected 1,246 healthy people and 54 patients in a hospital. Specificity was measured, and the study found that the positive predictive value was 70%.

However, internal validity should have been examined. The mortality threat may occur when uncommitted participants withdraw from a study (Branda et al., 2011). A total of 1,246 healthy individuals and 54 patients were randomly selected in the hospital; consequently, the results and findings cannot be generalized to other hospitals.

Nonetheless, this study was reported two decades after the testing for LD was initiated; the two-tiered testing with immunoblotting remains the standard for evaluation in testing patients for LD.

A clinician cannot accept ELISA and Western Block molecular test outcomes in two-tier testing for LD alone because they may yield false positive results (Marquez, 2015). These false positive results may be due to pre-existing conditions, such as Epstein-Barr virus or *Helicobacter pylori*. A false positive result is an issue because patients who do not have LD may show a positive test.

People who are aware of tick bites may be tested again for an increase in the *B. burgdorferi* antibodies after the first two weeks since ELISA and western blot tests may cause false negatives (Marquez, 2018). The proper time for testing with a two-tier kit for LD is between two and four weeks after the bite; this is when the antibodies for *Borrelia* species will develop and produce higher IgM than IgG. The low sensitivity of most two-tier testing systems commercially used in the United States for testing LD remains an issue because uninfected individuals may yield a positive test result. Additionally, others with early *B. burgdorferi* symptoms can be missed.

Testing should never be performed in the absence of appropriate history and clinical LD symptoms (Erthel, Nelson, & Carter, 2012). However, most laboratory clinicians prefer to use molecular biology tests with blood samples for bacteria diagnosis. Problems remain for testing serum samples from patients. Tests using serum samples from patients may yield a false positive due to issues with the specificity and sensitivity

of these tests, which can have cross-reacting antibodies against spirochetes in the normal flora (Ljøstad & Mygland, 2013).

Additionally, a polymerase chain reaction test is available to detect the tickborne bacteria (Greenwich Press, 2017; Hickling & Stromdahl, 2012). A polymerase chain reaction positive test performed on ticks is not a direct indication of LD infection. Instead, tick polymerase chain reaction testing for *B. burgdorferi* (Maurin*,* 2012) can provide valuable information about the probability of contracting an illness, especially if the tick was fully engorged and attached to a human host for over 48 hours (Marquez, 2015; Gasmi et al., 2017).

Although the CDC does not support the testing of ticks (CDC, 2017b), the Connecticut Agricultural Station (2019) and the Greenwich Health Department in Connecticut (2015) provide this service to the public. It may be beneficial to investigate whether the number and results of tick tests in Connecticut correspond with the highest incidence of LD. *Borrelia* DNA can be detected by a polymerase chain reaction test of synovial fluid and cerebrospinal fluid (e.g., CSF, synovial fluid, and blood) with varying levels of success (Bratton et al., 2008; Ljøstad & Mygland, 2013; Wright et al., 2012). It is important to note that *B. burgdorferi* is challenging to consistently cultivate from the synovial fluid (Marquez, 2015).

Polymerase chain reaction tests help identify bacteria species that are causing an infection (Maurin, 2012; Scott et al., 2017). The incubation period is 3 to 30 days after an infectious tick bite (CDC, 2017b; Kemperman, Bakken, & Kravitz, 2008). There is no

evidence for the person-to-person transmission of LD. There are some claims of maternal-to-child transmission, although there is little evidence (CDC, 2017b).

It is challenging to use microscopy, serology, or molecular testing to yield an accurate CLD/PTLDS diagnosis due to the lack of consensus between medical communities, as well as a lack of scientific evidence regarding its etiological agent(s). Scientists believe that CLD/PTLDS develops due to various factors related to the antibiotic treatment of *B. burgdorferi* in patients who were either undertreated, untreated, or treated late (Cameron, 2006; Wright et al., 2012). It is inappropriate and complicated to apply the same criteria used by most certified clinical labs to test for late-stage LD with a combination of ELISA and western blot tests (Ogden et al., 2017). Laboratory testing for *B. burgdorferi* is not standardized at the national level (Auwaerter, 2007). There is no known distinct testing method for CLD/PTLDS apart from the limited relationship to the approved serological testing for traditional cases of LD (Sigal, 2003; Strasheim, 2014).

Most patients with CLD/PTLDS have been accurately diagnosed based on the continuous symptoms that they have presented to a Lyme-literate medical doctor (Baker, 2012). The ILADS favors the use of long-term antibiotics and refers to many patients with CLD/PTLDS to Lyme-literate medical doctors, which is opposed by the Infectious Diseases Society of America. Infectious Diseases Society of America-affiliated physicians believe that long-term antibiotics are not a beneficial treatment for those who have late LD or CLD/PTLDS (Infectious Diseases Society of America, 2006, 2012, 2017; Marquez, 2008). Patients suffering from late cases of LD and CLD/PTLDS continue to

be symptomatic and seek a correct diagnosis and appropriate treatment for their condition at considerable personal and financial cost.

Problems for Physicians Reporting Chronic Lyme Disease

Unanswered questions remain regarding the existence of CLD/PTLDS. Therefore, the medical community is divided on the best approach for a diagnosis when presented with CLD/PTLDS symptoms. The root of the controversy lies in the fact that CLD lacks reliable biological markers and diagnostic tests to identify its origin.

Most patients visit a health professional for two reasons: to follow up with health plan appointments (e.g., annual checkups, surgeries, births) or to address immediate sickness. In both circumstances, patients may leave a health professional's office with a known diagnosis and an appropriate treatment to follow. In Connecticut, patients who believe that they have CLD/PTLDS do not encounter a fair process when visiting health care professionals and complain that they were denied or received limited or improper health care.

Physicians face difficulties in diagnosing CLD/PTLDS due to the lack of a clinical definition, symptom continuity, and systematic evidence that *B. burgdorferi* is associated with the etiology of CLD/PTLDS. Lantos (2011) found no proof that the bacteria that causes LD were present in certain patients who claimed to have CLD/PTLDS. These patients who claimed to have CLD/PTLDS had pre-existing conditions, such as rheumatoid arthritis, degenerative diseases of the spine, multiple sclerosis, or amyotrophic lateral sclerosis. Lantos's (2011) study also noted late-stage symptoms of LD, including severe pain in the joints and knees (e.g., in patients with

arthritis), chronic neurological complaints, short-term memory loss, cognitive issues, shooting pain, or numbness and tingling in the hands and feet. Lantos (2011) randomly selected patients who may have had CLD/PTLDS in the United States and successfully tested the research question; however, validity was mentioned in the study.

According to the Infectious Diseases Society of America (2017), patients who suffer from CLD/PTLDS have symptoms similar to the degenerative effects of untreated long-term LD. Therefore, there is confusion among Connecticut physicians as well as patients who believe that their illness is related to CLD/PTLDS or other diseases associated with LD. Many patients complain that their doctors refuse to diagnose and treat CLD/PTLDS and thereby withhold care. Patients' firsthand feelings are a result of their doctors' lack of knowledge about CLD/PTLDS and coinfections from *I. scapularis* bites (Cameron, 2010). If this is the case for health professionals who treat CLD/PTLDS patients, addressing physician education and training to ensure medical practice consistent with preventive care guidelines may be essential to aid in accurate diagnoses and to keep patients healthy (Gasmi et al., 2017; Strumpf, 2011).

Diagnosis, Treatment, and Management of Lyme Disease, Chronic Lyme Disease

There have been limited studies demonstrating the frequency of health practitioner diagnosis, treatment, and management of tick-borne disease, and, specifically for this study's purpose, about LD and CLD/PTLDS. PCPs may have difficulty in treating LD patients despite confirmation of the etiological agent and established antibiotic treatment regimens. Many areas remain open to exploration on how to control an LD infection that went untreated. CLD/PTLDS has many gaps and unanswered

questions, and there is a lack of information regarding the frequency of PCP diagnoses that use reliable and distinct laboratory testing.

Johnson and Feder (2010) found that fewer than 3% of physicians diagnosed patients with CLD/PTLDS in Connecticut. Johnson and Feder (2010) also discovered that 49% of physicians did not treat their patients for CLD/PTLDS because they did not believe it existed. Johnson and Feder (2010) performed descriptive statistics (but did not conduct MANOVA or t-tests). MANOVA is the most appropriate tool to measure differences between physicians because it assesses the effects of dependent variables simultaneously. T-tests can be valuable when using continuous data if the studied population is normally distributed (Parab & Bhalerao, 2010). If it not normally distributed, the data analysis should be complemented with non-parametric tests.

Ferrouillet et al. (2015) conducted a 2012 descriptive cross-sectional study to determine the knowledge and practices (in regards to the diagnosis and management of cases of LD using serology testing) of family physicians in two settings: (a) in one region with known infected ticks (Montérégie) and (b) in regions without infected ticks (Estrie and Lanaudière) in Southern Quebec, Canada. Ferrouillet et al. (2015) invited family participants to take part in the study by in-person invitations. A self-survey with 19 questions on two pages was given to those who accepted the invitation to participate. The survey questions were divided into three sections: (a) their experience with LD in the previous year, (b) questions regarding their knowledge, and (c) questions regarding their need for information.

A descriptive analysis on the two regions compared them using Fisher's exact test with SAS version 9.4. The participation rate in this study was 59% of the 201 participants. Ferrouillet et al. (2015) concluded that 201 participants were appropriate for representing the population of family physicians since the response rate of the survey was significant as a high response (n= 151 out of 201) among the primary care family physicians of Montérégie (p. 1). Some of the results were as follows: 56% never considered the diagnosis of LD, and 80% never prescribed antibiotics for LD patients. These results showed the based for internal validity. Ferrouillet et al. (2015) by conducting this study stated the importance that PCPs' knowledge and practices needed optimize the management of individual patients with LD.

Moreover, Ferrouillet et al.'s (2015) study's results were similar to Johnson and Feder's (2010) results. Johnson and Feder's (2010) study had identical conclusions regarding the differences in the KAPs of physicians related to LD and CLD/PTLDS. Johnson and Feder (2010) tested the assumption that there were significant differences in the KAP of physicians regarding the diagnosis, treatment, and management of LD. The hypothesis stated that there would be significant differences between PCPs concerning the diagnosis, treatment, and management of LD.

To test the hypothesis, Johnson and Feder (2010) performed descriptive statistics. Johnson and Feder (2010) randomly selected 3091 physicians and asked them to complete a mail survey. However, Johnson and Feder's (2010) study did not publish how the survey was developed, and its validity published.

Both Johnson and Feder's (2010) study and Ferrouillet et al.'s (2015) study focus on the differences in the KAPs of physicians regarding the diagnosis, treatment, and management of LD and CLD/PTLDS. The former discovered that there were significant differences. The latter also found that there were significant differences in the way physicians diagnosed and prescribed antibiotic treatment to potential LD patients. As evident in the study by Magri et al. (2002), most physicians preferred to recommend the LD vaccine to patients when the vaccine was still in use; it is essential to note that the vaccine is no longer prescribed to patients in the United States.

Magri et al.'s (2002) conclusion differs from Johnson and Feder's (2010) study and Ferrouillet et al.'s (2015) study. Magri et al. (2002) tested if there were significant differences in the KAPs of physicians concerning the diagnosis, treatment, and management of LD by performing Chi-square tests. Magri et al. (2002) randomly selected 600 physicians in New Hampshire and asked them to complete a survey.

However, internal validity should have been examined. Selection bias can occur when there are differences between physicians who return their questionnaires and physicians who do not answer their surveys. The mortality threat may occur when uncommitted physicians withdraw, such as in this study.

Diagnosis, Treatment, and Management of Post-Treatment Lyme Disease Syndrome

As stated in Chapter 1 and in this chapter, the term PTLDS (instead of CLD) it is more favorable used by the medical community (not the sick patients) (Delong, Hsus, and Kotsoris, 2019). Rebman et al. (2017) stated that 10 to 20% of patients after receiving treatment for LD experience multiple symptoms that sometimes the health professionals

find symptoms that vary from one patient to another) as prolonged fatigue, neurological dysfunction pains, that persist after being treated for LD (Delong et al., 2019a). There is no definite data collection or reporting it to the CDC as it is done for other infectious or chronic diseases. Nonetheless, Delong et al. (2019a) estimated an increase in the number of patients diagnosed with PTLDS from 2016 to 2020, with 68, 603 cases of PTLDS expected in 2020 (Delong et al., 2019a).

Thus, as well as CLD, there is not much information about how to conduct a standardized diagnosis and treatment to cure such patients with PTLDS (Delong et al., 2019). Rebman et al. (2017) stated the importance of investigating the clinical symptoms in patients living with PTLDS since it affects their quality of life. PTLDS bring financial burden to those patients with it; the problem is such a financial burden has never been investigated in the United States (Delong et al., 2019). But if PTLDS it turns out one day to be related to LD and CLD, it can cause more than a billion of dollars as it now the cost for health for patients known with LD (Delong et al., 2019). Therefore, in this study, although is investigating the validity of the finding founds by Johnson and Feder (2010) in regards to the diagnosis of CLD in Connecticut, it enhances insights about what would be the best implications or suggestions to recommends to PCPs in Connecticut to deal with cases of PTLDS (CLD). One clear objective recommendation is to have PCPs to accepts the term PTLDS to be able to create pathways to collect, document, and report possible cases of people sick with PTLDS (or CLD) that will eventually enable epidemiologists to how it is transmitted, what are the risk factors, and best treatment practices unknown presently. Further studies would be needed to find standardized

evidence based medical in regards to PTLDS to be substitute among professionals for CLD. Therefore, the term CLD/PTLDS was used concisely trough out the paper to recognized that is better for the future to recognized CLD/PTLDS as just "PTLDS". More on this topic is presented in chapter 5.

Summary and Conclusion

Johnson and Feder (2010) found that there were significant differences in the KAPs of PCPs regarding the diagnosis, treatment, and management of LD and CLD/PTLDS. Ferrouillet et al. (2015) also found that there were significant differences in the knowledge and practices of physicians concerning how physicians diagnosed and gave antibiotic treatment to potential LD patients. However, Magri et al. (2002) determined that most physicians preferred to recommend the LD vaccine to patients. It is necessary to examine the gap to yield new opportunities for future research if the topic of research has not been addressed appropriately by other researchers.

The study can help CT PCPs recognize PTLDS as a more appropriate diagnosis for those patients presumed has CLD. CT PCPs have difficulty dealing with the diagnosis and treatment of CLD/PTLDS patients. Thus, PTLDS can serve as a diagnosis for patients with CLD/PTLDS until more is known about it. Chapter 3 provides an overview of the research methods designed for the quantitative study and includes a discussion on the method of the study and the appropriateness of the design and data collection.

Chapter 3: Research Method

Introduction

Medical disagreements regarding CLD/PTLDS are caused by the unavailability of an acceptable standardized protocol to diagnose and treat it (Lantos, 2015a). Numerous medical doctors do not consider CLD/PTLDS an illness, which may be due to physician unawareness of evidence-based medical knowledge that corroborates the causal agent or the lack of surveillance systems that suggest that it is a new disease (Baker, 2008; Cameron, 2010; Feder et al., 2007; Johnson & Feder, 2010; Katz, 2007; Lantos, 2011, 2015a; McClellan, 2012; Wormser & Shapiro, 2009). Consequently, the cause, origin, and diagnostic criteria of CLD/PTLDS are unclear because most medical practitioners do not have data to guide treatment for affected patients (Lantos, 2011, 2015a).

The purpose of this quantitative nonexperimental, cross-sectional, comparative research was to validate Johnson and Feder's (2010) study and determine whether there were significant differences between two Connecticut PCPs regarding their knowledge, diagnosis, and treatment of LD and CLD (PTLDS). Statistical comparisons were made between survey responses provided by Connecticut PCPs in Johnson and Feder's study and the current study. I used the Connecticut knowledge, attitude, and practice (CT-KAP) survey, which was used by Johnson and Feder and was in the public domain for exact data comparisons.

This study's data may help physicians evaluate the current guidelines and methods for the diagnosis and treatment of CLD (PTLDS) patients. Within the limitation of having no approved case definition for CLD (PTLDS), in the survey mailed out, it was

defined "as the persistence (more than six months) of *Borrelia burgdorferi* infection, despite multiple standard courses of antibiotics)." Medical doctors are trained to conduct diagnosis using ICD codes, but in this study, an ICD code was not provided because it is not approved for CLD (PTLDS). This limitation accounts for the low response in this study, because some PCPs may not have felt comfortable to answer the KAP questionnaire or survey without knowing an ICD code with a definition associated for CLD/PTLDS, though I did provide a brief definition.

This chapter presents the study's methodology. The chapter begins with a summary of the research design and provides a rationale for its selection. The chapter continues with a discussion of the methodology with emphasis on the study population, sample, sampling procedures, participant recruitment and data collection procedures, the operationalization of study variables, the instrument and questions used to measure them, and the data analysis plan. Threats to validity of the study are then discussed, as are the ethical procedures of the study. A summary concludes the chapter.

Research Design and Rationale

I used a nonexperimental, cross-sectional, comparative (i.e., *ex post facto*) research design to examine whether there were significant differences regarding CLD/PTLDS KAPs between the sample of Connecticut PCPs who participated in Johnson and Feder's (2010) research and those who participated in this study. The study included five research questions. The independent variable for all research questions was the PCP group in this study compared to those who participated in Johnson and Feder's research. I used this the first research question acted as a validity check to examine

whether the two physician groups (the independent variable) had significant frequency distribution differences concerning the dependent variable of PCP types (i.e., family medicine, internal medicine, pediatric, other). The second research question helped examine whether the two PCP groups (the independent variable) had significant frequency distribution differences across three knowledge of LD categories (the dependent variable). The third research question helped examine whether the two physician groups (the independent variable) had significantly different frequency distributions across the knowledge of the four CLD (PTLDS) categories (the dependent variable). The fourth research question helped examine whether the two physician groups (the independent variable) significantly differed concerning the average number of patients they diagnosed as having CLD (PTLDS) within 3 years (the dependent variable). The fifth and final research question helped examine whether the two Connecticut PCPs (the independent variable) significantly differed concerning the average course of antibiotic treatment (in weeks) among the patients they diagnosed as having CLD/PTLDS within 3 years.

The quantitative approach in this study was guided by the positivist paradigm, which states that a single, objective, and measurable reality exists (Bowling, 2014; de Villiers, & Fouché, 2015). Quantitative research involves the scientific method where researchers develop questions and hypotheses that pertain to the tested theory or theories, use valid and reliable measures to obtain numerical data, and perform statistical analyses of numerical data; researchers then use the results to determine whether to reject or accept the null hypotheses (Bowling, 2014; de Villiers & Fouché, 2015). I chose the

quantitative research method over the qualitative method because it involves the scientific method to answer research questions. Hypotheses for each research question were formulated, and numerically-based data from surveys that were given to study participants (i.e., Connecticut PCPs) were collected. Statistical analyses from the data gathered in this study were conducted. Direct adjustment was conducted with population proportion 2015 to allow the PCP categories subgroups rates to have the same general trend as the population-proportion of 2006 PCP categories (Pagano-Gauvreau, 2000) before the data analysis was conducted.

Quantitative studies are delineated into three types: experimental, quasi-experimental, and nonexperimental (Bowling, 2014; Patten & Newhart, 2017). The quantitative experimental research design is used in studies where the researcher randomly selects participants from the population and randomly assigns them into study conditions such as an intervention group that receives some treatment and a control group that does not. The quantitative experimental research design is most appropriate for examining whether one or more dependent variables differ across intervention and control groups of participants. Nonexperimental research designs pertain to studies where neither random selection of participants is conducted nor when random assignment to conditions is relevant or applicable.

Further, nonexperimental research designs are commonly delineated into three types: (a) descriptive, in which the researcher presents and describes a phenomenon using descriptive statistics (as opposed to inferential); (b) correlational, in which the researcher wants to determine whether one or more independent variables (i.e., predictor variables)

are significantly associated with or related to one or more dependent variables (i.e., criterion variables) and utilizes inferential statistics such as correlational or regression models to determine the significance of these relationships; and (c) comparative, or *ex post facto*, in which the researcher wants to determine whether one or more naturally occurring groups (i.e., the independent variables) significantly differ in one or more dependent variables, which are also naturally occurring, and utilizes inferential statistics such as Chi-squares, *t* tests to determine if significant differences exist (Patten & Newhart, 2017; Reio & Reio, 2016). *Naturally occurring* refers to groups that cannot be manipulated. I did not choose a descriptive nonexperimental design because it does not involve inferential statistics (Reio & Reio, 2016). A correlational design was also not applicable because I did not determine temporal sequences or causal relationships between independent and dependent variables.

A comparative quantitative research design was suitable for this study to assess the validity of Johnson and Feder's (2010) study. I examined whether two naturally occurring groups of Connecticut PCPs (i.e., the independent variable) significantly differed among four dependent variables: (a) the type of PCP they identify as, (b) knowledge regarding LD and CLD(PTLDS), (c) the number of patients identified as having LD and CLD (PTLDS) per PCPs, and (d) the average course of antibiotic treatment (in weeks). These dependent variables are also naturally occurring. This study differs from other comparative studies in that the data were gathered at the same time from the groups of the study's focus. I compared the data collected from a new sample of

Connecticut PCPs to the archival proportion, frequency, and mean level data reported in Johnson and Feder's study conducted with Connecticut PCPs.

Finally, this study was designed to collect data from a single point in time and is therefore considered a cross-sectional study. Although data obtained in this study were compared to responses provided by Connecticut PCPs in Johnson and Feder's (2010) study, this study is not longitudinal. These two naturally occurring groups of Connecticut PCPs were not comprised of the same physicians, and they were not followed over the past 10 years, as would be done in a longitudinal study. Therefore, it was necessary to assess whether each study group (2006 and 2015) was representative of the Connecticut PCP population at the time of each survey so the appropriateness of generalization of the results (external validity) could be assessed.

Methodology

A quantitative, cross-sectional, comparative study was implemented similar to Johnson and Feder's (2010) study. The population of 2015 Connecticut PCPs was randomized using the same computer software (Excel) that Johnson and Feder used to obtain the 33% of PCP in the categories needed for the study to obtain the study sample. Participant recruitment and data collection procedures were also aligned. The study instrument was the CT-KAP 2006 questionnaire, and study variables were operationalized by survey item response coding. Further information is provided in the data analysis plan in this chapter.

Population

The population for this epidemiological investigation included 5,231 PCPs licensed to practice in the state of Connecticut as of 2015, based on information from the CT DPH (2015), which contained data on Connecticut physicians CT DPH MD/DO including physician work addresses for the 17,464 certified physicians who actively practiced medicine. Of these 17,464 physicians, 5,231 were classified as PCPs in the categories of primary health care practice specialties of pediatrics, primary/general/family medicine, and internal medicine as the main sampling frame needed to conduct the study (CT DPH, 2015). See Appendix F for the description of the sampling frame and PCPs for 2006 (Johnson & Feder, 2010) and 2015 (the current study).

The final population accountable for the data analysis in this study were 145 PCP survey responses (2015) and 285 PCP survey responses (2006). The total number of PCPs of 2006 was 15,424. Of these 15,424 physicians (MD/DO), 3,091 were classified as PCPs in the categories of primary health care practice specialties of pediatrics, primary/general/family medicine, and internal medicine as the main sampling frame needed to conduct the study (Benson & Eberle, 2009; CT DPH, 2006). The population proportion of 2006 was derived from the historical data in Johnson and Feder's (2010) study. Adjustment to the population proportion of 145 was conducted to make the data analysis appropriate, and the adjustment factor was 1.97 (285/145, 1.9655 = 1.97, 1.97 X 145 = 285). To be more specific, the 2006 population proportion derived from Johnson and Feder's study consisted of 57 family physicians, 113 internal medicine physicians, 107 pediatricians, and eight others (i.e., emergency physicians). In contrast, the 2015

population proportion in this study comprised 28 family physicians, 63 internal medicine physicians, 48 primary physicians, and six others (i.e., emergency physicians) before adjustments. After adjustments were made to bring the 145 PCP responses to be standardized for appropriate comparisons, the population proportion consisted of 55 family physicians, 124 internal medicine physicians, 48 pediatricians, and 12 others (i.e., emergency physicians). See Table 6 for more details.

Sample and Sampling Procedures

The recruitment of a sample of Connecticut PCPs were intended to form a similar sample size and type as that of Johnson and Feder's (2010) study. This study had the same inclusion/exclusion criteria for study participants as Johnson and Feder. Thus, adaption to the inclusion and exclusion criteria from those pages were applied (see Tables 4 and 5). The 2006 PCP population made up of 285 survey responses in the categories of family medicine practitioner, internist, pediatrician, or other PCPs (i.e., emergency physicians) after accounting for inclusion criteria. In this study, there were 145 PCP survey responses (population proportion) in 2015 for the data analysis (in the following categories: family medicine practitioner, internist, pediatrician, or other primary care practitioners). Physicians with specialization in areas unrelated to the primary care categories of pediatrics, family medicine, or internal medicine as explicitly described in the CT DPH database were excluded from this study. In alignment with the previous study, in this study, the sample frame was limited to physicians who are certified and actively practice primary care in Connecticut.

Johnson and Feder (2010) did not describe how they conducted the validation of the 2006 CT-KAP survey, but I assumed that it was validated because they were medical doctors. This lack of validity criteria is a basis to conduct a validity check to see if the PCPs in Johnson and Feder's study and in this study have changed after 10 years and to find the internal and external validity of the data for this study. Although the internal and external validity were not documented or not published, their survey will have a higher degree of internal validity because their response rate was 39.1 %, and the survey response rate with the 2015 population proportions in this study was 11.9%. In this study, the validation of data is presented in Chapter 4.

The overall sample size had similar population proportion based on the *z* score test. However, I still adjusted the 145 sample of PCP survey responses to the 285 sample of PCP survey responses before the data analysis because "equivalence testing performs best when sample sizes are equal" (Rusticus & Lovato, 2014, p. 1). A G*Power (Faul, Erdfelder, Lang, & Buchner, 2007) power analysis for a one-sample *t* test was used to determine the sample size needed to achieve adequate power for this study. The significance (alpha) level was set to $p < 0.05$, and power was set to 0.80. Because previous literature on LD and related disorders have reported small effect sizes, the effect size was set to small (Cohen's $d = 0.165$; Larsen, MacDonald, & Plantinga, 2014; Tonne, 2017). Based on the power analysis result, a sample size of $n = 300$ PCPs working in Connecticut was needed for the study (see Appendix H).

Because the 2015 PCP study population proportion did not achieve the sample size projected ($N = 300$), it was assumed that the margin of error in this study was greater

than the 285 PCP survey population proportion of 2006. The margin of error formula is margin of error = $z * \sqrt{p} * (1 - p) / \sqrt{n}$. The margin of error in this study was 0.01%, $p = <$ 0.05, 95% CI = 1.96. Further, under the expectation to receive 300 PCP survey responses and only receiving 145, the margin of error was ± 5.86%. Moreover, in this study when calculated for the 145 PCP survey responses with $p < 0.05$ (z score 1.96), the calculated margin error was ± 8.138%. In contrast, the margin of error for the samples in the Johnson and Feder (2010) 2006 population proportions of 285 was ±4.726%; therefore, the smaller sample size in this study had a larger margin of error. The larger the sample size, the smaller the margin of error. Thus, when the two cluster samples were added (i.e., n =145 for 2015 and n = 285 for 2006 = n = 430), the calculated margin of error was ± 4.73% (see Appendix G).

The sample was expected to be similar or greater in proportion to (with a response rate of 39.1%) Johnson and Feder's (2010) study sample to achieve equal representation and accurate data analysis. However, because the 2015 PCP proportion sample consisted of 145 from 179 PCP survey responses, I assumed that this response rate might affect the representation (internal validity) of the population in this study. The 2015 PCP specialty categories also had dissimilar frequency proportions in contrast to the 2006 PCP specialty categories. Z scores as presented in Chapter 4 show the variations within the PCP categories (see also Tables 4 and 5). Therefore, the n = 145 sample proportion of 2015 was adjusted for the data analysis stated the status of representation in this study before the data analysis was conducted. The adjustment was done using the larger number of P^1 / $P^{2.}$ Thus, P^1 (285) / P^2 (145) = 1.97.

Regarding sampling procedures, Johnson and Feder's (2010) sampling frame was from the CT DPH (2006) database of 3,091 PCPs licensed to practice in the state of Connecticut, which I also used for this study. Johnson and Feder used random sampling to select 33% of the 3,091 Connecticut PCPs (n = 1,034), whose data were available in the CT DPH database as the recruitment sample. The same random sampling strategy technique was also employed in this study. A randomization method was employed via a random number generator set between 1 and 5,231; these numbers corresponded to the numbered database entries of the 5,231 Connecticut PCPs. In this study, 1,726 physicians were randomly selected as the 33% of the Connecticut PCPs, whose data were available in the CT DPH (2015) database. These physicians made up the sample of participants necessary for this study (see Appendix E).

I mailed a study materials packet that included an informed consent form, directions on completing the study survey, the survey itself, and a stamped and addressed envelope to the physicians at their work addresses. As per the directions in the packet, physicians were asked to return the completed CT-KAP questionnaire using the stamped envelope, which was mailed to a designated P.O. box address. The questionnaire directions and CT-KAP questionnaire itself were identical to those used by Johnson and Feder (2010). Additionally, two other questions were included on whether the physician participated in Johnson and Feder's study (i.e., *Yes* or *No*) and to give consent to participate in this study (see Appendix A).

The consent form included my professional contact information, the reason for conducting the study, and information about (a) the goals and purpose of the study, (b)

the role of the study participant (i.e., what the physician were required to do), (c) the benefits and risk of participating in the study, (d) the procedures employed in the study to maintain confidentiality and anonymity, and (e) the voluntary nature of the study (i.e., the right of the physician to not participate in the study and/or to refuse to answer any questions on the CT-KAP questionnaire). Participants were not asked to sign their name on the consent form or to mail it back to maintain physician confidentiality and anonymity; instead, they were asked to check *Yes* or *No* on the consent form that was found in the mail out. If any physician selected *No* or did not mark the answer on the question as consent to participate yet returned a completed questionnaire, their data were not used in the study. It was not possible to mail reminder notices to encourage participation.

Johnson and Feder's (2010) study reported that of the 1,034 study packets mailed to the PCPs, 191 (18.5%) were returned unopened due to an incorrect address, which reduced the recruitment sample to 843 Connecticut PCPs (Johnson & Feder, 2010). A similar percentage (or proportions) rate of the 1,726 study materials packets was expected to be returned due to incorrect address, resulting in a recruitment sample of 1,507 physicians. Johnson and Feder (2010) reported that, of the 843 survey packets received by the physicians, only 330 surveys were returned (a 39% response rate; see Tables 4 and 5). Johnson and Feder's (2010) final response rate was 33.5%; 285 of the 843 surveys mailed to "Connecticut Primary Care Physicians 2018" were returned and had useable data. As response rates in health care and medicine studies using mailed questionnaires are notoriously low (i.e., approximately 30%), a response rate of 30% was anticipated (n

= 422) (Halbesleben & Whitman, 2013; Johnson & Wislar, 2012; Phillips, Friedman, & Durning, 2017).

Additionally, the study survey included a question inquiring as to whether the physician participated in Johnson and Feder's (2010) study. If a physician had participated, his or her response was used in this study. The likelihood that the same physicians in Johnson and Feder's (2010) study would also be recruited into this study was low, mainly since they and the researcher employed random sampling to obtain the initial recruitment sample. The expected sample of 422 physicians was large enough to allow for the removal of any of these cases – as well as the removal of cases with incomplete or otherwise unusable data – while achieving the desired sample size of 300.

Johnson and Feder (2010) did not seek to obtain equal numbers of PCPs per specialty category. Consequently, it was not sought in this study to align with Johnson and Feder's (2010) previous approach. The first research question was developed to act as a validity check and determine if the proportion of physicians per primary care category in this study was significantly different from those reported by Johnson and Feder (2010). In this study, it was hoped that this study sought to identify no significant differences in the proportion of physicians per primary care category because a lack of significance indicates that the two samples were similar.

The original data set used in Johnson and Feder's (2010) study was not fully accessible to the researcher. Therefore, the proportion, frequency, or mean level data that were reported in Johnson and Feder's (2010) study were also used in this study. The inability to access Johnson and Feder's (2010) full study data set required that the

statistical analyses used to test study hypotheses also treated the proportion, frequency, or mean data reported in their study as the expected or population data.

Instrumentation Operationalization of Study Variables

The instrument used in this study was Johnson and Feder's (2010) 9-item CT-KAP 2006 questionnaire on LD and CLD/PTLDS (see Appendix A). Murray and Feder (2001) developed and validated the CT-KAP questionnaire, and it was further refined in the study by Magri et al. (2002). Murray and Feder (2001) reported a 56% response rate, receiving completed questionnaires from 320 out of 573 PCPs in Connecticut that were solicited to participate. Of the 320 physicians in Murray and Feder's (2001) study, 267 (83%) reported having diagnosed patients with LD, a valid percent in a geographical region with a high LD prevalence rate. Most physicians said that they followed the established clinical guidelines for treating patients with LD; for example, the average course of antibiotic treatment was 21 days (Murray & Feder, 2001).

There is nearly a 20-year history of using the CT-KAP questionnaire in surveillance and epidemiological and clinical research studies on LD but little on CLD. Studies have provided evidence that the CT-KAP questionnaire provides a valid and reliable assessment of physicians' KAP regarding LD and CLD/PTLDS (Brett, Hinckley, Zielinski-Gutierrez, & Mead, 2014; McKinney et al., 2008). There is evidence of construct validity of the CT-KAP; that is, it effectively measures the KAP of physicians' clinical approach to CLD/PTLDS. Magri et al. (2002) provide evidence of criterion-related discriminant validity of the CT-KAP: they found that there was a significantly higher percentage (or proportions) of physicians with patients diagnosed with LD in high-

versus low-endemic areas (53.2% as compared to 29.1%, $p = 0.0003$). McKinney et al. (2008) note considerable overlap in KAP questions between the CT-KAP and related physician LD KAP questionnaires, providing evidence of the criterion-related concurrent validity of the CT-KAP.

The independent variable of this study was the physician group that is, the group of Connecticut PCPs who participated in Johnson and Feder's (2010) research and those who participated in this study. The inability to fully access and use Johnson and Feder's (2010) data set precludes the ability to analyze data at the item level for the group of Connecticut PCPs who participated in Johnson and Feder's (2010) study and those who participated in this study. Johnson and Feder's (2010) group was treated as a population, allowing for the use of proportion, frequency, and mean level data reported in their study. The response codes for each and all the nine items on the CT-KAP questionnaire was the same, which allowed the comparisons between the group of Connecticut PCPs who participated in Johnson and Feder's (2010) study and those who participated in this study to be made. The following section presents each dependent variable and its coding. Figure 5 presents a summary of the study independent and dependent variables, which are further discussed in the following sections.

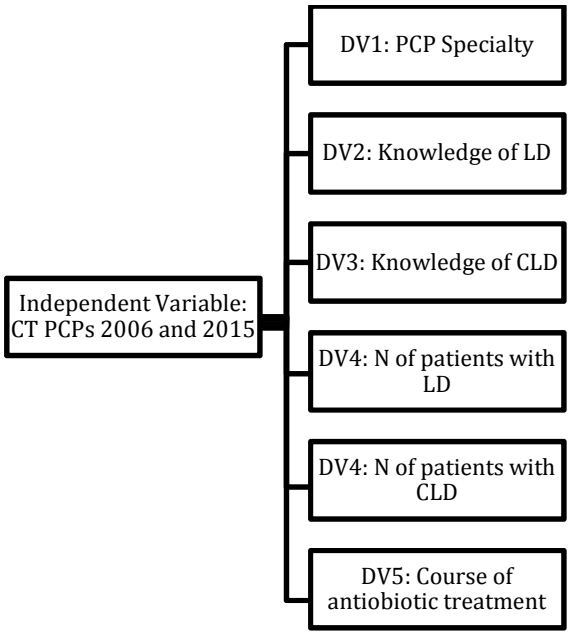

Figure 5. Study independent and dependent variables.

Dependent variable 1: Primary care physician specialty. The first dependent variable of PCP specialty was measured using CT-KAP item two: "What is your specialty?" This CT-KAP item two was coded as a categorical (nominal) item, where 1 = Family Medicine, 2 = Internist, 3 = Pediatrician, and 4 = Other Primary Care.

Dependent variable 2: Physician knowledge of Lyme disease. The second dependent variable of physician knowledge of LD was assessed using CT-KAP item 3: "How would you describe your knowledge of Lyme disease?" This CT-KAP item 3 was coded as a categorical (nominal) item, where 3 = I know the symptoms and feel comfortable diagnosing it, 2= I know the symptoms but don't feel comfortable diagnosing it, and 1 = I don't know the symptoms and don't feel comfortable diagnosing it.

Dependent variable 3: Physician knowledge of chronic Lyme disease. The third dependent variable of physician knowledge of CLD (PTLDS)was assessed using CT-KAP item four: "How would you describe your knowledge of CLD (PTLDS)?" This CT-KAP item four is coded as a categorical (nominal) item, where 4 = I know the symptoms and feel comfortable diagnosing it, 3 = I know the symptoms but don't feel comfortable diagnosing it, 2 = I don't know the symptoms and don't feel comfortable diagnosing it, and 1 = I don't believe it exists.

Dependent variable 4: Mean number of patients diagnosed and treated with Lyme disease and chronic Lyme disease. The fourth dependent variable of mean number of patients diagnosed and treated with LD and CLD (PTLDS) was measured using CT-KAP item seven: "Over the past 3 years, approximately how many patients have you diagnosed and treated with Lyme disease? "Over the past 3 years, approximately how many patients have you diagnosed and treated with Lyme disease?" This CT-KAP item seven was a ratio-coded variable that ranged from 0 to *n*.

Dependent variable 5: Average total course of antibiotic therapy (in weeks) for patients with chronic Lyme disease. The fifth dependent variable of average total course of antibiotic therapy (in weeks) was assessed using CT-KAP item seven a: "What has been the average total course (in weeks) of antibiotic therapy for patients with CLD (PTLDS)?" This CT-KAP item seven a was a ratio-coded variable that ranged from 0 to *n*.

Data Analysis Plan

The statistical software used to conduct all data analyses was SPSS 24.0. The data analysis plan involved a sequential process. Study participants used a paper questionnaire that necessitated the entry of questionnaire data into an SPSS 24.0 data set. Before entering these data, the researcher reviewed the surveys received from the physicians. Questionnaires with incomplete or otherwise unusable data were discarded, as were surveys in which the participant did not provide consent in the study. The researcher denoted the number of discarded questionnaires and the reasons why they were discarded (see Chapter 4).

The researcher assigned to each questionnaire an ID number and collated the questionnaires in order of the ID number. The data were documented and organized using SPSS 24.0 to create the data set, which was kept on a password-protected jump drive (not a computer hard-drive). The jump-drive was stored in a locked file cabinet at the researcher's home office in a separate compartment from paper questionnaires. The researcher reviewed the data and data set before and after the data were entered, searching for any data entry errors. Frequencies were performed on all item responses and conducted unusual cases analytics to ensure that all data entry errors were addressed.

Descriptive statistical analyses were conducted on all data, reporting responses for each of the first nine question items of the 2018 CT-KAP questionnaire. While certain CT-KAP 2018 items were used to measure dependent variables, descriptive statistics were used for all nine items. The researcher ran and reported the frequencies/percentages

of responses on categorical (nominal) variables as well as the mean, median, standard deviation, and minimum and maximum values for the ratio-coded variables.

The first, second, and third research questions required conducting Chi-square (χ^2) goodness-of-fit tests. The fourth and fifth research questions required one-sample t-tests. The appropriate effect size and power calculation results augmented the statistical findings for each research question.

Cohen's *W* is the indicator of effect size for a Chi-square (χ^2) goodness-of-fit test (Cohen, 1988; Cunningham & McCrum-Gardner, 2007; NCSS, n.d.). The mathematical formula for Cohen's *W* is $\sqrt{\chi^2/N}$ (Cohen, 1988; NCSS, n.d.). Cohen's *d* is the indicator of effect size for a one-sample t-test (Cohen, 1988; Lakens, 2013). The mathematical formula for Cohen's *d* for a one-sample test (i.e., Cohen's d_z) is $[t]/\sqrt{n}$, where [*t*] is the absolute *t*-value (i.e., no negative values used), and *n* is the sample size (Cohen, 1988; Lakens, 2013). Power was determined from the effect size and sample size values.

Research Questions Hypotheses and Statistical Analyses

The purpose of this quantitative comparative (i.e., *ex post facto)* study was to examine if significant differences regarding knowledge, diagnosis, and treatment of LD and CLD/ (PTLDS exist between two groups of Connecticut PCPs – those who participated in Johnson and Feder's (2010) study and those who participated in this study. The study posed five research questions with associated null and alternative hypotheses. These are restated below, followed by the proposed statistical analysis for each research question.

Research Question 1: Are the frequency distributions of the 2015 sample of Connecticut PCPs across the four primary practice specialty areas (i.e., family medicine, internal medicine, pediatrics, other) significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

$H_0$1: The frequency distributions of the 2015 sample of Connecticut PCPs across the four primary practice specialty areas (i.e., family medicine, internal medicine, pediatrics, other) are not significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

H_a1: The frequency distributions of the 2015 sample of Connecticut PCPs across the four primary practice specialty areas (i.e., family medicine, internal medicine, pediatrics, other) are significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

Analysis: Chi-square (χ^2) goodness-of-fit test. The researcher treated Johnson and Feder's (2010) physician data as population data and used data from CT-KAP questionnaire item two. Chi-square (χ^2) goodness-of-fit test was done by comparing the frequency/proportion distributions of physicians in each of the four specialty areas to the frequency/proportion distribution values reported in Johnson and Feder's (2010) study. This research question was unique, as it is the only one in the study in which the null hypothesis was intended to be retained or failed to be rejected.

Research Question 2: Are the frequency distributions of the 2015 sample of Connecticut PCPs across the two knowledge of LD categories (i.e., know symptoms of LD and feel comfortable diagnosing and treating LD vs. know LD but do not feel

comfortable diagnosing and treating LD) significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

$H_0$2: The frequency distributions of the 2015 sample of Connecticut PCPs across the two knowledge of LD categories (know symptoms of LD and feel comfortable diagnosing and treating LD versus know LD but do not feel comfortable diagnosing and treating LD) are not significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

H_a2: The frequency distributions of the 2015 sample of Connecticut PCPs across the two knowledge of LD categories (know symptoms of LD and feel comfortable diagnosing and treating LD versus know LD but do not feel comfortable diagnosing and treating LD) are significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

Analysis. Chi-square (χ^2) goodness-of-fit test. In this study, Johnson and Feder's (2010) physician data were treated as population data. Chi-square (χ^2) goodness-of-fit test was conducted by comparing the distributions of responses on CT-KAP questionnaire item three in this study data to the distribution values reported by Johnson and Feder (2010).

Research Question 3: Are the frequency distributions of the 2015 sample of Connecticut PCPs across the three knowledge of CLD/PTLDS categories (do not believe CLD exists, do not feel comfortable diagnosing and treating CLD/PTLDS, and feel comfortable diagnosing and treating CLD/PTLDS) significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

$H_0$3: The frequency distributions of the 2015 sample of Connecticut PCPs across the three knowledge of CLD/PTLDS categories (do not believe CLD exists, do not feel comfortable diagnosing and treating CLD/PTLDS, and feel comfortable diagnosing and treating CLD/PTLDS) are not significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

H_a3: The frequency distributions of the 2015 sample of Connecticut PCPs across the three knowledge of CLD/PTLDS categories (do not believe CLD/PTLDS exists, do not feel comfortable diagnosing and treating CLD/PTLDS, and feel comfortable diagnosing and treating CLD/PTLDS) are significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

Analysis. Chi-square (χ^2) goodness-of-fit test. The 2006 physician data were considered population data. Chi-square goodness-of-fit test was completed using the distribution data of physician responses per knowledge category for CT-KAP questionnaire item four and the distribution values reported by Johnson and Feder (2010).

Research Question 4: Is the estimated average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2015 sample of Connecticut PCPs significantly different from the average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

$H_0$4: The estimated average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2015 sample of Connecticut PCPs is not significantly

different from the average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

H_a4: The estimated average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2015 sample of Connecticut PCPs is significantly different from the average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

Analysis. One-sample *t*-test. The 2006 (Johnson & Feder, 2010) physician data were considered population data. One-sample *t*-test was used to test the difference between the study sample mean score for CT-KAP questionnaire item seven and the mean of 3.00 CLD cases reported per physician by Johnson and Feder (2010).

RQ5. Is the estimated average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2015 sample of Connecticut PCPs significantly different from the average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

Research Question 5: Is the estimated average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2015 sample of Connecticut PCPs significantly different from the average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

$H_0$5: The estimated average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2015 sample of Connecticut PCPs is not

significantly different from the average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCP.

H_a5: The estimated average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2015 sample of Connecticut PCPs is significantly different from the average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCP.

Analysis. One-sample t-test. The Johnson and Feder (2010) physician's data were considered the population data. One-sample *t*-test was used to test the difference between the study sample mean score for CT-KAP questionnaire 2018 item seven a and the mean of 20 weeks of antibiotic treatment by physicians in Johnson and Feder's (2010) study.

The two primary statistics used to test the hypotheses were the Chi-square (χ^2) goodness-of-fit test and the one-sample *t*-test. The non-parametric Chi-square (χ^2) goodness-of-fit test was used to determine if the frequency distribution of responses on a categorical variable for a sample is significantly different from the expected or population distribution (Salkind, 2016). The primary assumption to be met for a Chi-square (χ^2) goodness-of-fit test is that each variable category must have a sample size no smaller than five (Salkind, 2016). This assumption was met in this study. The smallest sample size per category was six, in reference to the number of PCPs who identified as other.

The one-sample *t*-test was used to determine if a sample variable mean score is significantly different from a known population mean score (Treiman et al., 2015). The

two fundamental assumptions of the one-sample *t*-test were that the dependent variable was measured using a ratio or interval scale and that the dependent variable had a normal distribution (Treiman et al., 2015). In this study, one-sample *t*-tests were used with ratio-coded dependent variables.

The assumption of normality was addressed by examining the skewness of the variables by computing $z_{skewness}$ values (i.e., by dividing the variable skewness by the skewness standard error; Kim, 2013). For medium-sized samples – that is, samples between 50 and 300 – a $z_{skewness}$ greater than 3.00 indicates variable skewness and a violation of the normality assumption (Kim, 2013). The assumption of normality was further tested by (a) conducting Kolmogorov-Smirnov tests, (b) utilizing SPSS 24.0 unusual cases function to identify outliers, and (c) computing box-plots.

As stated by Cousineau and Chartier (2010), "there is no single solution" to dealing with outliers (p. 66). There are three standard options to address outliers: (a) winsorizing the outlier (i.e., replacing the outlier value with the next lowest or highest score), (b) transforming the variable (i.e., using loglinear or square root transformations), or (c) removing the outliers (Cousineau & Chartier, 2010; Kim, 2013; Pollet & van der Meij, 2017). However, Winsorization and transformation of values do not always solve outlier issues (Cousineau & Chartier, 2010; Kim, 2013; Pollet & van der Meij, 2017).

The option for dealing with outliers selected for this study was removal of the outliers, especially as statistical findings may differ substantially based on whether "outliers are included or excluded" (Pollet & van der Meij, 2017, p. 54). A concern with removing outliers is that it may result in the loss of too many data points until the

statistical analysis cannot be conducted or is no longer applicable to the data set (Cousineau & Chartier, 2010; Kim, 2013; Pollet & van der Meij, 2017). However, one-sample t-tests were conducted for the fourth and fifth research questions, as it was important in this study to replicate the analyses conducted by Johnson and Feder (2010) and to address the null and alternative hypotheses for them.

Threats to Validity

Three types of validity in quantitative research studies pertain to study limitations in relation to the research methodology and design: (a) *internal validity*, or the degree to which it can be stated that the observed effects on the dependent variable(s) are due to the independent variables and not to uncontrolled confounding variables; (b) *external validity*, or the ability to generalize study results to the population or other samples, settings, and times; and (c) *construct validity*, or how well a study instrument operationally captured the constructs under study (Patten & Newhart, 2017). The internal and external validity were assessed by comparing the number or proportions of PCP survey responses and the PCP categories of 2006 (from the official list of CT MD/DO, and the ones that responded to the survey) and 2015 (from the official list of CT MD/DO, and the ones that responded to the survey). The calculations for internal and external validity are presented in Chapter 4. The internal and external validity was measure in this study when answering Hypothesis questions. Quantitative studies have threats to internal, external, and construct validity, but they differ according to the type of quantitative research design employed in the study (Reio & Reio, 2016). Threats as they pertain to internal, external, and construct validity are discussed in the following sections.

Threats to Internal Validity

Threats to internal validity are participant or study factors that compromise the ability to state that dependent variable effects were the result of the independent variable (Patten & Newhart, 2017). If a cross-sectional study has high level of internal validity will be measure in great part from the strength of the interferences of the study (Carlson, & Morrison, 2009). Most threats to internal validity concern experimental or quasi-experimental studies, but there are threats to the internal validity of nonexperimental research studies as well (Patten & Newhart, 2017). These threats to the internal validity of nonexperimental research studies include the following: (a) bias due to confounding, (b) self-selection bias, and (c) social desirability response (Patten & Newhart, 2017).

Bias due to confounding is the inability to conclude that the dependent variable effects are a result of the independent variable due to an unmeasured extraneous variable that was significantly associated with the independent and dependent variables (Bergman, 2011). A potential source of confounding bias in this study is that physicians who participated in Johnson and Feder's (2010) study may have been recruited into this study. There were a total of 14 PCP surveys responses of PCPs who believed they took the survey of 2006. Some of these respondents were not 100%, but they marked in the question 10 of the 2015 KAP survey used in this study as *Yes*.

Self-selection or volunteer bias occurs in studies that rely on a convenience sample as opposed to a random selection of study participants; participants who volunteer for a study tend to differ in "relevant clinical characteristics" from those who do not participate (Tripepi, Jager, Dekker, & Zoccali, 2010, p. 98). The self-selection bias may

be minimized by focusing on a subset of physicians—namely, PCPs in the state of Connecticut—and utilizing random selection to obtain the study recruitment sample. Klabunde, Willis, and Casalino (2013) identified four primary reasons why physicians do not participate in survey studies: (a) "lack of time," (b) perceptions that the study or study questionnaire has little value or importance, (c) confidentiality and anonymity concerns, and (d) views that the study questionnaire is "biased or not providing a full range of responses" (p. 286). Physicians who complete and mail the study survey may have more time in their schedule to complete the questionnaire and more positive attitudes about the study and/or study questionnaire and may be more assured that confidentiality will be maintained in the study than physicians who do not participate.

Another threat to the internal validity of nonexperimental studies (as this cross-sectional study) is social desirability response bias, or when the study participant provides answers to survey items that are socially acceptable irrespective of the truth (Bowling, 2014). As this study was a cross-sectional study, I am as the main researcher did not manipulate the independent variables and the random method used helped to control the present of extraneous variables. Nonetheless, social desirability response bias is more likely to occur when participants are asked sensitive questions – for example, questions about their weight, physical and mental health problems, and attitudes toward coworkers and supervisors (Klabunde et al., 2013). This study used a cross-sectional study (nonexperimental) to examine the physician's (PCPS in the categories family, internal medicine, pediatricians) work-related KAPs regarding LD and CLD. While the

study survey inquiries about controversial topics, it does not ask about personal or sensitive topics. Consequently, social desirability bias may be lessened.

The informed consent process wherein participants are informed about study confidentiality may further help reduce social desirability bias (Bowling, 2014). Conclusively, social desirability on self-reporting can affect the outcomes in the study in regard to the external and internal validity (Althubaiti, 2016). Althubaiti (2016) stated that an excellent way to eliminate the threat of social desirability not to affect the internal validity of a study is to validate the survey instrument before the data collection stage when possible. However, validating the survey instrument before the data collection stage is not applicable for cross-sectional study and better for experimental studies.

Threats to External Validity

External validity pertains to the ability to generalize study results beyond the study sample to the population (or other samples), to different points in time, and to other settings (Bowling, 2014). The external validity of a study is highly dependent upon the degree to which the study participants represent the population (Bowling, 2014). Random sampling to obtain the recruitment pool of physicians may increase the external validity of the study, as it can focus on a specific population of physicians. However, results from this study cannot be generalized to PCPs licensed to practice in states other than Connecticut, to physicians who are not PCPs, or to other health care workers (e.g., nurse, physician assistants), regardless of their specialty area. Results from this study cannot be used to predict physician responses on the CT-KAP or be compared to other LD or CLD questionnaires.

Threats to Construct Validity

Construct validity indicates that the study instrument is measuring the constructs it is intended to measure (Patten & Newhart, 2017). The *inadequate explication of constructs*, or the incorrect or inexact operationalization of study constructs, is a threat to construct validity (Patten & Newhart, 2017). The threat of inadequate explication of constructs is minimized in this study by a valid and reliable questionnaire. This study may be influenced by the construct validity threat of *mono-method bias*, or the use of a single type (vs. multiple types) of measurement (Patten & Newhart, 2017), primarily because individual items are used to measure study constructs. Conclusions from results can only be drawn concerning items on the CT-KAP questionnaire 2015.

Ethical Procedures

In conducting this study, the I adhered to the ethical standards for research with human subjects. I sought IRB approval from the Walden University IRB before implementing any part of this study. The study and data collection were approved by the Walden University IRB. Walden University's approval number for this study was 06-05-18-023461. I applied the highest level of ethical considerations to maintain the integrity of this study, especially with regard to informed consent and participant privacy and confidentiality, the management of data, data analyses, and the disposal of study materials (i.e., the checked consent forms, paper questionnaires, and data sets).

Per ethical guidelines for human subjects research, I required that study participants read and sign an informed consent form. The informed consent form included information on (a) the goals and purpose of the study, (b) the role of the

participants in the study, (c) their rights as human subjects, and (d) benefits and risks of participating in the study. I included my contact information (i.e., email and phone number) as well as the contact information for the Walden University IRB administrator on the consent form to enable physicians who had questions or concerns about the study. Only three physicians called with some questions regarding the study, and I received no emails from any physicians. The physicians had to check *Yes* next to the informed consent form statement to indicate they consented to participate in the study. I discarded any returned surveys if the PCP did not provide consent by checking *Yes*.

The CT-KAP questionnaire did not contain any questions that could identify the physician. While I knew names and work addresses of the 1,726 physicians of whom I mailed the survey packet, it was impossible to ascertain who did or did not complete and return the CT-KAP survey. I stored survey forms with the checked consent question mark from the CT-Survey of 2015 (conducted in 2018) in a locked file cabinet in a home work office.

After I entered the data from the paper questionnaires into an SPSS 24.0 data set, the data were checked carefully to avoid errors in the data entry process. The data set was stored on a password-protected jump-drive (not a computer hard drive), which was kept in a locked file cabinet separate from the consent forms and paper questionnaires. The informed consent forms and surveys are to be shredded, and the jump-drive is to be destroyed five years after completion of this study. Data from the study were reported on the aggregate level in the dissertation and any subsequent journal articles or conference presentations.

Summary

This quantitative study utilized a nonexperimental, cross-sectional, comparative research design to determine if two groups of Connecticut PCPs significantly differ in their knowledge, diagnosis, and treatment of LD and CLD/PTLDS. CLD/PTLDS definition was stated in the cover letter of the consent letter, which was mailed with the survey for this study. Survey responses provided by 145 Connecticut PCPs who participated in this study were compared to the frequency, proportion, and mean level data reported by Johnson and Feder (2010) in their research with 285 Connecticut PCPs.

The methodological practices, including the study participant recruitment and data collection procedures, were aligned with the practices outlined by Johnson and Feder (2010). The study used the CT-KAP questionnaire that Johnson and Feder (2010) utilized. One of two added questions (11) asked whether the physician took part in the previous study and was included on the questionnaire.

Data from physicians who participated in the previous study were used. The information from this study was expected to update the PCPs positions on CLD/PTLDS (e.g., see Chapter 4 and 5) and help to inform the need for the development of CLD/PTLDS diagnosis and treatment protocols since it lacks a case definition, reliable laboratory tests, surveillance, and standardized treatment practices as most identified infectious diseases do (National Institute of Allergy and Infectious Diseases, 2019; Wharton et al., 1990). This chapter provided a comprehensive review of the study methodology. The following chapter focuses on the study findings.

Chapter 4: Results

Introduction

CLD/PTLDS may be a new health condition (Marzec et al., 2017) that lacks a case definition, reliable laboratory tests, an ICD-10 code, data collection and surveillance, and standardized treatment practices (Infectious Diseases Society of America, 2006; Lantos, 2015a, National Institute of Allergy and Infectious Diseases, 2019). Johnson and Feder (2010) addressed this confusion regarding CLD/PTLDS by examining the knowledge and practices of LD and CLD/PTLDS diagnosis and treatment in 285 Connecticut PCPs. However, there has not been assessment of Connecticut PCPs' KAPs regarding LD and CLD/PTLDS since Johnson and Feder's seminal study.

In this study, I utilized a nonexperimental, cross-sectional, and comparative research design to validate Johnson and Feder's (2010) study outcomes. The key element of this study was to determine whether there were any significant differences between the two groups of Connecticut PCPs (i.e., the 2006 and 2015 samples) regarding their KAP responses on the diagnosis, treatment, and management of LD and CLD/PTLDS. I followed the same participant recruitment and data collection procedures as Johnson and Feder. I also utilized their KAP survey, which can be validated by statistically similar findings between the two Connecticut PCP groups (using the CT DPH bases for 2006 and 2015). Any significant differences between the two PCP groups suggest a need to conduct studies to further explore PCPs' KAPs regarding CLD/PTLDS. The data obtained in this study from the PCP survey responses were compared to the data

published in 2010. For purpose of representation, the data in this study was adjusted to the factor of 1.97 (see Table 6).

This study had five research questions. The first research question acted as a validity check to determine if the proportions of PCP specialties across this and the 2006 study specialty were similar, which they were. The second research question focused on PCP knowledge differences on LD. The last three questions helped examine knowledge, attitude, and treatment differences regarding CLD/CLD. The research questions and hypotheses were as follows:

Research Question 1: Are the frequency distributions of the 2015 sample of Connecticut PCPs across the four primary practice specialty areas (i.e., family medicine, internal medicine, pediatrics, other) significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

$H_0$1: The frequency distributions of the 2015 sample of Connecticut PCPs across the four primary practice specialty areas (i.e., family medicine, internal medicine, pediatrics, other) are not significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

H_a1: The frequency distributions of the 2015 sample of Connecticut PCPs across the four primary practice specialty areas (i.e., family medicine, internal medicine, pediatrics, other) are significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

Research Question 2: Are the frequency distributions of the 2015 sample of Connecticut PCPs across the two knowledge of LD categories (i.e., know symptoms of

LD and feel comfortable diagnosing and treating LD vs. know LD but do not feel comfortable diagnosing and treating LD) significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

$H_0$2: The frequency distributions of the 2015 sample of Connecticut PCPs across the two knowledge of LD categories (know symptoms of LD and feel comfortable diagnosing and treating LD versus know LD but do not feel comfortable diagnosing and treating LD) are not significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

H_a2: The frequency distributions of the 2015 sample of Connecticut PCPs across the two knowledge of LD categories (know symptoms of LD and feel comfortable diagnosing and treating LD versus know LD but do not feel comfortable diagnosing and treating LD) are significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

Research Question 3: Are the frequency distributions of the 2015 sample of Connecticut PCPs across the three knowledge of CLD/PTLDS categories (do not believe CLD exists, do not feel comfortable diagnosing and treating CLD/PTLDS, and feel comfortable diagnosing and treating CLD/PTLDS) significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

$H_0$3: The frequency distributions of the 2015 sample of Connecticut PCPs across the three knowledge of CLD/PTLDS categories (do not believe CLD exists, do not feel comfortable diagnosing and treating CLD/PTLDS, and feel comfortable diagnosing and

treating CLD/PTLDS) are not significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

H_a3: The frequency distributions of the 2015 sample of Connecticut PCPs across the three knowledge of CLD/PTLDS categories (do not believe CLD/PTLDS exists, do not feel comfortable diagnosing and treating CLD/PTLDS, and feel comfortable diagnosing and treating CLD/PTLDS) are significantly different from the distributions of the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

Research Question 4: Is the estimated average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2015 sample of Connecticut PCPs significantly different from the average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

$H_0 4$: The estimated average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2015 sample of Connecticut PCPs is not significantly different from the average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

$H_a 4$: The estimated average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2015 sample of Connecticut PCPs is significantly different from the average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs.

Research Question 5: Is the estimated average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2015 sample of Connecticut

PCPs significantly different from the average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCPs?

$H_0$5: The estimated average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2015 sample of Connecticut PCPs is not significantly different from the average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCP.

H_a5: The estimated average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2015 sample of Connecticut PCPs is significantly different from the average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2006 (Johnson & Feder, 2010) sample of Connecticut PCP.

This chapter starts with information on the data collection procedures, the initial and final response rate, and the specialty description of the 145 PCPs in this study. As this is a validation of Johnson and Feder's (2010) study, the discussion is focused on the similarities and differences found in this study with regard to study sample sizes and response rates. This chapter also provides a comprehensive examination of the descriptive and inferential statistical findings in this study. The presentation and discussion of these findings regarding the research questions comprise most of the Results section. The chapter concludes with a summary.

Data Collection

The data collection period for this study was June 18, 2018 to August 20, 2018. The data collection methods aligned with those conducted by Johnson and Feder (2010; see Chapter 3). The two groups under examination are the 285 PCPs (from the PCP sample of 2006) study and the 145 PCPs (from the sample of PCP of 2015) in this study. As this was a validation study, it was important to replicate the same sampling frame used by Johnson and Feder's research methodology, including the use of same survey instrument. Two extra questions were added to assess if the participants took the same survey before (Question 10) and to follow Walden University IRB requirements related to consent (Question 11) any relation with the variables in this study (see Appendix A).

The first step of the study was to determine if the 2006 and 2015 samples of Connecticut PCPs similarly represented Connecticut PCPs, especially regarding specialty areas. The first step of the validity process was to determine if the 2006 and 2015 samples adequately represented the population of Connecticut MDs/Dos as listed in the CT DPH database. The CT DPH MD/DO database had contact information on 15,424 PCPs for 2006 and 17, 464 PCPs for 2015. I mailed out CT-KAP surveys from the total list of MD/DO that were preselected of 2006 and 2015 populations proportions (see Figures 6 and 7).

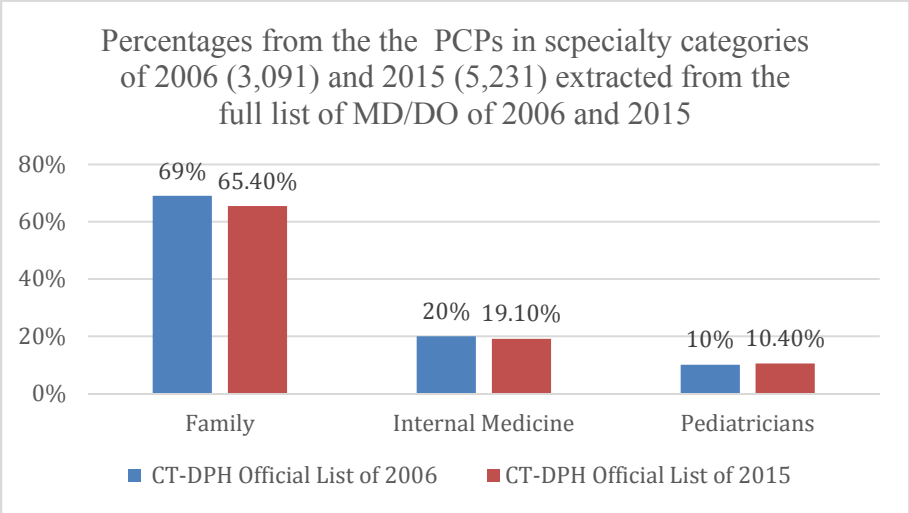

Figure 6. PCP Distributions from databases of CT DP MD/DO of 2006 and 2015. Database information was adapted from this study from the CT DPH List of Certified Medicare MD/DO. Database information were used to select the 33% of the PCPs in the list of 2006 (15,424) and in 2015 (15,464).

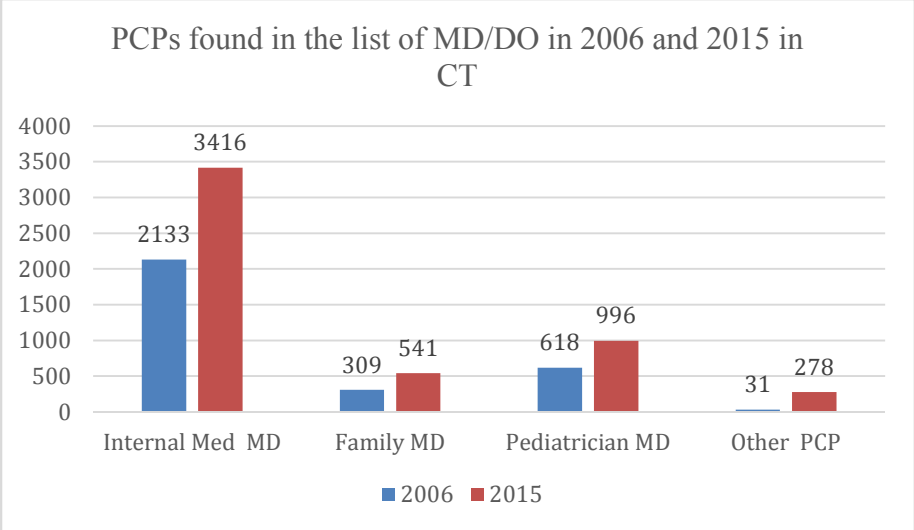

Figure 7. Frequency of specialty groups within the PCP category in distribution databases of MD/DO of 2006 and 2015. A Chi-square test result indicated that the two databases frequencies of 2006 and 2015 were not similar ($\chi 2$ (2) = 102, $p < .05$)

Therefore, the distribution of the three categories in year 2006 is not the same as the distribution in year 2015 taken from the original databases.

To further investigate the similarities and differences of categories, *z* tests were used to test which category differed between 2006 and 2015. Table 3 shows the results of the *z* test for each category. The proportions of internal medicine were not significantly difference between 2006 and 2015. Similarly, the proportions of family medicine were not significantly difference between 2006 and 2015. However, the proportions of pediatrician category were significantly different between the two years ($z = 2.492$, $p = 0.012$). Specifically, the percentage of pediatrician in 2006 (10.10%) was significantly less than that in 2015 (10.96%).

Table 3

Z Scores of Distributions from CT DPH Databases in 2006 and 2015

Category	*z*	*p*	Inference
Internal medicine	3.463	< 0.050	Significant difference
Family medicine	0.503	0.617	No significant difference
Pediatrician	1.062	0.289	No Significant difference
Other PCPs	10.05	< 0.050	Significant difference

Note. Pediatrician specialty and family were similar in the two population proportions of 2006 versus 2015, respectively ($z = 1.062$, $p = 0.289$; $z = 0.0503$, $p = 0.617$*). The internal medicine* specialty and the *other PCPs* specialty were no similar, respectively ($z = 3.463$, $p < 0.050$; $z = 10.05$, $p < 0.050$).

Therefore, it was found that the CT DPH MD/DO of 2015 was independent but not 100% similar to the CT DPH MD/DO of 2006. These findings are important to

answer the hypotheses, especially for Research Question 1 where the values to from the PCP population proportions were received in both surveys. Though the fact that the PCPs distributions or proportions were not the same in this validity study may have affected some results, the same protocols were followed to avoid bias (selection, information bias, and confounding; Kukull & Ganguli, 2012). It is important to maintain the correct association of the variables under the study to avoid errors in outcome frequencies exposures (Kukull & Ganguli, 2012). The selection of participants using randomization gave equal participants the capacity to take part in the study, which allows for inferences. One of the main criteria for sampling was to take the 33% of the group (PCPs in 2006 and PCPs in 2015). I also conducted a chi-square test to determine if this study was representative of the PCP sample or proportion found by Johnson and Feder (2010). The chi-square results indicated that the PCPs sample or proportion in this study was similar in terms of being representative of the PCPs of 2006. More of this discussion will be present when answering Research Question 1.

Tables 4 and 5 provide a review of the survey dissemination data, including the total number of potential participants, the selected number of potential participants, and the number and percentages (or proportions) of surveys sent and received in both studies. Johnson and Feder (2010) used the CT DPH MD/DO of 2006, whereas this study included the CT DPH MD/DO of 2015. The total number of Connecticut PCPs denoted in the CT DPH MD/DO of 2006 DPH list was 3,091, and the total number in the CT DPH MD/DO of 2015 list was 5,231. As per their research methodology, Johnson and Feder (2010) randomly selected 33% of the PCPs, which was 1,034. In this study, 33% of the

PCPS were also randomly selected, which was 1,726. Johnson and Feder reported an initial response rate of 39.1%, or 330 PCPs who completed and returned a study survey. In this study the initial response rate was 11.9% or 179 PCPs who returned a completed study survey. Therefore, the response rate was lower than the previous study done 10 years ago (see Table 4).

Table 4

Comparisons of Survey Dissemination Data

Category	PCP sample of 2006	PCP sample of 2015	*z*	*p*	Inference
Total number of the PCPs from the CT DPH database	15,424	17,464			
Number of PCPs on DPH-Certified list before randomization (original list).	3,091	5,231	20.64	< .001	Dissimilar (see Figure 8)
Randomly selected PCPs who were sent the study survey packet (33% of the original categorical list).	1,034 (33%)	1,726 (33%)	0.25	.804	Similar
Study survey packets returned to researcher due to wrong address.	191 (18.5%)	219 (12.7%)	4.06	< .001	Dissimilar
PCPs who received study survey packets.	843 (81.5%)	1,507 (87.3%)	3.75	< .001	Dissimilar
PCPS who returned study survey packets.	330 (39.1%)	179 (11.9%)	14.20	< .001	Dissimilar
Final population (proportion) of the number of PCP responses used for data analysis	285	145	1.59	0.118	Similar

Note. The data show the similarities of the two PCP responses received of the two PCP distributions of 2006 and 2015. The additional parameters presented in this table were closely similar in percentages (or proportions) based on the nonsignificance *z* scores.

The *z*-test procedure for testing the equality of two proportions was used to compare the responses to the survey between 2010 and 2015. The *z*-test statistic was computed as $z = (p1 - p2) / SE\ (p1\text{-}p2)$ where p1 is the estimate of the proportion in of 2006 (presented by Johnson & Feder, 2010) and p2 is the estimate of the proportion of

PCPs of 2015(in this study). *SE* (p1-p2) is the standard error of the difference in two proportions and can be estimated as: *SE* (p1-p2) = $\sqrt{p\ (1-p)(\frac{1}{n1}+\frac{1}{n2})}$ where n1, and n2 are sample sizes in 2006 and 2015, respectively.

The tests were performed at .05 level of significance which implies that the null hypothesis of equality of proportions will be rejected if the p value of the test is less than .05. The percentage of randomly selected PCPs of 2006 survey who were sent the study survey packet was 33.5% and it was very similar with the PCPs sample of 2015 (33.2%). Results of *z* test showed no significant difference in percentage of randomly selected PCPs who were sent the study packet between 2006 and 2015 ($z = 0.427$, $p = .669$). The percentage of study survey packets returned to the researcher due to wrong address was 18.5% in 2010 and the corresponding percentage in 2015 was (12.7%). Results of *z* test showed a significant difference in the two percentages between 2006 and 2015 ($z = 4.198$, $p < .001$). Specifically, the percentage of study survey packets returned to the researcher due to wrong address was significantly higher in 2006 sample compared with the 2015 sample (the difference in the proportions was 5.8%, 95% confidence interval for difference in percentage was 3.1% to 8.6% indicating that at 95% confidence, the difference in the percentage of survey packets returned due to wrong address was between 3.1% to 8.6%).

The percentage of randomly selected PCPs who received the survey packets was 81.5% od 2006 sample and the corresponding percentage of the 2015 sample was 87.3%. Results of *z* test showed a significant difference between the two proportions in 2010 and 2015 ($z = 3.748$, $p < .001$). Specifically, the proportion of randomly selected PCPs who

received the survey packets was significantly lower in 2006 sample compared with 2015 sample. The difference in the two proportions was – 5.3%, 95% confidence interval of the difference in proportions was -8.0% to -2.5% indicating that at 95% confidence, the difference in the proportion of randomly selected PCPs who received the survey packets in 2006 sample compared with the 2015 sample is between 2% to 8%.

The percentage of PCPs who returned the survey packets was 39.1% of 2006 sample and the corresponding percentage of 2015 sample was 11.9%. Results of *z* test showed a significant difference in the proportions between 2006 and 2015 samples ($z = 14.200$, $p < .001$). Specifically, the proportion of PCPs who returned the survey packets of 2006 sample was higher compared with that in 2015 sample. The difference in the proportions was 21.6%, 95% confidence interval for difference in proportions was 18.6% to 24.6% indicating that at 95% confidence, the difference in the proportion of randomly selected PCPs who returned the survey packets in 2006 sample compared with that in 2015 sample was between 18.6% to 24.6%. More surveys were returned in this study due to wrong addresses than the one of 2006. This fact implies in this study the percent of nonresponse may be greater than in the previous study. Additionally, the facts of having more survey returned because wrong address may imply that fact maybe a greater number of PCPs moved out and maybe retired. Returned survey can increase the percent of error in regard to the margin error in this study and decrease the reliability.

Table 5

Comparison of Surveys Received and Discarded

Category	Johnson & Feder (PCPs 2006 sample)	Current Study - 2015 PCPs sample	χ^2	*p*	Inference
Number of Returned Study Surveys. (Similar).	330	179	1.509	.219	
Number of Discarded Surveys	45 (13.6%)	34 (19%)			
Rationale for Discarding Survey Data*			*Z*	*p*	
Physician who completed survey was not a PCP.	20 (44.4%)	16 (47.0 %)	0.231	.817	Similar
PCP reported he/she was no longer in practice	10 (22.2%)	10 (29.4 %)	0.727	.233	Similar
PCP had not diagnosed patients within the last 3 years.	5 (11.1%)	3 (8.8%)	0.334	.739	Similar
Undecipherable survey responses.	8 (17.8%)	1 (2.9%)	2.055	.039	Dissimilar
Health care provider other than PCP answered survey.	2 (4.4%)	0 (0.0%)	1.245	.213	Similar

Note. *Percentages (or proportions) are derived from the respective 45 or 34 discarded surveys. The 0.0% values could not be used for *z* tests using SPSS. Nonetheless, it was calculated here with the value that was no 0 to compensate the analysis.

As illustrated in Table 5, A Chi-square (χ^2) test of independence was used to test the difference in distribution of surveys received and discarded for 2006 versus 2015 PCPs. In the study by Johnson and Feder, (2010) 86.4% of surveys were returned and 13.6% were discarded. In the current study, 81% of surveys were returned and 19% were discarded. Results of the Chi-square (χ^2) test for independence showed that there was no significant difference in the distribution of surveys returned or discarded between the two samples (2006 and 2015) ($\chi 2$ (1) = 1.509, p = .219). *Z* tests for testing the equality of two proportions was also used to compare which rationale of discarding the surveys was significantly different between 2006 sample and 2015 sample. *Z*-test statistic was computed as Z = (p1 – p2) / SE (p1-p2) where p1 is the estimate of the proportion of 2006 sample and p2 is the estimate of the proportion in 2015 sample. SE (p1-p2) is the standard error of the difference in two sample proportions and can be computed using the following formulae: SE (p1-p2) = $\sqrt{p\ (1-p)(\frac{1}{n1}+\frac{1}{n2})}$ where n1, and n2 are the sample sizes in 2006 sample and 2015 sample , respectively. This test was carried out at .05 level of significance which implies that the null hypothesis of equality of proportions will be rejected if the p value of the test is less than .05.

The percentage of surveys discarded because the physician who completed the survey was not a PCP was 44.4% in the 2006 sample and the corresponding percentage in the 2015 sample that was 47.1%. Results of the *z* test indicated no significant difference between the two proportions ($z = 0.231$, $p = .817$).

The percentage of surveys discarded because the PCP reported he/she was no longer in practice was 22.2% for the 2006 sample and the corresponding percentage in

2015 sample was 29.4%. Results of the *z* test indicated no significant difference between the two proportions ($z = 0.727$, $p = .233$). This may suggest that medical doctors may had changed their medical specialty from PCPs to other types of medical doctors (i.e. in this study in the exclusion list two PCPs stated they were now cardiologists, others stated they were neurologists, etc.). This fact may imply LD and CLD are terms more popular among doctors and patients presently than in 2006 (i.e. as the CDC had documented how LD cases had increased after 2006; see Figure 3).

The percentage of surveys discarded because the PCP had not diagnosed the patients in the last three years was 11.1% in the 2006 sample and the corresponding percentage in the 2015 sample was 8.8%. Results of the *z* test indicated no significant difference between the two proportions ($z = 0.334$, $p = .739$).

The percentage of surveys discarded because of undecipherable survey responses was 17.8% in the 2006 sample and the corresponding percentage in 2015 sample was 2.9%. Results of the *z* test showed a significant difference between the two proportions ($z = 2.055$, $p = .039$). Specifically, the proportion of surveys discarded because of undecipherable survey responses was significantly higher in the 2006 sample compared with 2015 sample. The difference between the two years was 14.8%, 95% confidence interval for difference was 0.7% to 28.9% indicating that at 95% CI, the difference in percentage of surveys discarded because of undecipherable survey responses between 2006 sample and 2015 sample was between 0.7% to 28.9%.

The percentage of surveys discarded because the health care provider other than PCP answered the survey was 4.4% in 2006 sample and the corresponding percentage in

2015 sample was 0%. Results of the *z* test indicated no significant difference between the two proportions ($z = 1.245$, $p = .213$).

The percentage of surveys discarded because the PCP did not provide informed consent was 0%% for the 2006 sample, and the corresponding percentage in 2015 sample was 11.8%. Results of the *z* test showed a significant difference between the two proportions ($z = 2.361$, $p = .018$). Specifically, the proportion of surveys discarded because PCP did not provide informed consent was significantly lesser in 2006 sample compared with 2015 sample. The difference between the two samples was 11.8%, (95% CI: -21.53% to -2.0% at 95% CI, the difference in percentage of surveys discarded because the PCP did not provide informed consent for the 2006 versus and 2015 sample was between -21.53% to -2.0%.

For each research question, a post hoc power analysis was conducted after the analysis to determinate the degree of probability that the results could be said to be true. The post hoc effect size and power are reported in this study in those research questions needed.

Descriptive statistics: PCP specialty. Table 6 provides the PCP specialty group frequencies and percentages, and Figure 8 details the frequencies per PCP specialty category. The largest group of PCPs in this study self-identified as internists ($n = 63$, 43.4%). Forty-eight (33.1%) reported that they were pediatricians, while 28 (19.3%) were family physicians. Six (4.1%) reported having another primary care specialty (i.e., all six reported being in emergency medicine). The data was adjusted to present the representation of 2015 in contrast with 2006 population frequencies. The 2006 PCP

frequencies and percentages (or proportions) of 2006 specialty of $n = 285$ from the study done by Johnson and Feder (2010) are presented in Table 7.

Table 6

Frequencies for Primary Care Physician Specialties in 2015

PCP Specialty	Frequency (*n*)	2015 Non-adjusted proportion (%)	2015 Adjusted Frequency (%)	2015 Adjusted Proportion (%)	CT DPH MD/DO) of 2015(%)
Internist	63	43.4%	124	43.4%	65.4%
Pediatrician	48	33.2%	94	33.2%	19.1%
Family physician	28	19.3%	55	19.3%	10.4%
Other (i.e., Emergency Physicians)	6	4.1%	12	4.1%	5.1%

Note. The 2015 PCPs of 2015 in the categories presented here internist, pediatrician, family physician, pediatrician and other were adjusted to present the representation status of it in this study. The percentages (or proportions) did not change, but the frequencies of PCPs did. The respective frequencies presented here from 2015 data were 63, 48,28, and 6. When the data was adjusted by a factor of 1.97 (285/145) the frequencies of PCPs in this study are 124, 94, 55, and 12. Samples were similar after adjusted Samples had different frequencies (X^2) $= 0.0017$, $p < 00001$, no significant at $p < 0.05$. Therefore, the it may limit generalizations and the external validity of the data found in this study.

Table 7

Frequencies for Primary Care Physician Specialties in 2006

PCP Specialty	Frequency (*n*) 2006 study	Proportion (%) 2006 study	CT DPH MD/DO) of 2006(%)
Internist	113	39.6	69*
Pediatrician	107	37.5	20*
Family physician	57	20	10*
Other (i.e., Emergency Physicians)	8	2.9	1*

Note. * The whole data of MD/DO was not available to me. Therefore, estimation was adapted from figures from three sources (a) http://www.publichealth.uconn.edu/assets/primarycarereport_02_09.pdf, (b) https://portal.ct.gov/DPH/Practitioner-Licensing--Investigations/PLIS/Licensing-Statistics, and (c) data from the Johnson and Feder (2010). Therefore, it was found that samples had different frequencies ($X^2 = 2706$, $p < 00001$, significant at $p < 0.05$. Thus the 2006 population proportion who participated in Johnson and Feder study ($n = 285$) was not similar to the list of 2006 CT Md/DO of 2006. Therefore, the external validity is limited within these populations.

Comparison of PCP specialty groups between the PCPs in this study and the 285 PCPs from Johnson and Feder (2010) study is the topic of the first research question (see Figure 8). The percentages (or proportions) of PCPs by specialty were compared to the percentage of the 5,231 PCPs in the CT DPH (2015) database of active registered medical doctors (including PCPs) in Connecticut (see Table 6). The data in Table 6 establish the true state of representation in this study when comparing the PCP data

obtained with the original CT DPH MD/DO of 2015. The CT DPH MD/DO keep changes within less than 20% (see Appendix D).

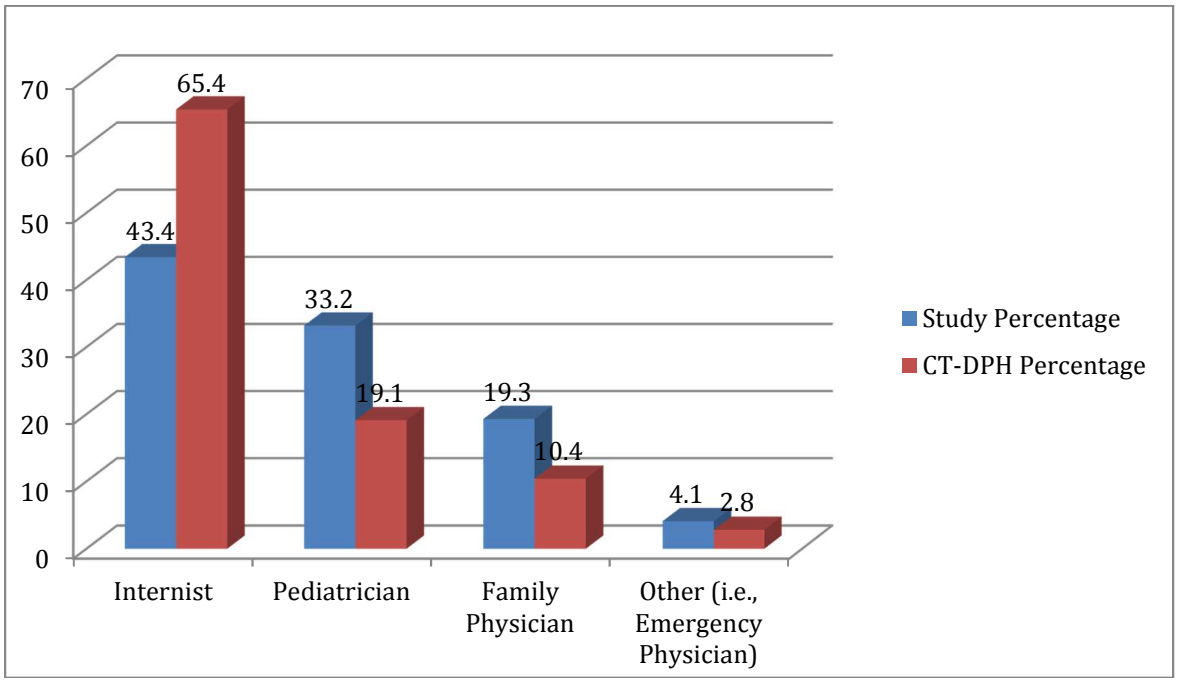

Figure 8. Primary care physician specialty category frequencies from 2015 survey responses versus CT DPH List of Certified MD/Surgeons. The PCPs distribution in this study and the CT DPH (MD/DO of PCPs) were not similar. Therefore, the it may limit generalizations and the external validity of the data found in this study. The x-axis is the PCPs categories of 2015. The y-axis is the percentages of those PCPs categories.

Results

This section contains descriptive and inferential findings from the present study and opens with a summary of key descriptive statistics. The remaining sections are devoted to the statistical analyses and findings to address the study's questions. The data obtained did not require adjustments. Because this was a validation study, it was

important to ensure that the 2006 and 2015 samples were equivalent. As presented in Figure 9, the two groups of PCPs had similar sampling frames. The *z* test was not significant (z =1.50, p = 0.118). There were no significant differences between the sample proportion of 2006 (n = 285 PCPs) and sample proportion of 2015 (n = 145 PCPs; see Figure 9).

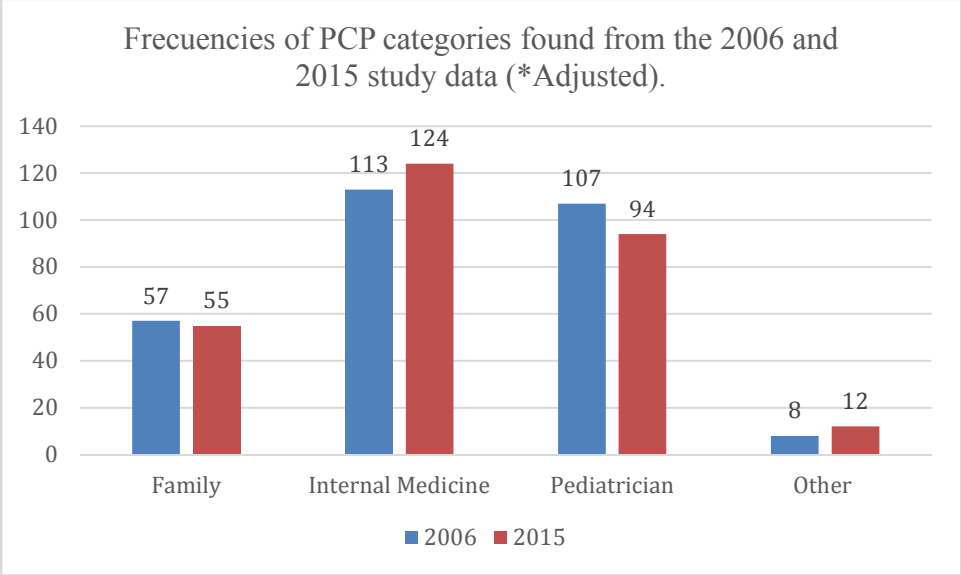

Figure 9. Data of primary care physician proportions from Johnson and Feder (2010). The proportions from Johnson and Feder had a population proportion of 285, and this study had 145 PCP responses. After adjustment of the data was done with a factor of 1.97, the frequencies of 2006 PCP were similar to the 2015 PCP obtained in this study. Taking the responses more in detail when looking to the category data, the data frequencies showed to be similar. (X^2 = 2.1871), p-value 0.534502. The result is *not* significant at $p < .05$. The null hypothesis is accepted.

Prior to hypothesis testing, descriptive statistics were computed for the five research questions in this study. Of the 145 PCPs in this study, 79.3 (n = 115) stated they knew LD symptoms and felt comfortable diagnosing LD. Almost half (n = 70, 48.3%) of the PCPs reported that they do not believe CLD/PTLDS exists. A third (n = 44, 30.3%) reported that they believe CLD/PTLDS may exist but are not comfortable diagnosing CLD/PTLDS. The smallest group of PCPs (n = 31, 21.4%) reported feeling comfortable diagnosing and treating CLD/PTLDS. Due to the substantial differences in responses for all three groups, which resulted in high variance and substantial skewness, the frequencies and proportions of responses are reported (see Figures10 through 13).

Results for Physicians who Believe Chronic Lyme Disease Does Not Exist

Of the 70 PCPs who reported not believing that CLD/PTLDS exists, 69 (98.6%) reported the number estimated patients they diagnosed and treated for LD. The mean number of patients diagnosed and treated for LD was M = 28.00 (Md = 15.00, SD = 42.09). Figure 11 presents (as an asymmetrical bar chart that was converted) in a box plot of the estimated number of patients (cases) diagnosed with and treated for LD in the past 3 years greatly differed across the individual PCPs who believed CLD/PTLDS does not exist with a range from no patients (cases) to 300 patients (cases). See Figure 10.

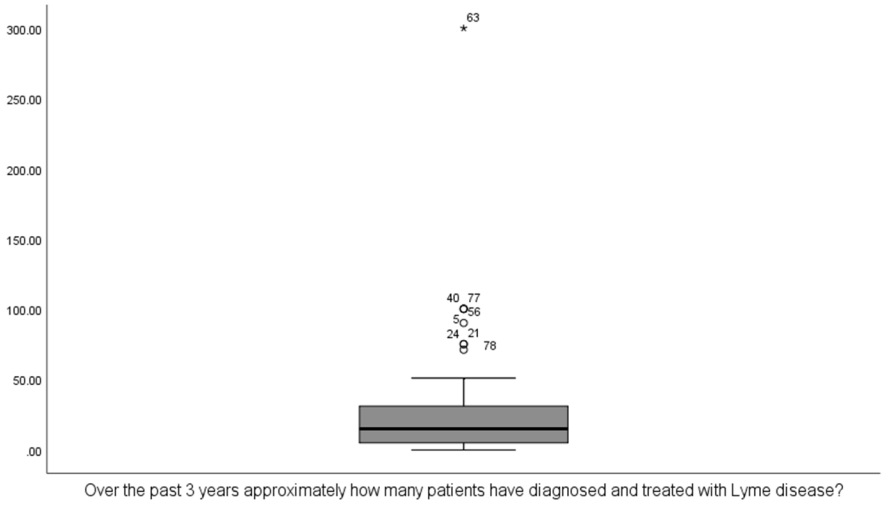

Figure 10. Boxplot of number of estimated patients (cases) diagnosed with and treated for Lyme disease in past 3 years. Based on *n* = 69 PCPs who stated they did not believe CLD/PTLDS exists. Case #5 through Case #78 had between 50 and 100 patients diagnosed and treated for LD, while Case #63 had 300 patients diagnosed and treated for LD in the past 3 years. Scaling is asymmetric.

In Johnson and Feder's (2010) study, results showed that PCPs diagnosed a total of 11,970 cases for LD. Sixty-nine (24.2%) PCPs estimated they had diagnosed and treated 10 to 20 patients for LD in the past 3 years. Six (8.6%) PCPs estimated having diagnosed and treated no patients for LD in the past 3 years. Five (7.1%) PCPs each estimated having diagnosed and treated five or 25 patients for LD in the past 3 years. There were between one and three PCPs, who estimated the numbers of patients they had diagnosed with and treated for LD. Moreover, in the 2006 sample, the two (2) PCPs who believed CLD/PTLDS existed, had a mean average of 3.1 patients.

Results for Physicians who were Unsure and Uncomfortable Diagnosing Chronic Lyme Disease

All 44 PCPs who felt uncomfortable diagnosing CLD estimated the number of patients they treated for LD in the past 3 years. The mean number of patients diagnosed and treated for LD for these 44 PCPs was $M = 18.86$ ($Md = 10.00$, $SD = 23.19$). Figure 13 presents the estimated number of patients diagnosed and treated for LD for these 44 PCPs. The estimated number of patients (cases) diagnosed with and treated for LD in the past 3 years by the 44 PCPs who were unsure that CLD exists and felt uncomfortable diagnosing CLD greatly ranged from no patients (cases) to 100 patients (cases). The largest groups of PCPs were eight (18.2%) and estimated having diagnosed and treated no patients for LD. The next largest groups of PCPs were 5 (11.4%) and estimated having diagnosed and treated 5 or 20 patients for LD in the past 3 years. Four (9.1%) PCPS estimated having diagnosed and treated 30 patients for LD in the past 3 years. There were between 1 and 3 PCPs who estimated the numbers of patients they had diagnosed with and treated for LD. See Figure 11.

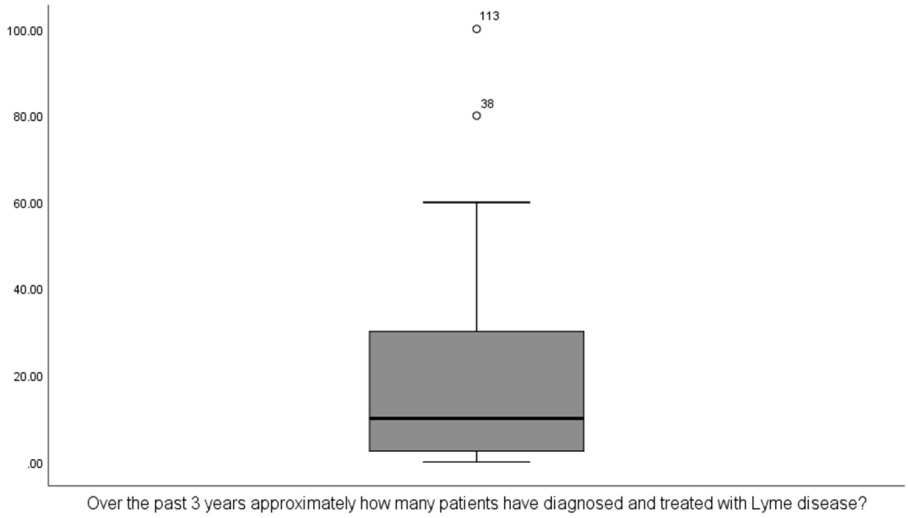

Figure 11. Boxplot of the number of patients estimated to have been diagnosed with and treated for LD in past 3 years. Based on $n = 44$ PCPs who stated they believe CLD may exist but felt uncomfortable diagnosing CLD. Case #38 had 80 patients diagnosed and treated for LD while Case # 113 had 100 patients diagnosed and treated for LD in the past 3 years.

Results for Physicians who were Comfortable Diagnosing and Treating Chronic Lyme Disease

Of the 31 PCPs who reported feeling comfortable diagnosing and treating patients for CLD, 28 (90.3%) provided the estimated number of patients they diagnosed as having LD in the past three years. The mean number of patients diagnosed and treated for LD for these 28 PCPs was $M = 26.75$ ($Md = 20.00$, $SD = 23.47$). Figure 14 presents the frequencies of the number of patients estimated to have been diagnosed and treated for LD, as reported by these 28 PCPs who responded. Responses as to the number of patients (cases) estimated to have been diagnosed with and treated for CLD/PTLDS in the past 3

years ranged from no patients (cases) to 100 patients (cases). Three (9.7%) of the PCPs each estimated having diagnosed and treated 20 or 30 patients for LD in the past 3 years. Between 1 and 2 PCPs each respectively estimated having diagnosed and treated between 0 and 100 patients for LD in the past 3 years.

Figure 12. Boxplot for estimated number of patients (cases) diagnosed with and treated for LD in past 3 years. Based on $n = 28$ PCPs who stated they diagnosed and treated patients for LD. Case #138 had 100 patients diagnosed with and treated for LD in past 3 years.

The estimated number of patients diagnosed with and treated for CLD in the past 3 years were also calculated for the group of 31 PCPs who stated they diagnosed and treated patients for CLD/PTLDS. All 31 PCPs that provided an answer; the mean number of patients diagnosed and treated for CLD/PTLDS in the past three years was $M = 5.84$ ($Md = 3.00$, $SD = 10.15$). Figure 15 provides the frequencies of patients diagnosed and treated for CLD/PTLDS in the past three years. The range of estimated patients diagnosed with and treated for CLD/PTLDS in the past 3 years was from 0 to 51 patients.

The largest group was the 7 (22.6%) PCPs who estimated diagnosing 0 or 3 patients for CLD/PTLDS in the past three years, respectively. Four (12.9%) PCPs estimated having diagnosed and treated patient for CLD/PTLDS within the past three years. Three (9.7%) PCPs estimated diagnosing and treating 5 patients for CLD/PTLDS in the past three years. Two (6.5%) PCPs estimated diagnosing and treating 2 or 10 patients each for CLD/PTLDS in the past three years. One PCP each estimated having diagnosed and treated 4, 10, 11, or 51 patients for CLD/PTLDS in the past 3 years.

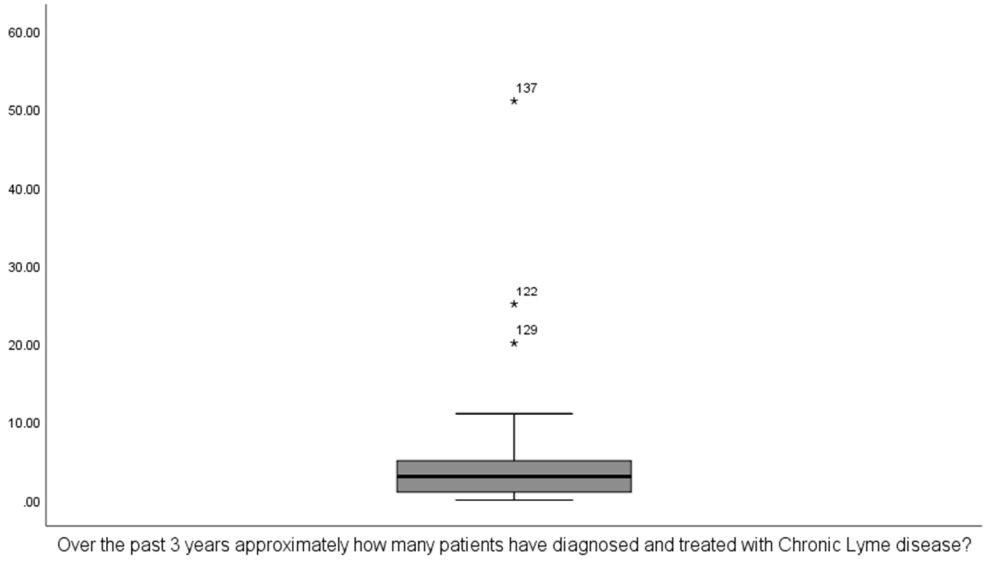

Figure 13. Box plot of estimated number of patients (cases) diagnosed with and treated for CLD/PTLDS in past 3 years. Based on $n = 31$ PCPs who stated they diagnosed and treated patients for CLD/PTLDS. Case #129 had 20 patients, Case #122 had 25 patients, and Case #137 had 51 patients diagnosed with and treated for CLD/PTLDs in the past three years.

Dependent Variable Descriptive Statistics

This study had two dependent variables: the estimated number of patients diagnosed and treated for CLD/PTLDS in the past three years and the estimated course of antibiotic treatment (in weeks), as reported by the PCPs who felt comfortable diagnosing CLD/PTLDS. Table 8 provides the descriptive statistics for the 31 PCPs who reported feeling comfortable diagnosing and treating patients for CLD/PTLDS. One (3.2%) PCP estimated diagnosing and treating 51 patients for CLD/PTLDS in the past 3 years (i.e., the maximum score). Twenty-four of the 31 (77.4%) PCPs who reported feeling comfortable diagnosing and treating CLD/PTLDS answered the question about average antibiotic treatment (in weeks). The descriptive statistics for the course of antibiotic treatment (in weeks) dependent variable were recorded (Table 8). The estimated average (mean) course of antibiotic treatment was 12.33 weeks (*Md* = 8.00, *SD* = 12.34). Two (6.5%) PCPs reported an antibiotic treatment course of no weeks (i.e., the lowest value), and one PCP (3.2%) reported an antibiotic treatment course of 52 weeks (i.e., the highest value).

Table 8

Estimated Number of Patients Diagnosed and Treated by Primary Care Physicians who Reported Feeling Comfortable Diagnosing and Treating Chronic Lyme Disease

	n	*M*	*Md*	*SD*	*Min*	*Max*
Number of patients diagnosed and treated for CLD	31	5.84	3.00	10.15	0.00	51.00
Course of antibiotic treatment (in weeks)	24	12.33	8.00	12.34	0.00	52.00

Testing of the Normality Assumption

An assumption of the independent samples t-test is that the data is normally distributed. Normality – must show a normal distribution= around the mean (Kim, 2013). Samples, $Z_{skewness}$ values, Kolmogorov-Smirnov (K-S) tests, and boxplots were calculated to test the normality assumption for the variables of CLD/PTLDS case numbers and course of antibiotic treatment (in weeks). $Z_{skewness}$ values were computed by dividing the variable skewness value by the skewness standard error (see Table 9). The number of patients diagnosed and treated for CLD/PTLDS in the past three years had a $z_{skewness}$ value of 8.10, indicating a violation of the normality assumption. Thus, the normality assumption was not met and for the analysis of this data it was required to conduct a non-parametric testing. The significant K-S test, shown in Table 9, provided confirmation of variable skewness and resultant non-normality for the course of antibiotic treatment (in weeks) variables. The assumption of normality was met. The $z_{skewness}$ value for the antibiotic treatment course variable was 3.57, also indicative of skewness.

Table 9

Test Values for Estimated Number of Patients Diagnosed and Treated by Primary Care Physicians Comfortable Diagnosing and Treating Chronic Lyme Disease

	N	$Z_{skewness}$	*K-S Value (p)*
Number of patients diagnosed and treated for CLD	31	8.10	0.32 (p = .001)
Course of antibiotic treatment (in weeks)	24	3.57	0.22 (p = .004)

The SPSS unusual cases function indicated that the number of patients diagnosed and treated for CLD/PTLDS variable had three outlier cases with values of 20, 25, and 51, respectively. Figure 14 presents the boxplot with outliers. Note that the case ID is presented in the boxplot not the actual variable score. SPSS output does not give the outlier values, but it does provide ID numbers of the cases. Case 15 had a score of 20, case 8 had a score of 25, and case 23 had a score of 51. The SPSS unusual cases function indicated that the course of antibiotic treatment (in weeks) variable had one outlier case. Figure 15 presents the boxplot with outliers. Case 123 had a score of 52 weeks.

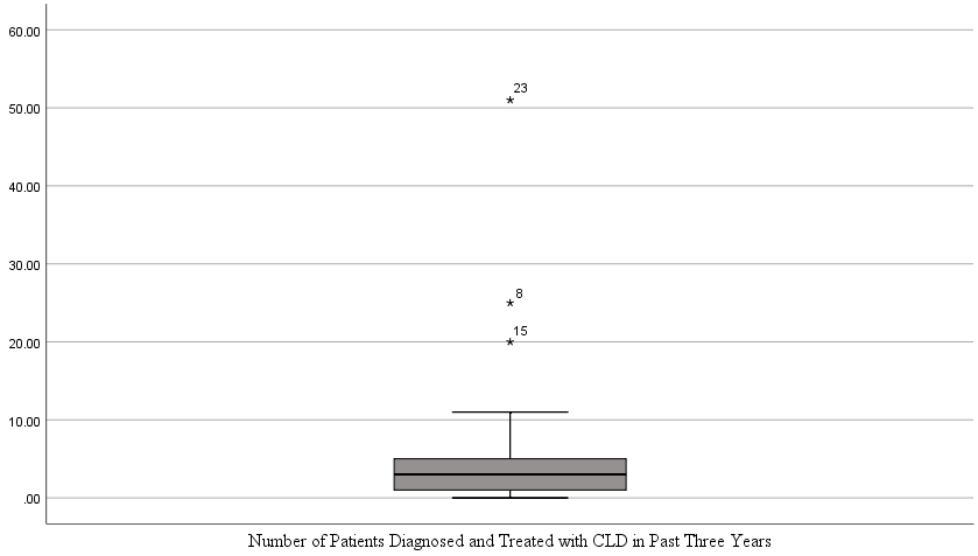

Figure 14. Course of antibiotic treatment in weeks (n = 24). The horizontal line in the box interior represents the estimated median. Outlier 123 represents the score of 52 weeks.

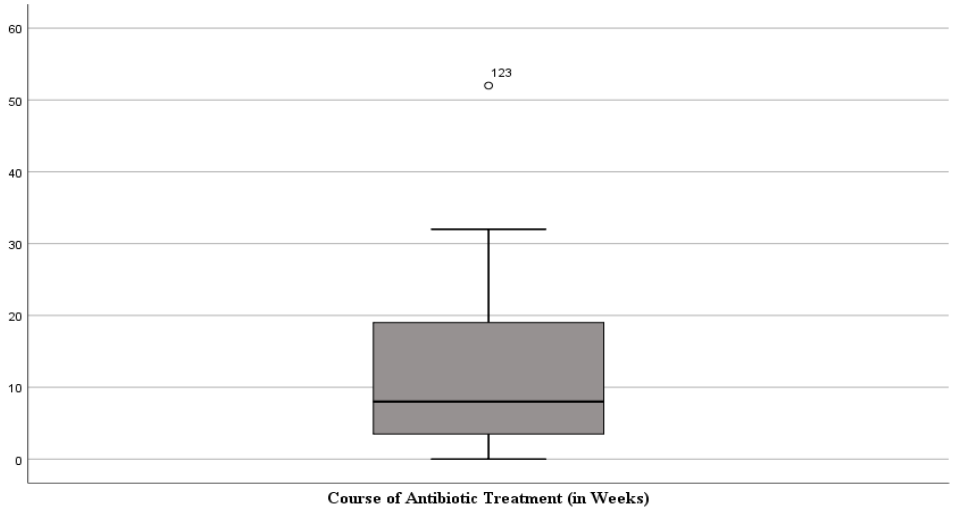

Figure 15. Course of antibiotic treatment in weeks (n = 24). The horizontal line in the box interior represents the estimated median. Outlier 123 represents the score of 52 weeks.

The data collected in this study yielded a non-normal distribution of values for the estimated number of course of antibiotic treatment PCPs used with patients with CLD from the distribution of PCPs in 2018. Since the estimated samples mean came from a small sample size, it was necessary to eliminate outliers to make an estimated sample mean closer to the true value.

The removal of the three outliers for the number of patients diagnosed and treated for CLD/PTLDS variable reduced the $z_{skewness}$ value to 2.93, which was lower than the critical value of 3.00. The removal of the outliers may result in the loss of data points in this study. It will also affect the mean and median values. When one is removing higher values, like it is the case here, the mean and the media will decrease, but the mean will decrease by more than the media. The K-S test remained significant (K-S (28) = 0.219, p =0.001). The removal of the one outlier for the course of antibiotic treatment (in weeks)

reduced the $z_{skewness}$ value to 1.87, which was below the $z_{skewness}$ critical value of 3.00. Moreover, the K-S test was marginally significant, (K-S (23) = 0.18, p = 0.054). The boxplot indicated no outliers for the number of patients diagnosed and treated for CLD/PTLDS variable (see Figures 16 & 17).

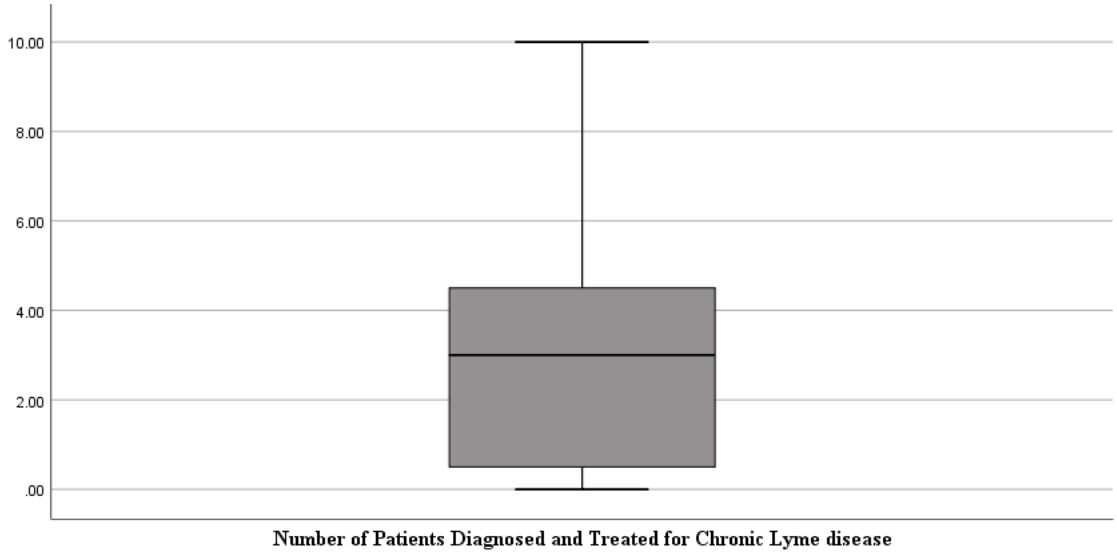

Figure 16. Number of patients diagnosed and treated for CLD/PTLDS (n = 28). The boxplot indicated no outliers for the course of antibiotic treatment (in weeks) variable, as seen in Figure 17.

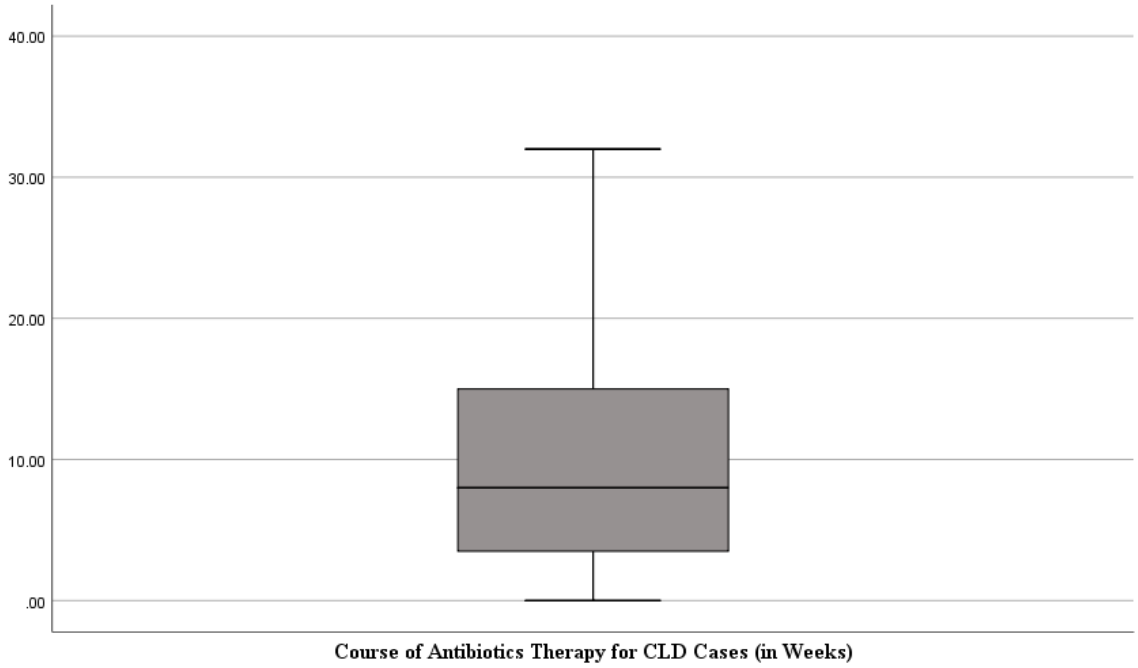

Figure 17. Course of antibiotic treatment in weeks (n = 23). The exclusion of outliers may cause the loss of data and may limited the finding in this study since the survey response was low. Results need to be taking with caution.

Descriptive statistics for the estimated number of patients diagnosed and treated for CLD/PTLDS and course of antibiotic treatment (in weeks) variables with outliers removed are presented in Table 10. The estimated average (mean) number of patients diagnosed and treated for CLD/PTLDS was M = 3.04 (SD = 3.13), which is very similar to the median value of Md = 3.00. The estimated number of patients diagnosed and treated for CLD/PTLDS ranged from 0 to 11. The estimated course of antibiotic treatment variable mean was M = 10.61 (Md = 8.00, SD = 9.19). Antibiotic treatment

course ranged from 0 to 32 weeks. The non-skewed dependable variables with mean scores of 3.04 and 10.61 were used for hypothesis testing of Research Questions 4 and 5.

Table 10

Descriptive Statistics for Estimated Number of Patients Diagnosed and Treated with Outliers Removed

	n	*M*	*Md*	*SD*	*Min*	*Max*
Number of patients diagnosed and treated for CLD	28	3.04	3.00	3.13	0.00	11.00
Course of antibiotic treatment (in weeks)	23	10.61	8.00	9.19	0.00	32.00

Answers to the Research Questions

Research Question 1

The first research question posed in this study was as follows: "Are the frequency distributions of the 2015 sample of Connecticut PCPs across the four primary practice specialty areas (i.e., family medicine, internal medicine, pediatrics, other) significantly different from the distributions of the 2006 sample of Connecticut PCPs?"

In this study, the sample was comprised of 28 (19.3%) family physicians, 63 (43.4%) internists, 48 (33.1%) pediatricians, and 6 (4.1%) other PCPs (i.e., emergency medicine). As this study treated Johnson and Feder's (2010) 2006 physician data as population data, a Chi-Square (χ^2) goodness-of-fit test was conducted to address the first research question. A Chi-square (χ^2) goodness-of-fit test computes the expected sample frequencies (numbers) per variable categories based on population category proportions and compares these computed frequencies to the actual observed sample group

frequencies (Sharpe, 2015). The expected frequencies (*n*s) denoted in the following chi-square table represent the expected number of participants per category based on the 2006 and 2015 survey proportions. A non-significant chi-square value ($p > 0.05$) indicates that the sample frequency distributions are similar between the 2006 sample (done in 2008) and the 2015 sample (done in 2018).

The chi-square (χ^2) test conducted for Research Question 1 was not significant ($\chi^2(3, n = 145) = 1.41, p = .703$) Therefore, the null hypothesis was accepted since there were no significant differences and the alternative hypothesis was rejected. The actual observed PCP group specialty proportions were similar for the 2006 and 2015 samples (see Table 11). This research question was unique, as it was the only one in the study in which the null hypothesis failed to be rejected. The non-significant findings indicate that the 2015 PCP specialty proportional distribution in this study was similar to the historical data of 2006 (Johnson & Feder, 2010).

Table 11

Chi-Square Test for Primary Care Physician Frequencies in 2006 Versus 2015

		Observed (n)	*Expected (n*)*
Family Physician		28	29
Internist		63	59
Pediatrician		48	52
Other PCP		6	5
Chi-Square (χ^2)	1.410		
Df	3		
Significance (*p*)	.703		

Note. PCP Categories for the 2006 and 2015 samples were similar

Research Question 2

The second research question pertained specifically to LD: "Are the frequency distributions of the 2015 sample of Connecticut PCPs among the two knowledge of LD categories (i.e., know symptoms of LD and feel comfortable diagnosing and treating LD vs. know LD but do not feel comfortable diagnosing and treating LD) significantly different from the distributions of the 2006 sample of Connecticut PCPs?" In the 2006 study, 282 (98.9%) of PCPs reported knowing symptoms of LD and feeling comfortable diagnosing and treating LD while 3 (1.1%) PCPs reported knowing LD symptoms but not feeling comfortable diagnosing LD. The frequencies of PCPs per knowledge of LD categories are presented in Figure 18 and Table 12.

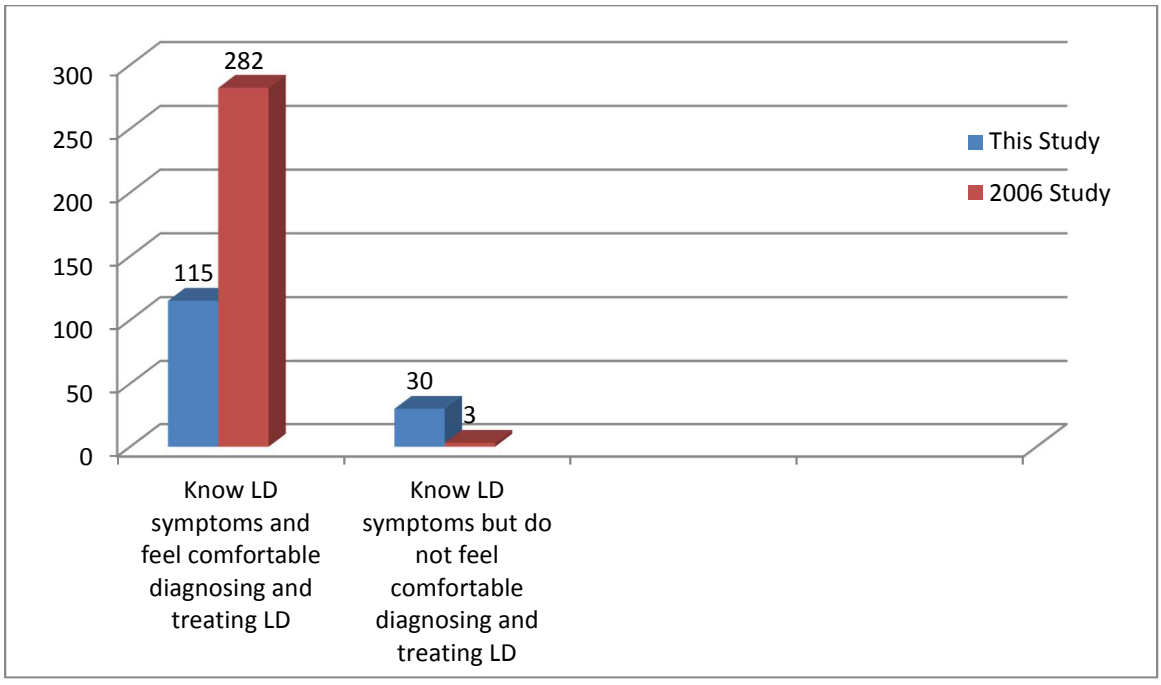

Figure 18. Frequencies of primary care physicians per knowledge of Lyme disease categories in this and the 2006 study. Chi-square (χ^2) results were significant (χ^2 (df1, n = 145) = 536.83, $p < 0.001$).

The observed frequency of 30 PCPs in this study who reported knowing the symptoms of LD but not feeling comfortable diagnosing LD was significantly higher than the expected frequency of 2 PCPs who reported knowing LD but not feeling comfortable diagnosing LD. Moreover, the observed frequency of 115 PCPs in this study who reported knowing the symptoms of LD and feeling comfortable diagnosing LD was significantly lower than the expected frequency of 144 PCPs who reported feeling comfortable diagnosing LD. Results of the Chi-square(χ^2) test were significant (χ^2 (1, n = 145) = 536.83, p <.001). Due to the significant findings, the null hypothesis was rejected (failed to be retained) and the alternative hypothesis was retained for the second research question, denoting significant differences in the frequencies of PCPs who felt comfortable (or not) diagnosing LD across the two studies.

Table 12

Chi-square (χ^2) Goodness-of-fit Test: Observed and Expected Comfort in Diagnosing LD Categories (n = 145)

	Observed (n)	*Expected (n*)*
Not comfortable diagnosing LD	30[a]	2[a]
Comfortable diagnosing LD	115[b]	144[b]
Chi-square (χ^2)	536.83	
df	1	

Significance (*p*)	<0.001

Note. *The expected frequencies are derived from the category percentages (or proportions) reported by Johnson and Feder (2010). They are not the actual frequencies.
[a] The observed frequency of 30 is significantly higher than the expected frequency of 2.
[b] The observed frequency of 115 is significantly lower than the expected frequency of 144.

Cohen's *w* (Cohen, 1988; Cunningham & McCrum-Gardner, 2007; NCSS, n.d.) was calculated. The mathematical formula for Cohen's *w* is $\sqrt{\chi^2/N}$ (Cohen, 1988; NCSS, n.d.). Cohen's *w* was 1.9, a very large effect size (Cohen, 1988; NCSS, n.d.). Like Cohen's *d*, Cohen's *w* can be greater than 1.00, and it indicates a large magnitude in the frequency or proportion differences between the sample and population (Becker, 2000; Cohen, 1988). A post hoc power analysis using G*Power was conducted on the total sample of 145, with an effect size of 1.9, α err prob of .05, and *df* of 1. The output provided a noncentrality parameter λ of 523.45, critical χ^2 of 3.84, and the power was very high, 1- β= 1.00.

Research Question 3

The third research question was as follows: "Are the frequency distributions of the 2018 sample of Connecticut PCPs across the 3 knowledge of CLD/PTLDS categories (i.e., do not believe CLD exists, do not feel comfortable diagnosing and treating CLD/PTLDS, and feel comfortable diagnosing and treating CLD/PTLDS) significantly different from the distributions of the 2010 sample of Connecticut PCPs?" Of the 145 PCPs in this study, 70 (48.3%) PCPs reported that they do not believe CLD/PTLDS exists, 44 (30.3%) reported that they believe CLD/PTLDS may exist but are not comfortable diagnosing CLD/PTLDS, and 31 (21.4%) reported feeling comfortable

diagnosing CLD/PTLDS. Johnson and Feder (2010) reported that, of the 285 participants in their study, 142 (49.8%) PCPs reported that they felt CLD/PTLDS did not exist, 137 (48.1%) stated that they believed CLD/PTLDS might exist but did not feel comfortable diagnosing CLD/PTLDS, and 6 (2.1%) PCPs reported that they felt comfortable diagnosing CLD/PTLDS. The frequencies of PCPs per knowledge of CLD categories are presented in Figure 19.

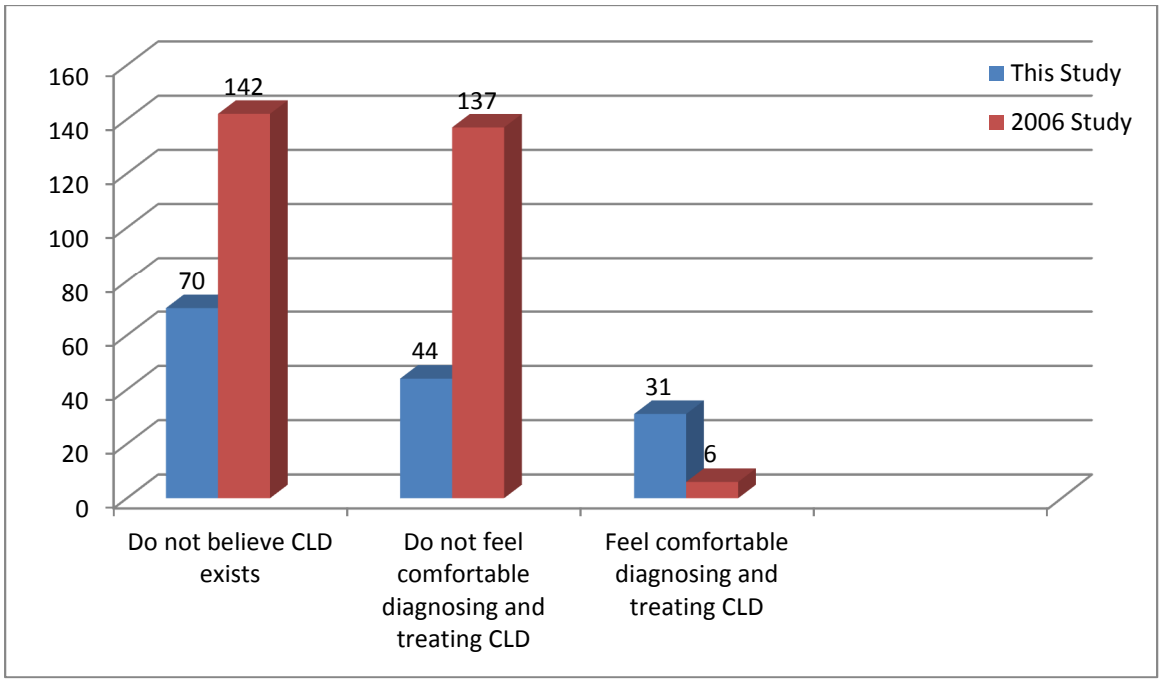

Figure 19. Frequencies of primary care physicians per knowledge of chronic Lyme disease categories. Results from the Chi-square (χ^2) goodness-of-fit test, were significant (χ^2 (2, N = 145) = 265.41, p < 0.001).

A Chi-square (χ^2) goodness-of-fit test was conducted to address the third research question. Results from the Chi-square (χ^2) goodness-of-fit test were significant (χ^2 (2, n = 145) = 265.41, p <.001) (see Table 14). The observed frequency of 44 PCPs in this study who reported that they believe that CLD/PTLDS may exist but do not feel comfortable

diagnosing CLD/PTLDS was significantly lower than the expected frequency of 70 PCPs who reported that they believe that CLD/PTLDS may exist but do not feel comfortable diagnosing CLD/PTLDS, which was based on the population percentages (or proportions) derived from Johnson and Feder's (2010) of the historical data. Moreover, the observed frequency of 31 PCPs in this study who reported feeling comfortable diagnosing CLD/PTLDS was significantly higher than the expected frequency of 3 PCPs who reported feeling comfortable diagnosing CLD/PTLDS, which was based on the population percentages (or proportions) derived from Johnson and Feder's (2010) from the historical data. The observed frequency of 70 PCPs who believed that CLD/PTLDS does not exist was similar to the expected frequency of 72, which was also based on Johnson and Feder's (2010) databased on the historical data. Due to the significant findings, the null hypothesis was rejected (failed to be retained), and the alternative hypothesis was retained for the third research question, indicating significant differences the frequency of PCPs who felt comfortable (or not) diagnosing CLD/PTLDS across studies.

Table 13

Chi-square (χ^2) Goodness-of-fit Test: Observed and Expected Comfort in Diagnosing CLD/PTLDS Categories (n = 145)

		Observed (n)	*Expected (n*)*
Do not believe CLD exists		70	72
Not comfortable diagnosing CLD		44[a]	70[a]
Comfortable diagnosing CLD		31[b]	3[b]
Chi-square (χ^2) goodness-of-fit test	265.41		
df	2		

Significance (*p*)	<0.001

Note. *The expected frequencies are derived from the category percentages (or proportions) reported by Johnson and Feder. They are not the actual frequencies.
[a] The observed frequency of 44 is significantly lower than the expected frequency of 70.
[b]There observed frequency of 31 is significantly higher than the expected frequency of 3.

The Cohen's was 1.35, a very large effect size (Cohen, 1988; NCSS, n.d.). Like Cohen's *d*, Cohen's *w* can be greater than 1.00, and it indicates a large magnitude in the frequency or proportion differences between the sample and population (Becker, 2000; Cohen, 1988). A post hoc power analysis using G*Power was conducted on the total sample of 145, with an effect size of 1.35, α err prob of .05, and *df* of 1. The output provided a noncentrality parameter λ of 264.26, critical χ^2 of 3.84, and the power was very high (1- β=1.00).

Research Question 4

The fourth research question was as follows: "Is the average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2018 sample of Connecticut PCPs significantly different from the average number of patients diagnosed as having CLD/PTLDS within a 3-year period by the 2010 sample of Connecticut PCPs?" This research question required comparisons of data from the PCPs who reported feeling comfortable diagnosing CLD/PTLDS to data from the population of PCPs who reported feeling comfortable diagnosing CLD/PTLDS in Johnson and Feder's (2010) study.

A one-sample *t*-test, using data from the adjusted diagnosed or treated for CLD/PTLDS PCPC group mean (outliers removed) was conducted to address the fourth research question. In Johnson and Feder's (2010) study, the average number of patients

diagnosed and treated for CLD/PTLDS in past years by these 6 PCPs was $M = 3.10$. Consequently, the test value mean was 3.10. Results from the first one-sample t-test were not significant (t (27) = -0.11, $p = 0.914$). The estimated mean number of patients diagnosed and treated for CLD/PTLDS in the past three years as reported by the 28 PCPs ($M = 3.04$) was not significantly different than the mean of 3.10, as reported in Johnson and Feder's (2010) study.

Research Question 5

The fifth research question was as follows: "Is the average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2018 sample of Connecticut PCPs significantly different from the average course of antibiotic treatment (in weeks) for patients diagnosed as having CLD/PTLDS by the 2010 sample of Connecticut PCPs?" The fifth research question required comparing data from the 23 PCPs (one outlier removed) that provided an answer to the antibiotic treatment course variable. The population was the 6 PCPs who reported feeling comfortable diagnosing CLD/PTLDS in Johnson and Feder's (2010) study.

To address the fifth research question, a one-sample t-test, using the antibiotic course of treatment (in weeks) variable estimated mean of 9.74, was conducted. In Johnson and Feder's (2010) study, the estimated average course of antibiotic treatment (in weeks) for the 6 PCPs who felt comfortable diagnosing and treating patients for CLD/PTLDS $M = 20.00$. Consequently, the test value mean was 20.00. Results from the second one-sample t test were significant (t (22) = -4.90, $p < 0.001$). The estimated average course of antibiotic treatment (in weeks) as reported by the 23 PCPs in this study

(M = 10.61) was significantly lower than the mean of 20.00 weeks, as reported in Johnson and Feder's (2010) study. Consequently, the null hypothesis was retained, and the alternative hypothesis was rejected.

Summary

The purpose of this nonexperimental cross-sectional comparative research study was to determine if two groups of PCPs working in Connecticut – the 285 PCPs in Johnson and Feder's (2010) study and the 145 PCPs in this study – reported significant differences in their KAP in the diagnosis, treatment, and management of LD (LD) and CLD/PTLDS. Data collection occurred in the summer of 2018, utilizing a USPS-mailed survey process. Of the 1,726 survey packets mailed to the PCPs, 219 (12.7%) were returned due to an incorrect address. 1,507 (87.4%) PCPs received the study packet via USPS mail. The number of survey packets returned to the researcher was 179, resulting in an initial 11.7% response rate. The removal of 34 surveys from the data set for various reasons (e.g., the PCP not providing informed consent, PCP was retired) yielded a final sample of 145 and a final response rate of 11.9%.

Due to the inability to obtain Johnson and Feder's raw data, the comparison data were drawn from the information presented in Johnson and Feder's (2010) their published study. The data from their study were treated as population data, and these data from the 285 PCPs were compared to the data from the sample of 145 PCPs in this study. The five research questions were answered using population-based statistical analyses, namely Chi-square (χ^2) goodness-of-fit tests and one- sample t-tests. These inferential

analyses coupled with descriptive statistical analyses yielded pertinent information on key LD and CLD/PTLDS diagnosis and treatment factors.

The first research question inquired as to whether the PCP specialty area frequency distributions (i.e., family medicine, internal medicine, pediatrics, other) of the 145 PCPs in this study were significantly different from the PCP specialty area frequency distributions of the 285 PCPs in Johnson and Feder's (2010) study. Results from a (χ^2) goodness-of-fit test were not significant. This research question was unique, because it was the only one in the study in which the null hypothesis failed to be rejected. The nonsignificant findings indicated that the PCP specialty frequency distributions of family physicians, internists, pediatricians, and other PCPs (i.e., emergency medicine) in this study were similar to the PCP specialty frequency distributions in Johnson and Feder's (2010) study.

The second research question examined if the knowledge of LD category frequency distributions in this study significantly differed from the LD knowledge category frequency distributions in Johnson and Feder's (2010) study. Results from the Chi-square (χ^2) goodness-of-fit test, which was conducted to address the second research question, were significant. There was a significantly lower frequency of PCPs (n = 115, 79.3%) in this study who reported that they knew LD symptoms and felt comfortable diagnosing LD than the frequency of PCPs (*n* = 282, 98.9%) who reported that they knew LD symptoms and felt comfortable diagnosing LD in Johnson and Feder's study. Due to the significant findings, the null hypothesis was rejected (failed to be retained) for the second research question.

The third research question examined if the frequency distributions across the 3 knowledge of CLD/PTLDS categories in this study were significantly different from the CLD knowledge category frequency distributions in Johnson and Feder's study. Results from the Chi-square (χ^2) goodness-of-fit test conducted to address the third research question were significant. There was a significantly higher frequency of PCPs (n = 31, 21.4%) in this study who reported feeling comfortable diagnosing CLD/PTLDS as compared to the frequency of (2.1%) PCPs who reported feeling comfortable diagnosing CLD/PTLDS in Johnson and Feder's (2010) study. There was a significantly lower frequency of PCPs (n = 44, 30.3%) in this study who believed CLD/PTLDS might exist but did not feel comfortable diagnosing CLD/PTLDS as compared to the frequency of 137 (48.1%) PCPs in Johnson and Feder's study who stated that they believed CLD/PTLDS might exist but did not feel comfortable diagnosing CLD/PTLDS. It should be noted, however, that the frequency distributions of PCPs who reported that they did not believe CLD/PTLDS exists were similar for both studies: 70 (48.3%) PCPs in this study and 142 (49.8%) PCPs in Johnson and Feder's study reported that CLD/PTLDS did not exist. Due to the significant findings, the null hypothesis was rejected (failed to be retained) for the third research question.

The fourth research question inquired as to whether the average number of patients diagnosed as having CLD/PTLDS within a 3-year period as reported by the PCPs in this study significantly differed from the average number of patients diagnosed as having CLD/PTLDS within a 3-year period as reported by those in the previous study. This research question required statistical comparisons of data from the 31 PCPs who

reported feeling comfortable diagnosing CLD/PTLDS to data from the population of 6 PCPs who reported feeling comfortable diagnosing CLD/PTLDS in Johnson and Feder's study. Statistical testing for skewness (i.e., computation of $z_{skewness}$ values and K-S test) revealed that the number of patients diagnosed and treated for CLD/PTLDS among these 31 PCPs was considerably skewed. The removal of 3 outliers reduced the degree of skewness. While the $z_{skewness}$ value was acceptable, the K-S test remained significant. Results from the one-sample t-test conducted with 28 PCPs (outliers removed) were not significant. The 28 PCPs reported an average of 3.04 patients whom they had diagnosed as having CLD/PTLDS within the past 3 years, which was remarkably similar to the mean of 3.10 patients diagnosed with CLD/PTLDS in the previous study. The null hypothesis for the fourth research question was retained (failed to be rejected).

The fifth and final research question for this study assessed if the median course of antibiotic treatment (in weeks) range of response for patients diagnosed as having CLD/PTLDS significantly differed between 23 PCPs in this study and the PCPs in Johnson and Feder's study. Statistical testing for skewness (i.e., computation of $z_{skewness}$ values and K-S tests) revealed that the course of antibiotic treatment (in weeks) variable was skewed. However, after the removal of one outlier, the $z_{skewness}$ value was acceptable, and the K-S tests was no longer significant. A one-sample t-test conducted for the fifth research question was significant. The approximately 10 week course of antibiotic treatment reported by PCPs in this study was significantly lower than the 20-week course. Is this consistent with your previous description of the answer to RQ5 reported by the PCPs in Johnson and Feder's (2010) study. Due to significant findings, the null

hypothesis for the fifth research question was rejected (failed to be retained). The following chapter ends the dissertation study. It provides discussions in relation to the guiding theories of this and previous research studies as well as the study's le limitations and recommendations for application or practice and future research.

Chapter 5: Discussion, Conclusions, and Recommendations

Introduction

Due to the absence of a case definition, known biological agent, and lack of reliable laboratory testing, CLD/PTLDS remains a controversial diagnosis (Johnson & Feder, 2010; Lantos, 2015a; Maloney, 2016, Stricker & Fesler, 2018). The controversy and lack of clarity surrounding CLD/PTLDS have impeded understanding of health care providers' diagnosis, treatment, and management of patients (Lantos, 2015a; Maloney, 2016). Further research is necessary to understand and improve the health practices and methods for PCPs when addressing a diagnosis of CLD/PTLDS (Johnson & Feder, 2010; Lantos, et al., 2010; Lantos, 2015a; Stricker & Johnson, 2008).

The purpose of this nonexperimental, cross-sectional, comparative study was to compare CLD/PTLDS knowledge, attitudes, and treatment/practice differences on the how frequently they diagnosed and treated (antibiotics used) patients for LD and CLD/PTLDS in the last 3 years. This study was a replication of Johnson and Feder's (2010) seminal study, with the same sampling and methodological practices and survey instrument. The sampling frames for the two studies was the CT DPH database of MD/DOs, with Johnson and Feder (2010) using 2006 data and this study using 2015 data. As Johnson and Feder's whole dataset could not be obtained, comparisons were made between the data in this study and the available data reported in their study, with their sample treated as the population. Additional data used to complement those in Johnson and Feder's (2010) study were retrieved from https://portal.ct.gov and http://www.publichealth.uconn.edu.

The initial data analyses was focused on assessing whether the survey dissemination and aspects of the two samples were similar. The response rate of 11.7% was significantly lower than the response rate of 39.1% reported by Johnson and Feder (2010). The survey dissemination factors were largely similar. Moreover, it was found that the two Connecticut PCPs were similar with regard to PCP specialty.

This study had five research questions. Results for the first question were not significant, indicating that both studies had similar numbers of PCPs across specialty areas (i.e., family medicine, internal medicine, pediatricians, and other). The similarities between the two study samples allowed for an increased accuracy in statistical comparisons and enhanced the internal validity of the study. Results for the second and third research questions showed a smaller percentage of PCPs reported feeling comfortable diagnosing LD compared to the percentage of the 2006 sample of PCPs. In contrast, there was a much larger percentage of PCPs who reported feeling comfortable diagnosing CLD in this study compared to the percentage of the 2006 sample of PCPs. This finding shows the need for social change in the ways PCPs may be dealing with such patients versus the PCPs who do not believe in the diagnosis for CLD/PTLDS.

The fourth research question required the use of a one-sample *t* test, using the adjusted sample mean value of 3.04. The population sample mean was 3.10 patients. The *t* test was not significant, indicating that the number of patients diagnosed and treated for CLD/PTLDS did not significantly differ across the two groups of PCPs. The fifth research question also involved a one-sample *t* test to determine if the adjusted mean of 10.61 weeks found in this study was significantly different from the mean of 20 weeks

reported by Johnson and Feder. Results from the *t* test indicated that PCPs in this study reported a significantly lower course of antibiotic treatment (in weeks) compared to the 2006 sample of PCPs.

This chapter provides a comprehensive overview of the study findings. The chapter opens with an interpretation of findings section, which includes a review and discussion of findings concerning prior literature, especially Johnson and Feder's (2010) study, and the guiding theories of the study. The chapter continues with a Study Limitations section, where recommendations for future health care practices and suggestions for future empirical study are denoted. The topics under discussion in the penultimate section of the chapter, Implications, pertain to the study's potential for positive social change. Recommendations and a Conclusion section end the chapter.

Interpretation of Findings

The intent of this study was to validate Johnson and Feder's (2010) seminal study to examine the differences between two groups of Connecticut PCPs regarding their diagnosis, treatment, and management of LD and CLD/PTLDS (health professionals tend to prefer to use PTLDS instead of CLD, and *PTLDS* is a term accepted by the CDC). This study emphasized the potential differences in the responses provided by the PCPs regarding their knowledge and attitudes about LD and CLD/PTLDS when Johnson and Feder conducted their study using PCPs distributions in 2006 and PCP distributions in 2015 (the data in this study). In alignment with Johnson and Feder, I focused on PCPs who work in the state of Connecticut, as this type of physician is most likely to engage with patients who demonstrate symptoms of LD and CLD/PTLDS (Ali et al., 2014;

Johnson et al., 2014). The emphasis on differences required a guiding theory that suggests why a medical idea or concept is adopted by the medical community. The diffusion of innovations theory provided the lens to examine potential differences between the two groups of PCPs in this study, which aligned with the KAP approach of this study. In the following sections of the chapter, I present and discuss the findings in relation to prior research, especially Johnson and Feder's study and the diffusion of innovation theory.

This study was a replication of Johnson and Feder's (2010) study conducted with 285 PCPs working in the state of Connecticut. The first research question acted as a validity check to determine if the PCP specialty area frequency distributions were similar in this study and Johnson and Feder's study. The lack of significant findings indicated that both studies had similar numbers of PCPs across specialty areas (i.e., family medicine, internal medicine, pediatricians, and other). The similarities between the two study samples allowed for an increased accuracy in statistical comparisons and enhanced the internal validity of the study.

The second and third research questions helped examine whether there were significant differences in the frequency distributions of PCPs who felt comfortable diagnosing LD or CLD in this study as compared to Johnson and Feder's (2010) study. In this study, a smaller percentage of PCPs reported feeling comfortable diagnosing LD (79.3%) compared to the percentage of PCPs who reported feeling comfortable diagnosing LD (98.9%) in Johnson and Feder's study and the percentage (99%) in a previous study by Ferrouillet et al. (2015). In contrast, there was a much larger

percentage of PCPs who reported feeling comfortable diagnosing CLD (12.6%) in this study compared to the percentage of PCPs who reported that feeling comfortable diagnosing CLD (2.1%) in Johnson and Feder's study. The significant findings for the second and third research question suggest that PCPs in Connecticut may feel increasingly comfortable diagnosing and treating CLD. However, there are still many gaps in implementing a common case definition for CLD using evidence-based research, something that is limited at this time.

The diffusion of innovation theory provided the framework to understand these findings. In this study, the innovative health care practice was the diagnosis and treatment of CLD/PTLDS. The diffusion process pertained to changes in PCP knowledge, attitudes, and practices regarding CLD/PTLDS over a 10-year period (i.e., between 2008 and 2018). Study findings support diffusion of innovation's theoretical intent regarding the diagnosis and treatment of CLD/PTLDS. The six (2.1%) PCPs in Johnson and Feder's (2010) study can be considered innovators, rare physicians who felt that CLD/PTLDS was a meaningful, real, and diagnosable disorder. The increase from 2.1% to 21.4% of PCPs who felt comfortable diagnosing CLD in the past 10 years suggests that CLD/PTLDS diagnosis and treatment has gone from the innovation stage to the early adoption stage.

The diffusion of innovation theory also has implications for the findings regarding the average course of antibiotic treatment. The average course of treatment reported by the 17 PCPs who felt comfortable diagnosing and treating CLD in this study was significantly lower than the course of treatment reported by the six PCPs in Johnson and

Feder's (2010) study. However, when considering this finding within the context of diffusion of innovation, it could be that the change from the innovation to adoption stage of CLD diagnosis and treatment has resulted in an improved treatment procedure. That is, being wary of the problems associated with antibiotic treatment (e.g., over-prescribing. Increasing resistance, side effects), the PCPs in this study may have learned that a shorter effective antibiotic treatment course was as effective as a longer one.

The diffusion of innovation theory has less clear implications for the findings regarding the number of patients diagnosed and treated for CLD/PTLDS in the past 3 years. The mean of 3.10 patients reported by Johnson and Feder (2010) and used in analyses is an adjusted value. Johnson and Feder removed one outlier to obtain this value. The number of patients diagnosed as having CLD/PTLDS was twice as high in this study as compared to Johnson and Feder's study when the two outliers were retained in the data set (i.e., 6 to 3). In contrast, the adjusted mean value of 3.04 patients—obtained by removing two outliers—was similar to the 3.10 patients reported by the six PCPs in Johnson and Feder's study. However, the course of antibiotic treatment (in weeks) was significantly lower in this study compared to Johnson and Feder's study. These differing findings suggest that, despite an increase in the number of PCPs who report feeling comfortable diagnosing and treating CLD in the past 10 years, PCPs are hesitant to diagnose and treat their patients for CLD and are cautious about prescribing a long course of antibiotic treatment for CLD. Although the *acceptance* of CLD diagnosis and treatment has gone from the innovation to the adoption stage, the *actual diagnosis and*

treatment of CLD remains in the innovation stage. There were limitations in this study that likely influenced the findings in this study, which are discussed in the next section.

Limitations of the Study

This study had some limitations. One weakness was the small response rate of 11.9 %, especially when comparing it to the response rate of 33.9% reported by Johnson and Feder (2010). Although 179 surveys were returned by the PCPs, 34 surveys had to be discarded for a variety of reasons, most notably that the physician who completed the survey was not a PCP or that the physician was a PCP but no longer practiced or did not provide informed consent. When comparing both distributions with and without the 34 omitted surveys untabulated in this study, the loss of data did not seem to affect the frequency distributions of the PCP specialty areas, as they were similar across this study and Johnson and Feder's study. Related problems were the small sample size of 31 PCPs who reported feeling comfortable diagnosing and treating CLD/PTLDS. In addition, there were missing data or outliers in the responses related to the number of patients diagnosed and treated for CLD/PTLDS in the past 3 years and the average course of antibiotic treatment for them. Therefore, the results from the one-sample *t* test regarding the number of patients diagnosed and treated for CLD/PTLDS should be interpreted with caution.

Other limitations concerned the PCPs' survey answers and the survey itself. Despite being asked to provide a numerical value when answering the questions regarding the number of patients diagnosed and treated for LD or CLD/PTLDS, a small number of PCPs provided answers such as "many, many" or "a few." These responses

made it difficult to interpret the exact number of diagnosed and treated patients. Moreover, when answering the question regarding the average course of antibiotic treatment for patients with CLD/PTLDS, some PCPs provided answers in months or days instead of weeks, and a small number of PCPS provided a range of values (i.e., 3 to 6 months). These types of responses resulted in having to estimate values. Additionally, there was limitation with the survey because of a small inconsistency in the language used with the term CLD, which should have been consistently stated as CLD/PTLDS. Nonetheless, the questions used in the survey were the same Questions 1-9 used by the previous researchers, so it should not affect much the construct validity of the study.

Another limitation of this study concerned methodological biases that may have influenced study findings. The percentage (or proportion) of PCPs who were comfortable diagnosing CLD/PTLDS (21.4%) in this study was significantly higher than the 2.1% of the PCPs reported in Johnson and Feder's (2010) study. The participation bias may play a role in this finding. PCPs who believe that CLD/PTLDS exists may have been more likely to participate in this study, so the 21.4% value may not reflect the actual population percentage (or proportion), which is an issue when considering the low response rate. Alternatively, the 21.4% value may be a result of the social desirability bias. That is, some PCPs may not have reported their actual belief—that CLD/PTLDS exists—as this belief contradicts the current mainstream medical opinion.

Another potential concern in this study was recall bias. PCPs were asked to recall the number of patients they diagnosed and treated for LD and CLD/PTLDS in the past three years. A 3-year span is quite long, especially considering the number of patients

that PCPs see daily. As such, the PCPs may have under- or over-reported the number of patients they diagnosed as having LD or CLD/PTLDS.

Another limitation of the study pertained to the study recruitment period as it relates to the mailing of the survey packets. Recruitment and the mailing of survey packets occurred during summer. The summer is a difficult season to recruit study participants, especially physicians, as professionals often take extended time off for vacations and traveling (Johnston et al., 2010). Physician recruitment seems to improve during the spring and winters (Johnston et al., 2010; PRA, n.d). Moreover, the survey packets were mailed on Mondays or Saturdays, with physicians receiving the packets early or late in the workweek. Study survey completion rates contribute to be higher on Tuesdays or Wednesdays (Bowling, 2014; PRA, n.d.). These two-timing factors may have contributed to the poor return rate response. It is possible that an electronic survey would be better, as other researchers have suggested that they are faster and cheaper to reach to PCPs through their medical societies or in conferences that they will be attending (Dobrow et al., 2008). However, due to the increase of cyberattacks, PCPs may be reluctant to take part in electronic surveys because they care about keeping their patient records safe. For example, out of 10 medical doctors, eight had experienced a cyberattack in practice (American Medical Association, 2017).

Lastly, the study database used in this study have limited information about the participants in this study. This kind of database only keeps the license number, first name, last name, address (most of the time is work), city, state, zip code, issue date, expiration date, degree type, and specialty. This type of MD/DO database does not have

information about gender, age, or race, meaning certain data descriptive data from the participants to describe the populations under the study were unavailable. Thus, it was challenging to provide evidence that the samples of the two surveys (2006 vs. 2015) were comparable, and it is not possible to make inferences about the gender, age, and race presented in this study from the PCPs who responded to the surveys.

Recommendations

There is a 10-year gap between this and Johnson and Feder's (2010) seminal study. There remains a relative absence of contemporary studies—quantitative or qualitative—on physicians' knowledge, attitudes, and treatment of CLD/PTLDS. Moreover, both this and Johnson and Feder's study were conducted with Connecticut PCPs, with contact information gathered from the CT DPH MD/DO databases for 2006 and 2015. Thus, the findings can only be generalized to the PCPs who responded and whose contact information is listed in the CT DPH MD/DO databases. These two factors emphasize the need to conduct more epidemiological/public health empirical work to refine knowledge and understanding of the CLD/PTLDS diagnosis rates among PCPs and physicians in general.

As findings in this study can only be generalized to PCPs in Connecticut, a need exists for replication studies that extend beyond the Connecticut PCP population to include state and preferably national samples of PCPs. There is a need for cross-state studies on whether KAP differences regarding PTLDS/CLD occur across PCPs practicing in different geographical regions, states, or even countries. Studies that compare PTLDS/CLD KAPs among PCPs who practice in states with low versus high rates of

PTLDS/CLD would be especially beneficial. Other types of needed studies are (a) causal comparative studies that examine PTLDS/CLD KAP differences between PCPs that differ with regard to demographics (gender, age), education, and training experience; (b) correlational studies that examine if significant relationships exist between PCPs' attitudes toward PTLDS/CLD diagnosis, primary symptomatology, and perceived severity/health impact and the number of patients diagnosed with and treated for PTLDS/CLD; and (c) longitudinal studies that follow one set of physicians/PCPs over time and measure changes in PTLDS/CLD (and LD) diagnostic and treatment practices. Qualitative empirical work, such as phenomenological studies that capture PCPs' experiences diagnosing and treating PTLDS/CLD and case studies on PTLDS/CLD diagnostic and treatment modalities, would complement the quantitative research on the study topic.

As this was a validation study of Johnson and Feder's (2010) work, it utilized these authors' survey. There exists a need for validation studies that assess the psychometric quality of Johnson and Feder's (2010) study. Do to the controversy surrounding the term CLD and the lack of a case definition for this disease (Borcher et al., 2015), it would be interesting to see if differences emerge if different groups of PCPs answer questionnaires that have the same questions but use the terms CLD, PTLDS, or PTLDS/CLD. There is also a need to develop and psychometrically test more comprehensive questionnaires that inquire not only about PCPs' demographics (e.g., age, gender) and education and training, but also delve into PCPs knowledge about

PTLDS/CLD, its diagnostic criteria, and recommended treatment protocols, as well their actual treatment protocols for their own patients diagnosed with PTLDS/CLD.

Specific aspects of this study and study findings provide a guide for future studies. Findings in this study indicated that a lower percentage (or proportions) of PCPs reported feeling comfortable diagnosing LD as compared to the PCPs in Johnson and Feder's (2010) study. This finding is intriguing and suggests that studies examining changes in LD diagnostic rates among PCPs and physicians would be beneficial. The estimated course of antibiotic treatment (in weeks) for patients with CLD/PTLDS was similar in this and Johnson and Feder's (2010) study**.** It is unknown whether the course of treatment reported by the PCPs in this and Johnson and Feder's (2010) study is typical among Connecticut PCPs and PCPs in general. Additional work is needed to obtain a better understanding of PCPs' reported average course of antibiotic treatment for CLD/PTLDS as well as the type and dosage of antibiotic prescribed for CLD/PTLDS, as this type of information is currently unknown. Finally, CLD/PTLDS antibiotic treatment efficacy studies are warranted, especially experimental studies that examine the effects of different antibiotic types, dosages, and course lengths on CLD/PTLDS symptomatology. However, it would unethical to conduct clinical trials when there is not a known etiological agent to understand its susceptibility to antibiotics. Conducting epidemiology research would be an appropriate starting point.

The uncertainty regarding the cause, origin, and specific diagnostic criteria of CLD/PTLDS is concern among physicians (Greenberg, 2017; Halperin, 2015). Olson, Graber, and Singh (2018) stated the difficulty that medical doctors may have when

coming across “undesirable diagnostic events (UdesF)” due in significant part to the lack of standardization making impossible to have health professionals to make an accurate and timely diagnosis. The majority of the PCPs in Connecticut, as well as the CDC, and the National Institute of Allergy and Infectious Diseases may want to adopt a reconciliation position that will eventually help CLD/PTLDS patients indirectly since they may feel the same way as Olson et al. (2018). One way to adopt a reconciliation position is by utilizing a new practice diagnosis as PTLDS.

By adopting a new practice diagnosis as PTLDS, the CDC, the National Institute of Allergy and Infectious Diseases, and the PCPs in Connecticut can do and document PTLDS diagnosis. At the same time, it will be a good thing for the patients because they can get most of their medical bills accepted by their health insurance, which is not a perfect solution to alleviate the tensions between PCPs and presumed CLD/PTLDS patients. However, it is a position in the middle that may unite PCPs from that belongs to the Infectious Diseases Society of America and ILADS.

It would also be beneficial if CT DPH, the Connecticut Medical School, Connecticut Convergence Institute for Translation in Regenerative Engineering would initiate “blood serum clinics” from those people or patients who are feeling afflicted with PLTDS/CLD. In the past, serological surveys and clinics have generated new insights for the discovery and cure of infectious agents that became new diseases in the United States (e.g., AIDS, syphilis) and nowadays, there are a standardized diagnosis and acceptable treatment protocols (Metcalf et al., 2016). Additionally, parallel applications should be dedicated to finding more about CLD/PTLDS. Without a CLD/PTLDS’s case definition,

it would be unfair to assess what are the best PCP practices to diagnose and treat patients for CLD/PTLDS. There should be resources to find more important issues pending and presently unsolved pertinent to the uncertainty of CLD/PTLDS as new disease (if this is the case) as: (a) aids in the identification, if applicable, of a known biological agent involved in CLD/PTLDS; (b) reconcile concerns regarding *Borrelia burgdorferi* exposure studies that refine the laboratory testing of LD and CLD/PTLDS agents; and (c) move toward a medically-informed consensus of CL/PTLDS symptomatology and diagnostic indicators (Greenberg, 2017).

Implications

Epidemiological studies that will assess CLD/PTLDS prevalence/incidence rates and LD-CLD/PTLDS correspondence rate (i.e., how many patients diagnosed with LD go on to develop CLD/PTLDS) would be especially worthwhile. Epidemiological studies that will assess CL/PTLDS prevalence/incidence rates and LD-CLD/PTLDS correspondence rate will help to minimize the current polarized understanding regarding CLD/PTLDS that has created a dispute among many medical professionals, including mainstream community PCPs (Marzec et al., 2017). Since there is not a case definition for CLD/PTLDS, PCPs in Connecticut should compromise to accept PTLDS and start collecting information about PTLDS.

The comparative findings found between this study and Johnson and Feder's (2010) study presented in this cross-sectional investigation contradict and complement one another within the same alignment of the literature review presented in chapter 2. This study and Johnson and Feder's (2010) study have similar findings to affirm the need

for more studies to find (a) the identification (if any) of a biological agent involved in CLD/PTLDS; (b) associations between LD and CLD/PTLDS (d) CLD/PTLDS diagnostic criteria; and (e) CLD/PTLDS treatment ‘best practices. It would be improper for PCPs to have an effective standardized treatment if they do not know if the agent causing CLD/PTLDS is infectious or not. Moreover, there is the pressing need for more studies to find if there are any relationships between LD biofilms and late antibiotic treatment, associated the prevalence of CLD/PTLDS, that at this time is unknown.

Moreover, without any doubts, the study findings affirm the need for new conversations between PCPs, government officials (local, state, and federal), and patients to allocate financial resources for further medical and epidemiological investigations regarding CLD/PTLDS. In addition, the study findings will help to create universal guidelines for the best optimal treatment for patients affected by CLD. Additionally, results from this study suggest that medical doctors may find it challenging to treat patients potentially suffering from CLD/PTLDS.

It is hoped that the knowledge generated in this study can be applied by physicians to understand their pursuit of eliminating and minimizing morbidity and mortality among their patients. Facing the need to force better practices for the CLD/PTLDS diagnostic and treatment acumen will promote their sensitivity and understanding when dealing with patients who report CLD/PTLDS symptoms. The increasing rate of PCPs who diagnose and treat CLD/PTLDS, as evidenced in this study, denotes a need for change in medical policies to make the CLD/PTLDS diagnosis more cost-effective, and legitimate to be documented in a new electronic surveillance system.

Additionally, the results of the study may help federal and state government health care organizations (e.g., CT DPH, CDC) to urgently fund more studies to find the etiological agents of CLD/PTLDS, to consequently develop and implement educational programs, new policies and services that equip PCPs to have a standardized diagnosis and treatment system across all medical doctors' categories.

It is the intent of the researcher to develop, complete, and publish empirical manuscripts from this study. Attention will be given to publishing in peer-reviewed epidemiology and public health journals, in partnership with the previous researchers (i.e., Johnson & Feder, 2000) and Walden University mentors. The study data set is robust enough to publish results noted in this study as well as findings on additional information gleaned from the data set. The dissertation manuscript will be published through ProQuest and made available to Walden University professors and students.

Conclusion, Future Research, and the Need for Social Change

As posited by Johnson and Feder (2010), the diagnosis and subsequent treatment of CLD/PTLDS remain challenging and controversial issues for PCPs in Connecticut. PCPs, such as internists, pediatricians, family, and emergency medicine physicians, are often the first to diagnose and treat LD. Nonetheless, in this study it was found that LD is not as straightforward diagnosed and treated as in the previous study done 10 years ago or maybe not as many physicians feel comfortable diagnosing regular LD anymore. This is an interesting point to move the message in this research to create social change and it is interesting since it looks like especially LD has strong scientific evidence to back it up. Nonetheless I think physicians may prefer evidence-based medicine, but when a disease

emerges that they do not know how to treat or have treated unsuccessfully using the standard of care, they resort to case based reports or expert opinions, lower levels of evidence. Thus, the data from this study process show how PCPs diagnose and treat CLD/PLTSDS as an emerging disease that still requires a scientific explanation and more research is needed. PCPs must remain attentive to the possibility that 3 to 28% of these patients may develop CLD/PTLDS. Often, PCPs do not have the means or the time to explore and investigate the causes of CLD/PTLDS symptoms, nor are they able to provide a holistic and ongoing evaluation and treatment protocol for CLD/PTLDS patients. Patients with CLD/PTLDS, both self-diagnosed or diagnosed by a PCP, frequently suffer in silence. Ultimately, CLD/PTLDS patients' health-related quality of life and daily functioning may be impaired due to these controversies.

Despite the substantially higher number of 285 PCPs in the previous study, the proportional distributions of internists, pediatricians, and family and emergency medicine physicians were similar to those in this study (Figure 20). It can be accounted that in Connecticut, the numbers of PCPs grow or diminish not more than 20% of any previous year. The mean number of patients diagnosed for CLD/PTLDS by PCPs and the estimated average course of antibiotic treatment (in weeks) did not significantly differ between this study and Johnson and Feder's (2010) study. However, significantly fewer PCPs were comfortable diagnosing and treating LD in this study. This study and Johnson and Feder's (2010) study may collectively provide insight regarding PCPs' KAP on CLD/PTLDS based on their survey responses.

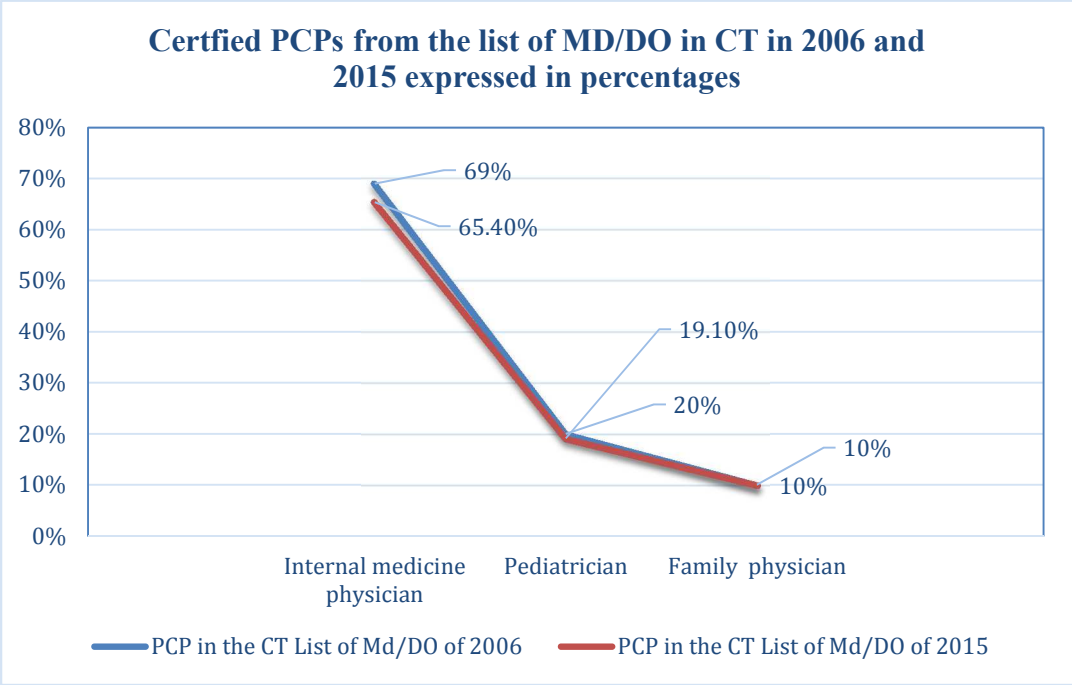

Figure 20. Percentages (or proportions) of the total numbers of primary care physicians in the categories used in this study. Total numbers did not change more than 20%. This type of information is very limited to be share. Thus, it would be more meaningful to be able to show how the how the PCPs increase or decrease in such specialty, but such information is well protected by at the CT DPH.

Moreover, this manuscript points out how the substantial majority of PCPs voice discomfort and concern when diagnosing and treating LD and CLD/PTLDS. Some patients diagnosed with LD, much less CLD/PTLDS, may never have reported a tick bite or show the EM rash (Allen et al., 2016; Gasmi et al., 2017). There are existing PCP customary practices (meaning PCPs want to diagnose their patients adopting an evidence-based approach); PCPs and other health care providers want to diagnose and treat all patients without any bias, which means they want to conduct a proper medical health

assessment on their patients to find why they are sick (Ebell, Sokol, Lee, Simons, & Early, 2017). There may be some limitations when requesting an exact diagnostic test for CLD/PTLDS patients because there is no known biological agent, which prevents potential medical tests for CLD/PTLDS (Lantos, 2015c). Therefore, PCPs may not be comfortable with CLD/PTLDS diagnosis because there is no cost-effective clinical testing to back it up and recommended treatment (Ebell et al., 2017; Lantos, 2015a).

Consequently, the lack of a consensus on a CLD/PTLDS case definition among leading medical organizations will continue until there are further discoveries related to this condition (Stanek et al., 2010; Stricker & Fesler, 2018). The lack of a case definition has important implications. The World Health Organization (2016) who developed ICD classification codes (see Table 2) to identify a patient's specific health condition, as well as the respective billing code to health insurance companies, has not assigned an ICD classification code for either CLD/PTLDS (CDC, 2017; World Health Organization, 2016). PCPs may be highly reticent in diagnosing a patient with CLD/PTLDS if they cannot follow standardized protocols to have their patients be reimbursed by their insurance companies or non-coverage policies.

This study may instigate a consciousness of how difficult it may be for a PCP to better assist patients with CLD/PTLDS; this may be because the existing guidelines for infectious diseases do not consider CLD a disease that affects people in Connecticut (where LD was discovered) or in the United States. For example, the American Academy of Pediatrics presently (as 2017) stated that they do not consider CLD/PTLDS a medical diagnosis (Korioth, 2017). It is necessary for organizations (i.e., World Health

Organization, CDC, National Institute of Health, and the CT DPH) to hold conversations that contribute to future innovations and practices. However, to accomplish this, they need a consensus on the most recent data collected from the care given to patients with CLD/PTLDS.

In the study, the survey was random and anonymous, so there was limited opportunity for the participants to exchange an active dialogue with the researcher of this study. Nonetheless, there was at the end of the survey space for PCPs to write comments (see Appendix A). This chapter ends with a list of specific gaps in knowledge as well as applied practice recommendations:

- The current treatment data lack specificity since the previous data on standardized "treatments" (including alternative treatments) can be applied to persons under specific CLD/PTLDS clinical conditions.
- The present CLD/PTLDS data published up to 2019 cannot be well characterized and it will be not useful for surveillance, prevention, or control of disease to eliminate mortality and morbidity.
- In the future, it helps to determinate the geographical locations of patients afflicted by CLD/PTLDS, but the reporting of cases will need to meet the specific case definitions (possible, probable, confirmed) – without this, geographical mapping can be misleading so that future researchers can determine the incidence and prevalence of CLD/PTLDS.
- There is still lack of knowledge to find or corroborate if environmental factors play a role in the symptomatology and developmental pathophysiology of

such patients with CLD/PTLDS, because it is meaningless without beginning with well pedigreed data – that is, data developed with careful forethought and scientific objectivity, including the development and use of standardized definitions and establishment of a representative surveillance and monitoring system.

- There is the need for more studies to find their effects of climate change on tick-borne diseases (Connecticut Agricultural Experimental Station,2017; Dumic & Severnini, 2018), notably when the CDC reports that the ticks population keeps increasing in the last decades (CDC, 2015b)
- There is no confirmation of the etiological agent of CLD/PTLDS thus, clinical testing is limited, and the use of the term "CLD/PTLDS" implies the present LD diagnostic tests have very low sensitivity and can produce many false negatives.
- There is a need for new innovative technologies that can help identify vector-borne diseases from non-vector bone disease since most scientists think that CLD/PTLDS is a vector borne disease related with B. Burgdorferi (the spirochete that causes LD).
- There is a need for organizations such as the CDC, World Health Organization and the Infectious Diseases Society of America to investigate if patients with CLD/PTLDS are related to LD because LD has a standardized case definition, and clinical care guidelines exist to develop an ICD code for CLD/PTLDS and better medical guidelines that PCPs can follow (see Table 2)

- If CLD/PTLDS becomes established as an infectious disease, the Institute of Medicine and National Center for Complementary and Integrative Health may wish to review the applications of the Koch's Postulates in the 21st Century through a rigorous scientific approach and to decide what would be the best for patients with it.
- According to Ali at al. (2014), and Johnson et al. (2014), patients that presumed to have CLD/PTLDS is a problem at the national level since, in their studies, patients were recruited at large. Thus, it is necessary for some legislation to benefit both presumed patients with CLD/PTLDS and PCPs. To develop such legislation (local and Federal), the health organizations such as the World Health Organization, CDC, Council of State and Territorial Epidemiologists, International Society for Disease Surveillance, and state and local health departments need to identify what will be the next step towards such legislative changes. If this legislative process will be met, patients can get their health insurance to pay for the treatments needed, and PCPs do not need to be afraid about the care given to such presumed CLD/PTLDS patients.
- From the biotechnological point of view, there is a need to conduct more studies in the fields of molecular biology, immunology, and genetics to determine the role of *Borrelia burgdorferi* and other Borrelia species, as well as other bacteriological agents found in deer ticks to find potential relationships with patients afflicted by CLD/PTLDS.

Medical education for PCPs will continue to be a challenge and will be limited until scientists, health professionals, organizations like the World Health Organization, CDC, Council of State and Territorial Epidemiologists, and Infectious Diseases Society of America resolve present existing disagreements for a standardized case definition and ICD code for CLD/PTLDS (Id one day will have the merit to be identified as disease alone). Once a case definition and an ICD code will be established, PCPs can follow the same protocols and guidelines to diagnose and treat patients with CLD/PTLDS (or in some cases with PTLDS). The main limitation for PCPs for not having a standardized case definition for surveillance is because patients with CLD/PTLDS do not exhibit specific symptoms for their illness like with other infectious or not infectious diseases.

While the global disease burden has been shifting towards chronic conditions, health systems, and moreover, including primary health systems, it is crucial to have the system that evoked the concept of CLD/PTLDS. In addition, new opportunities for research, as well for CLD/PTLDS and LD studies, should further continue to be funded in the United States to benefit both PCPs and their patients (World Health Organization, 2003). Finally, for CLD/PLTDS or just CLD or PTLDS, definitions usually have to come from the medical literature and evolve over time. In this study, it is expected that the information presented here most likely will help PCPs to come together to help that happen by building on others and clearly defining the terms presented in this study.

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Appendix A: CT-KAP Johnson and Feder's (2010) questions 1-9, update CT KAP 2018 (questions 10 and 11)

1. Are you in clinical practice seeing patients?

☐Yes ☐ No

2. What is your specialty?

☐ Family Physician ☐ Internist ☐ Pediatrician ☐Other (please indicate) _____

3. How would you describe your knowledge of Lyme disease?

☐ I know the symptoms and feel comfortable diagnosing it.
☐ I know the symptoms, but I don't feel comfortable diagnosing it.
☐ I don't know the symptoms and I don't diagnose it.

4. How would you describe your knowledge of Chronic Lyme disease?

☐ I know the symptoms and feel comfortable diagnosing it.
☐ I know the symptoms, but I don't feel comfortable diagnosing it.
☐ I don't know the symptoms and I don't feel comfortable diagnosing it.
☐ I don't believe it exists. (**Go to question #6**.)

5. In your experience Chronic Lyme disease includes which of the following? Check all that apply; you may check none, or more than one.

☐ Following the treatment for Lyme disease, a patient has persistent symptoms like headache, trouble concentrating, fatigue, myalgias, and/or arthralgias. Some of these patients have **Chronic Lyme disease** and require prolonged antibiotic therapy.

☐ A patient has never previously been diagnosed with Lyme Disease but has persistent headache, trouble concentrating, fatigue, myalgias, and /or is seropositive

for *Borrelia burgdorferi* antibodies. Some of these patients have **Chronic Lyme disease** and require prolonged antibiotic therapy.

☐ A patient has never been diagnosed with Lyme Disease but has persistent headache, trouble concentrating, fatigue, myalgias, and/or arthralgias is seronegative for *Borrelia burgdorferi* antibodies. Some of these patients have **Chronic Lyme disease** and require prolonged antibiotic therapy.

☐ Other-please describe _____

6. Over the past 3 years approximately how many patients have you diagnosed and treated with Lyme disease? _____

7. Over the past 3 years approximately how many patients have you diagnosed and treated with Chronic Lyme disease? _____ (if "0", please go to question 8.)

a. What has been the average total course of antibiotics therapy for these patients with Chronic Lyme disease? _____

b. In your opinion, have these patients diagnosed with patients with Chronic Lyme disease been helped by the antibiotics?

☐ Yes ☐ No ☐ I don't know

8. Over the past 3 years approximately how many patients have you diagnosed and treated with Chronic Lyme disease (or PTLDS) by other physicians?

_____

8a. In your opinion have these patients diagnosed with Chronic Lyme disease been helped by antibiotics?

☐ Yes ☐ No ☐ I don't know

9. In your opinion, how frequently does Chronic Lyme disease occur in Connecticut?

☐ Commonly ☐ Uncommonly ☐ Never ☐ I don't know

10. Did you participate in the same previous same mailed survey done in 2006 by Johnson& Feder (2010).

☐ Yes ☐ No

11. I should understand that the fact that you mailed the survey back to me is the corroboration that you have given me consent to use your anonymous data in this study?

☐ Yes ☐ No

Extra: Comments (optional): write below.

Appendix B: The Reportable Disease Confidential Case Report Form PD-23

REPORTABLE LABORATORY FINDINGS—2018

The director of a clinical laboratory must report laboratory evidence suggestive of reportable diseases. The Laboratory Report of Significant Findings form (OL-15C) can be found on the DPH website or by calling 860-509-7994. The OL-15C is a supplement to the physician report, and is used for verification of diagnosis. Pathogens on the OL-15C are listed in alphabetic order; however, there is a separate section for possible disease indicators of bioterrorism. Changes for 2018 are noted in **bold** and an asterisk (*).

Anaplasma phagocytophilum by PCR only
Babesia: ☐ IFA IgM (titer) _____ IgG (titer) _____
☐ Blood smear ☐ PCR ☐ Other _____
☐ *microti* ☐ *divergens* ☐ *duncani* ☐ Unspeciated
Bordetella pertussis (titer) _____
☐ Culture (1) ☐ Non-pertussis *Bordetella* (1) (specify) _____
☐ DFA ☐ PCR
Borrelia burgdorferi (2)
California group virus (3) spp _____
Campylobacter (3) spp_____ ☐ Culture ☐ PCR ☐ EIA
***Candida auris* (1,4) ***
Carbapenem-resistant *Acinetobacter baumannii* (CRAB) (1,5)
Carbapenem-resistant Enterobacteriaceae (CRE) (1,5)
Genus _____spp_____
Carboxyhemoglobin ≥ 5% _____% COHb
Chikungunya virus
Chlamydia trachomatis (test type) _____
Clostridium difficile (6)
Corynebacterium diphtheria (1)
Cryptosporidium spp _____ ☐ Culture ☐ PCR ☐ EIA
☐ Microscopy ☐ Other:_____
Cyclospora spp _____ ☐ PCR ☐ Microscopy ☐ Other:_____
Dengue virus
Eastern equine encephalitis virus
Ehrlichia chaffeensis by PCR only
Escherichia coli O157 (1) ☐ Culture ☐ PCR
Giardia spp _____
Group A *Streptococcus*, invasive (1,5) ☐ Culture ☐ Other _____
Group B *Streptococcus*, invasive (5) ☐ Culture ☐ Other _____
Haemophilus ducreyi
Haemophilus influenzae, invasive (1,5) ☐ Culture ☐ Other _____
Hepatitis A virus (HAV) IgM anti-HAV (7) ALT___ AST ___ ☐ Not Done
Hepatitis B HBsAg ☐ Positive ☐ Negative (7) ☐ IgM anti-HBc
☐ **HBeAg (2)*** ☐ **HBV DNA (2)***
anti-HBs (8) ☐ Positive (titer) _____ ☐ Negative
Hepatitis C virus (HCV) ☐Rapid antibody ☐RNA (9) ☐ Genotype (9)
Herpes simplex virus (infants ≤ 60 days of age) (specify type) _____
☐ Culture ☐ PCR ☐ IFA ☐ Ag detection
HIV Related Testing (report only to the State) (10)
☐ Detectable Screen (IA)
Antibody Confirmation (WB/IFA/Type-diff) (1,10)
HIV 1 ☐ Positive ☐Neg/Ind HIV 2 ☐Positive ☐ Neg/Ind
☐ HIV NAAT (or qualitative RNA) ☐ Detectable ☐ Not Detectable
☐ HIV Viral Load (all results) (10)
☐ HIV genotype (10)
☐ CD4 count: _____ cells/uL: _____% (10)
HPV (report only to the State) (11)
Biopsy proven ☐ CIN 2 ☐ CIN 3 ☐ AIS
or their equivalent (specify) _____
Influenza virus: ☐ Rapid antigen (2) ☐ RT-PCR ☐ Culture-confirmed
☐ Type A ☐ Type B ☐ Type Unknown
☐ Subtype _____
Lead poisoning (blood lead ≥ 10 µg/dL <48 hrs; 0-9 µg/dL monthly) (12)
☐ Finger stick level _____µg/dL ☐ Venous level _____ µg/dL
Legionella pneumophila
☐ Culture ☐ DFA ☐ Ag positive
☐ Four-fold serologic change (titers) _____

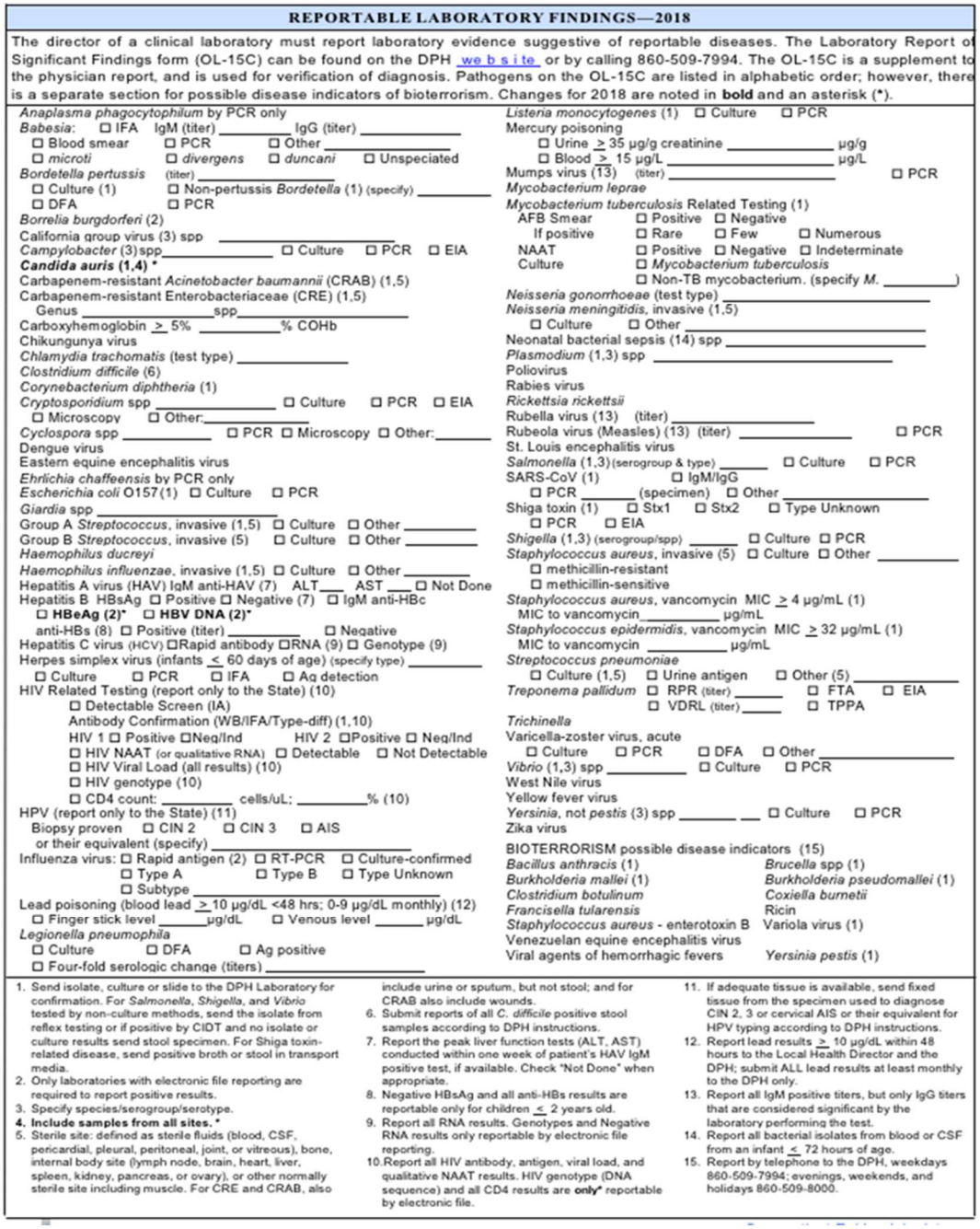
Listeria monocytogenes (1) ☐ Culture ☐ PCR
Mercury poisoning
☐ Urine ≥ 35 µg/g creatinine _____ µg/g
☐ Blood ≥ 15 µg/L _____ µg/L
Mumps virus (13) (titer) _____ ☐ PCR
Mycobacterium leprae
Mycobacterium tuberculosis Related Testing (1)
AFB Smear ☐ Positive ☐ Negative
If positive ☐ Rare ☐ Few ☐ Numerous
NAAT ☐ Positive ☐ Negative ☐ Indeterminate
Culture ☐ *Mycobacterium tuberculosis*
☐ Non-TB mycobacterium. (specify *M.* _____)
Neisseria gonorrhoeae (test type) _____
Neisseria meningitidis, invasive (1,5)
☐ Culture ☐ Other _____
Neonatal bacterial sepsis (14) spp _____
Plasmodium (1,3) spp _____
Poliovirus
Rabies virus
Rickettsia rickettsii
Rubella virus (13) (titer) _____
Rubeola virus (Measles) (13) (titer) _____ ☐ PCR
St. Louis encephalitis virus
Salmonella (1,3) (serogroup & type) _____ ☐ Culture ☐ PCR
SARS-CoV (1) ☐ IgM/IgG
☐ PCR _____ (specimen) ☐ Other _____
Shiga toxin (1) ☐ Stx1 ☐ Stx2 ☐ Type Unknown
☐ PCR ☐ EIA
Shigella (1,3) (serogroup/spp) _____ ☐ Culture ☐ PCR
Staphylococcus aureus, invasive (5) ☐ Culture ☐ Other _____
☐ methicillin-resistant
☐ methicillin-sensitive
Staphylococcus aureus, vancomycin MIC ≥ 4 µg/mL (1)
MIC to vancomycin_____ µg/mL
Staphylococcus epidermidis, vancomycin MIC ≥ 32 µg/mL (1)
MIC to vancomycin _____ µg/mL
Streptococcus pneumoniae
☐ Culture (1,5) ☐ Urine antigen ☐ Other (5) _____
Treponema pallidum ☐ RPR (titer) _____ ☐ FTA ☐ EIA
☐ VDRL (titer) _____ ☐ TPPA
Trichinella
Varicella-zoster virus, acute
☐ Culture ☐ PCR ☐ DFA ☐ Other _____
Vibrio (1,3) spp _____ ☐ Culture ☐ PCR
West Nile virus
Yellow fever virus
Yersinia, not *pestis* (3) spp _____ ☐ Culture ☐ PCR
Zika virus

BIOTERRORISM possible disease indicators (15)
Bacillus anthracis (1)
Brucella spp (1)
Burkholderia mallei (1)
Burkholderia pseudomallei (1)
Clostridium botulinum
Coxiella burnetii
Francisella tularensis
Ricin
Staphylococcus aureus - enterotoxin B
Variola virus (1)
Venezuelan equine encephalitis virus
Viral agents of hemorrhagic fevers
Yersinia pestis (1)

1. Send isolate, culture or slide to the DPH Laboratory for confirmation. For *Salmonella*, *Shigella*, and *Vibrio* tested by non-culture methods, send the isolate from reflex testing or if positive by CIDT and no isolate or culture results send stool specimen. For Shiga toxin-related disease, send positive broth or stool in transport media.
2. Only laboratories with electronic file reporting are required to report positive results.
3. Specify species/serogroup/serotype.
4. **Include samples from all sites. ***
5. Sterile site: defined as sterile fluids (blood, CSF, pericardial, pleural, peritoneal, joint, or vitreous), bone, internal body site (lymph node, brain, heart, liver, spleen, kidney, pancreas, or ovary), or other normally sterile site including muscle. For CRE and CRAB, also include urine or sputum, but not stool; and for CRAB also include wounds.
6. Submit reports of all *C. difficile* positive stool samples according to DPH instructions.
7. Report the peak liver function tests (ALT, AST) conducted within one week of patient's HAV IgM positive test, if available. Check "Not Done" when appropriate.
8. Negative HBsAg and all anti-HBs results are reportable only for children ≤ 2 years old.
9. Report all RNA results. Genotypes and Negative RNA results only reportable by electronic file reporting.
10. Report all HIV antibody, antigen, viral load, and qualitative NAAT results. HIV genotype (DNA sequence) and all CD4 results are **only*** reportable by electronic file.
11. If adequate tissue is available, send fixed tissue from the specimen used to diagnose CIN 2, 3 or cervical AIS or their equivalent for HPV typing according to DPH instructions.
12. Report lead results ≥ 10 µg/dL within 48 hours to the Local Health Director and the DPH; submit ALL lead results at least monthly to the DPH only.
13. Report all IgM positive titers, but only IgG titers that are considered significant by the laboratory performing the test.
14. Report all bacterial isolates from blood or CSF from an infant ≤ 72 hours of age.
15. Report by telephone to the DPH, weekdays 860-509-7994; evenings, weekends, and holidays 860-509-8000.

Retrieved from https://portal.ct.gov/-/media/Departments-and-Agencies/DPH/dph/infectious_diseases/CTEPINEWS/Vol38No1.pdf?la=en

Appendix C: Laboratory Finding Report- Form OL-15C



REPORTABLE LABORATORY FINDINGS—2018

The director of a clinical laboratory must report laboratory evidence suggestive of reportable diseases. The Laboratory Report of Significant Findings form (OL-15C) can be found on the DPH website or by calling 860-509-7994. The OL-15C is a supplement to the physician report, and is used for verification of diagnosis. Pathogens on the OL-15C are listed in alphabetic order; however, there is a separate section for possible disease indicators of bioterrorism. Changes for 2018 are noted in **bold** and an asterisk (*).

Anaplasma phagocytophilum by PCR only
Babesia: ☐ IFA IgM (titer) _____ IgG (titer) _____
☐ Blood smear ☐ PCR ☐ Other _____
☐ *microti* ☐ *divergens* ☐ *duncani* ☐ Unspeciated
Bordetella pertussis (titer) _____
☐ Culture (1) ☐ Non-pertussis *Bordetella* (1) (specify) _____
☐ DFA ☐ PCR
Borrelia burgdorferi (2)
California group virus (3) spp _____
Campylobacter (3) spp _____ ☐ Culture ☐ PCR ☐ EIA
***Candida auris* (1,4) ***
Carbapenem-resistant *Acinetobacter baumannii* (CRAB) (1,5)
Carbapenem-resistant Enterobacteriaceae (CRE) (1,5)
Genus _____ spp _____
Carboxyhemoglobin ≥ 5% _____% COHb
Chikungunya virus
Chlamydia trachomatis (test type) _____
Clostridium difficile (6)
Corynebacterium diphtheria (1)
Cryptosporidium spp _____ ☐ Culture ☐ PCR ☐ EIA
☐ Microscopy ☐ Other: _____
Cyclospora spp _____ ☐ PCR ☐ Microscopy ☐ Other: _____
Dengue virus
Eastern equine encephalitis virus
Ehrlichia chaffeensis by PCR only
Escherichia coli O157 (1) ☐ Culture ☐ PCR
Giardia spp _____
Group A *Streptococcus*, invasive (1,5) ☐ Culture ☐ Other _____
Group B *Streptococcus*, invasive (5) ☐ Culture ☐ Other _____
Haemophilus ducreyi
Haemophilus influenzae, invasive (1,5) ☐ Culture ☐ Other _____
Hepatitis A virus (HAV) IgM anti-HAV (7) ALT ___ AST ___ ☐ Not Done
Hepatitis B HBsAg ☐ Positive ☐ Negative (7) ☐ IgM anti-HBc
☐ **HBeAg (2)*** ☐ **HBV DNA (2)***
anti-HBs (8) ☐ Positive (titer) _____ ☐ Negative
Hepatitis C virus (HCV) ☐ Rapid antibody ☐ RNA (9) ☐ Genotype (9)
Herpes simplex virus (infants ≤ 60 days of age) (specify type) _____
☐ Culture ☐ PCR ☐ IFA ☐ Ag detection
HIV Related Testing (report only to the State) (10)
☐ Detectable Screen (IA)
Antibody Confirmation (WB/IFA/Type-diff) (1,10)
HIV 1 ☐ Positive ☐ Neg/Ind HIV 2 ☐ Positive ☐ Neg/Ind
☐ HIV NAAT (or qualitative RNA) ☐ Detectable ☐ Not Detectable
☐ HIV Viral Load (all results) (10)
☐ HIV genotype (10)
☐ CD4 count: _____ cells/uL; _____% (10)
HPV (report only to the State) (11)
Biopsy proven ☐ CIN 2 ☐ CIN 3 ☐ AIS
or their equivalent (specify) _____
Influenza virus: ☐ Rapid antigen (2) ☐ RT-PCR ☐ Culture-confirmed
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☐ Subtype _____
Lead poisoning (blood lead ≥ 10 µg/dL <48 hrs; 0-9 µg/dL monthly) (12)
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If positive ☐ Rare ☐ Few ☐ Numerous
NAAT ☐ Positive ☐ Negative ☐ Indeterminate
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☐ Non-TB mycobacterium. (specify *M.* _____)
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Neisseria meningitidis, invasive (1,5)
☐ Culture ☐ Other _____
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Plasmodium (1,3) spp _____
Poliovirus
Rabies virus
Rickettsia rickettsii
Rubella virus (13) (titer) _____
Rubeola virus (Measles) (13) (titer) _____ ☐ PCR
St. Louis encephalitis virus
Salmonella (1,3) (serogroup & type) _____ ☐ Culture ☐ PCR
SARS-CoV (1) ☐ IgM/IgG
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Staphylococcus aureus, vancomycin MIC ≥ 4 µg/mL (1)
MIC to vancomycin _____ µg/mL
Staphylococcus epidermidis, vancomycin MIC ≥ 32 µg/mL (1)
MIC to vancomycin _____ µg/mL
Streptococcus pneumoniae
☐ Culture (1,5) ☐ Urine antigen ☐ Other (5) _____
Treponema pallidum ☐ RPR (titer) _____ ☐ FTA ☐ EIA
☐ VDRL (titer) _____ ☐ TPPA
Trichinella
Varicella-zoster virus, acute
☐ Culture ☐ PCR ☐ DFA ☐ Other _____
Vibrio (1,3) spp _____ ☐ Culture ☐ PCR
West Nile virus
Yellow fever virus
Yersinia, not pestis (3) spp _____ ☐ Culture ☐ PCR
Zika virus

BIOTERRORISM possible disease indicators (15)

Bacillus anthracis (1)	*Brucella* spp (1)
Burkholderia mallei (1)	*Burkholderia pseudomallei* (1)
Clostridium botulinum	*Coxiella burnetii*
Francisella tularensis	Ricin
Staphylococcus aureus - enterotoxin B	Variola virus (1)
Venezuelan equine encephalitis virus	
Viral agents of hemorrhagic fevers	*Yersinia pestis* (1)

1. Send isolate, culture or slide to the DPH Laboratory for confirmation. For *Salmonella*, *Shigella*, and *Vibrio* tested by non-culture methods, send the isolate from reflex testing or if positive by CIDT and no isolate or culture results send stool specimen. For Shiga toxin-related disease, send positive broth or stool in transport media.
2. Only laboratories with electronic file reporting are required to report positive results.
3. Specify species/serogroup/serotype.
4. **Include samples from all sites. ***
5. Sterile site: defined as sterile fluids (blood, CSF, pericardial, pleural, peritoneal, joint, or vitreous), bone, internal body site (lymph node, brain, heart, liver, spleen, kidney, pancreas, or ovary), or other normally sterile site including muscle. For CRE and CRAB, also include urine or sputum, but not stool; and for CRAB also include wounds.
6. Submit reports of all *C. difficile* positive stool samples according to DPH instructions.
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14. Report all bacterial isolates from blood or CSF from an infant ≤ 72 hours of age.
15. Report by telephone to the DPH, weekdays 860-509-7994; evenings, weekends, and holidays 860-509-8000.

CT Epidemiologist, 2018. Retrieved from https://portal.ct.gov/-/media/Departments-and Agencies/DPH/dph/infectious_diseases/CTEPINEWS/Vol38No1.pdf?la=en

Appendix D: Frequencies of Primary Care Physicians in Connecticut from 2005 to 2016

Table D1

Frequency of Primary Care Physicians

Year	Number total MD/DO in CT from 1998 to 2018
2005	15047
2006	15424
2007	15831
2008	16238
2009	16604
2010	17904
2011	16692
2012	17130
2013	17294
2014	17428
2015	17464
2016	17664

Note. Adapted from the Connecticut Department of Health (2019). The year before 2006 and after 2015 have minimal changes in the total frequencies of PCPs. The PCP population in Connecticut shows stable growth.

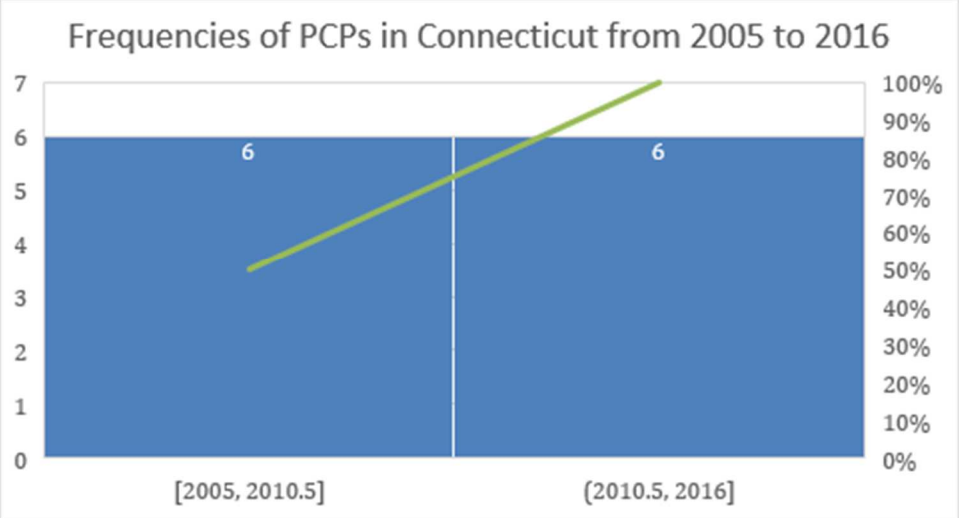


Figure D1. Histogram for frequency of primary care physicians.

Appendix E: Original Data About Connecticut Primary Care Physicians of 2006 and 2015

Table E1

Data on Primary Care Physicians Based on Category

PCP Category or Specialty	CT DPH of total data of PCPS of 2006 (original) in %.	CT DPH of total data of PCPS of 2006 proportions.	CT DPH of total data of PCPs 2015 (original) in %.	CT DPH of total data of PCPS of 2017proportions.
Total number of MD/DO from original data	15,424		17,464	
Family physicians	*69%	10643	65.4	11422
Internal Medecine	*20%	3085	19.1%	3336
Pediatricians	*10%	1542	10.4%	1816
Other		1155		890
Total		1524		17464
Total number of PCPs selected to participate in this study taking a 33%	1034 (33 % of 3091)		1726 (33% of 5231).	

Table E2

Frequency Results Based on Category

	Results											
	Family MD			Internal Medicine			Pediatricians			Other			***Row Totals***
Frequencies of 2006 PCPs before randomization	3085	(3011.36)	[1.80]	10643	(10348.17)	[8.40]	1542	(1574.85)	[0.69]	154	(489.62)	[230.06]	15424
Frequencies of PCPs of 2015 before randomization	3336	(3409.64)	[1.59]	11422	(11716.83)	[7.42]	1816	(1783.15)	[0.61]	890	(554.38)	[203.18]	17464
Column Totals	6421			22065			3358			1044			**32888 (Grand Total)**

Note. * Adapted from three sources (a) http://www.publichealth.uconn.edu/assets/primarycarereport_02_09.pdf, (b) https://portal.ct.gov/DPH/Practitioner-Licensing--Investigations/PLIS/Licensing-Statistics and (c) the data from the Johnson and Feder (2010).
The chi-square statistic is 453.7446. The *p*-value is < 0.00001. The result is significant at $p < .05$.

Appendix F: Distribution of the Population Used in this Study (2006 vs. 2015)

Population	2006 Population from Johnson & Feder (2010)	2015 Population from This Study	***z*** Score	***p*** value
Total number of the original population of PCPs from the databases from CT Public Health Department years (2006 vs. 2015)	15424	17464		
Population (proportion) after the selection of PCP in the categories (F,IM, P) needed for the study from Original population of PCPs from the CT DPH MD/DO list.	3091	5231	20.6351	$p < .0001$ $p < .05$ Significant Dissimilar
Population (proportion) within the pre-selection of the 33 % from the population of PCPs from the CT DPH MD/DO list randomized to receive the survey.	1034	1726	0.4273	$p < .0001$ $p <. 05$ Not Significant Similar
Population (proportion) of the Number of PCPs that responses were received successfully from the survey and were mailed back to the researchers.	843	1507	4.1353	$p < .0001$ $p < .05$ Significant Dissimilar
Population(proportion) of the number of PCP that responses were received before exclusions were applied in the studies.	330	179	-15.3912	$p < .0001$ $p < .05$ Significant Dissimilar
Final Population (proportion) of the number of PCPs that responses were received used for data analysis in the studies.	285	145	1.594	$p = 0.1184$ (no significant). *Proportions are Similar

Note. The population proportions for this study were similar (2006 vs. 2015).

Appendix G: The Margin of Error Calculated for this Study

The margin of error (with finite population expected of 300, but I only got 145 (2015P) is ±5.86%
Where: z = 1.96 for a confidence level (α) of 95%, p = proportion (expressed as a decimal), N = population size, n = sample size.
z = 1.96, p = 0.5, N = 300, n = 145
margin of error = 1.96 * √0.5 * (1 - 0.5) / √ (300 - 1) * 145 / (300 - 145); margin of error = 0.98 / 16.725 * 100 = 5.86%
The margin of error (with finite population correction) is ±5.86%
The margin of error 145 (2015) PCP survey responses received is ±8.138%
Where: z = 1.96 for a confidence level (α) of 95%, p = proportion (expressed as a decimal), n = sample size.
z = 1.96, p = 0.5, n = 145
margin of error = 1.96 * √0.5 * (1 - 0.5) / √145= margin of error = 0.98 / 12.042 * 100 = 8.138%
The margin of error is ±8.138%
The margin of error (145 PCP survey responses only) is ±5.805%
Where: z = 1.96 for a confidence level (α) of 95%, p = proportion (expressed as a decimal), n = sample size.
z = 1.96, p = 0.5, n = 285
margin of error = 1.96 * √0.5 * (1 - 0.5) / √285; margin of error = 0.98 / 16.882 * 100 = 5.805%
The margin of error is ±5.805%
The margin of error for the whole population of 2006(285 & 145 PCP survey) 430 PCP survey responses is ±4.726%
The margin of error is calculated according to the formula: margin of error = z * √p * (1 - p) / √n
Where: z = 1.96 for a confidence level (α) of 95%, p = proportion (expressed as a decimal), n = sample size.
z = 1.96, p = 0.5, n = 430
margin of error = 1.96 * √0.5 * (1 - 0.5) / √430 = margin of error = 0.98 / 20.736 * 100 = 4.726%
The margin of error is ±4.726%

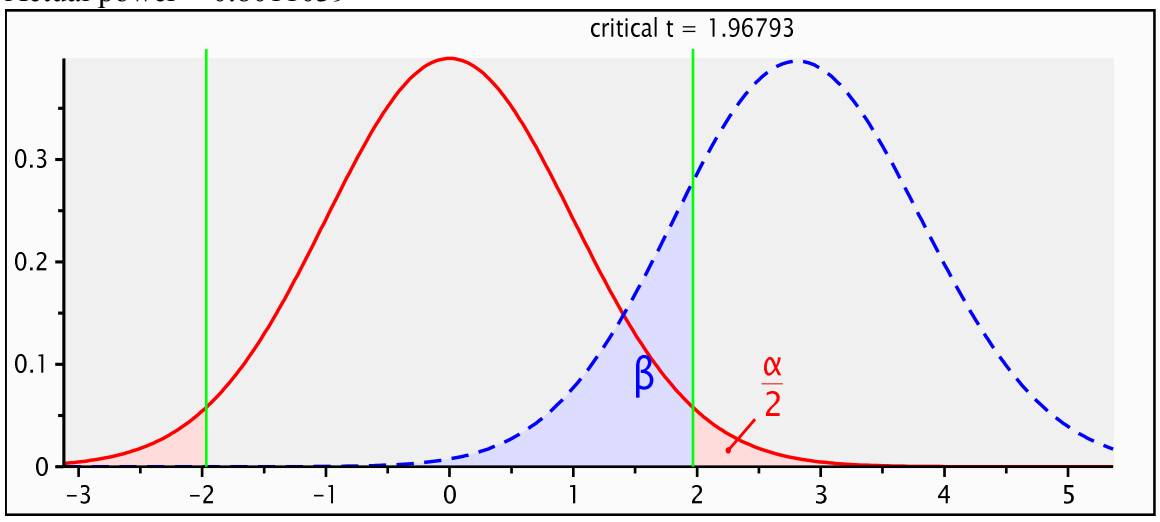
Appendix H: Representation of the Two Population Proportions After Adjustment

	Results				
	Family MD	Internal Medicine MD	Pediatrician MD	Other (i.e. Emergency MD)	***Row Totals***
Frequencies of PCPs of 2006 in the study of J&F	57 (56.00) [0.02]	113 (118.50) [0.26]	107 (100.50) [0.42]	8 (10.00) [0.40]	285
Frequencies of 2015 adjusted in this study	55 (56.00) [0.02]	124 (118.50) [0.26]	94 (100.50) [0.42]	12 (10.00) [0.40]	285
Column Totals	112	237	201	20	**570 (Grand Total)**

The Chi-square statistic is 2.1871. The *p*-value is .534502. The result is *not* significant at $p < .05$. (dependent variable).

Appendix I: G*Power Analysis Findings

t-tests :Means: Difference from constant (one sample case)
Analysis: a priori: Compute required sample size
Input: Tail(s) = two
Effect size (d)= 0.1625
α err prob = 0.05
Power (1-β err prob)= 0.80
Output: Noncentrality parameter δ = 2.8145826
Critical t= 1.9679297
df=299
Total sample size = 300
Actual power = 0.8011039



Note. Source from Erdfelder et al. (2007). Retrieved from

https://link.springer.com/article/10.3758/BRM.41.4.1149