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Prevalence of Lyme Disease Across the United States with a Focus on Pennsylvania

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Abstract

The focus of this study is on the prevalence of Lyme disease and the common factors that contribute to this prevalence. *Borrelia burgdorferi*, hereafter referred to as *B. burgdorferi*, is the bacterium that causes Lyme disease. *B. burgdorferi* is a zoonotic bacterium found in *Ixodes scapularis*, commonly referred to as the Blacklegged tick or the deer tick. The purpose of this literature review is to analyze peer-reviewed resources to determine the prevalence of Lyme disease across the United States of America. An emphasis on Pennsylvania will be analyzed. Pennsylvania is the "ground zero" of this tick-borne disease. The common factors that may contribute to this prevalence is also established. Determining prevalence allows us to understand the extent to which the disease is impacting citizens of the United States. This is the first step in determining how to prevent or eliminate Lyme disease altogether an important concept due to the detrimental effect that Lyme disease can have on both humans and animals when diagnosed. Finally, treatment and control options are also reviewed.

Abbreviations: Borrelia burgdorferi; Spirochete bacterium; Ixodes scapularis; Lyme disease; Prevalence; Zoonotic; Vector; Reservoir host; Endemic; Acaricide.

Introduction

Lyme disease is an inflammatory disease caused by the spirochete bacterium *B. burgdorferi*. *B. burgdorferi* is listed in the Order *Spirochaetales* and the Family *Spirochaetaceae* [1] and is spreading rapidly across the United States [2]. Lyme disease is zoonotic, which means it can be spread between animals and humans [3]. Commonly, cases pop up in late spring or the summer months [1].

Lyme disease first became apparent in 1975 in Lyme, Connecticut, when local children started to become diagnosed with rheumatoid arthritis [4]. In 1982, this diagnosis led to the discovery of the bacterial infection, Lyme [4]. Since 1991, Lyme disease has been a "nationally notifiable condition in the United States" so that the disease can be monitored and surveyed over time [5]. In turn, every case must be reported when diagnosed in humans [1].

Since Lyme disease is a vector-borne disease, it requires a pathogen bacteria, viral or parasitic to survive and transmit [6]. In the lecture given by Roopnarine, the risk of zoonotic infection requires both a biological vector and a reservoir host [1]. In terms of Lyme disease, the biological vector is a tick referred to as *I. scapularis*. A long list of wild animal species are the reservoir hosts [1]. *Ixodidae* ticks are commonly referred to as the Blacklegged tick or more often, the deer tick [7].

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Research question

What is the prevalence of Lyme disease across the United States of America and how does this compare to the prevalence within Pennsylvania?

Review of literature

Materials and methods

Searches regarding medical literature were designed to compare the species of ticks across the United States and the presence of Lyme disease within those ticks. Common factors that contribute to the prevalence of ticks that carry Lyme disease were also discussed.

Performed was a Boolean search of Medline through PubMed. Embase, a biomedical research engine, was also utilized. MayoClinic and MedicineNet were used to identify the causes and symptoms of Lyme disease for the introduction aspect of this research. Many research articles for the analysis section of this literature review were obtained through google scholar. Keywords including "Lyme disease", "*Borrelia burgdorferi*", "Pennsylvania" and "prevalence". For Medline, the first search contained "*Borrelia* OR Lyme" AND "prevalence" AND "United States" OR "America" OR "ticks". Articles were only included in the reported prevalence within the United States, if they reported the number of ticks present across the United States and/or they contained similar factors relative to possible transmission of Lyme Disease. Articles that were excluded were those with other tick-borne diseases not relevant to Lyme Disease or those containing data outside of the United States.

Databases are restricted to a time length of articles within the past 15 years. Supporting appendices are within the past 20 years. Reference lists of each study have been searched and reviewed. Relevant articles, reviews and editorials had also been analyzed. Any results that lack peer review or sufficient detail to analyze the observation of the article, were excluded.

Analysis

Lyme disease is an important zoonotic disease across North America. It is known as the most common vector-borne disease in the United States [8]. According to Applegren and Kraus [9], annual cases of the disease have increased from 10,000 in 1991 to greater than 25,000 in 2014 [9]. Contributions to this increase prevalence also has to do with geographic expansion and an exponential increase in number of infected ticks [9]. Although it is still unclear what reasons there are for this expansion in geological spread of ticks, there are various factors that are evident. There are many changes in land use patterns, which includes reforestation and suburban development [10]. People are in closer contact with wildlife that carry ticks, including deer, mice and chipmunks [10]. Another factor is the climate change and its effect on seasonality for these ticks. In fact, according to the CDC [11], between 1993 through 2012, the risk of Lyme disease within the northeastern and upper midwestern United States has increased by 300% [10].

Studies are continually being done to understand the evolutionary battle between vector, host and pathogen. Pathogens continuously develop mechanisms to undermine the host immune system response to its' invasion [12]. Because of this, most research towards *B. burgdorferi* pathogenesis "has been devoted to understanding the mammalian host response to the bacterium" [12]. There are no known homolog of *B. burgdorferi* and other bacteria [12]. Several reviews have been established in the article titled *Lyme Disease: Recent Advances and Perspectives,* to analyze "the most recent advances and future studies to be undertaken in the field of *B. burgdorferi* biology" [12].

Lyme disease and its effects on humans

Most humans contract Lyme through a bite of an infected immature tick. An immature tick is called a nymph. Nymphs generally feed through the spring and summer months [3]. This vector borne disease has tripled over the last two decades and has affected around 300,000 Americans annually across the United States [2]. Lyme disease can affect the central nervous system, muscles, eyes, joints and the heart [13]. In turn, Lyme may lead to fatigue, rashes, achy joints, headaches, fevers, sleep disturbances, cognitive decline and neurological problems.

Signs of Lyme disease may begin between three to 30 days post-exposure or may not show until months later. However, it is important to recognize that the tick requires 24 hours of skin exposure prior to releasing the spirochete bacteria into the bloodstream of its victim [1]. The first common sign of Lyme includes a classic *Erythema migrans* rash. This rash occurs in approximately 70-80% of infected persons within the first three to 30 days [14]. The rash appears as a small red bump that forms into a bullseye appearance [14].

Lyme disease and its effects on animals

The way in which Lyme disease effects animals is extremely similar to its effects on humans. Dogs are the prime species that will develop Lyme due to their frequent exposure to ticks. Of all the dogs that live in endemic regions of the United States, 75% of them are exposed to infected ticks [15]. Cats, cattle and horse are also at risk. The main clinical sign reported in dogs when positive for Lyme disease include a sense of generalized pain with a decreased appetite [16]. Swollen joints, lameness and fever are also reported. However, 95% of seropositive dogs will not show any signs of disease [1]. Unlike their human relatives, the bulls-eye rash is not commonly found in animals. Finally, non-specific signs of Lyme include its direct effect on the kidneys due to chronic disease because of formation of antigen-antibody complexes within the glomerulus [1]. Anorexia, lethargy, vomiting and weight loss can also be found [16].

Pennsylvania as "Ground Zero"

In 2018, the CDC provided information regarding the number of cases across the United States, by region, and subdivided into states (See appendix A). In 2018 alone, the United States reported a total of 33,666 cases-23,558 were confirmed and 10,108 were probable [5]. The Mid-Atlantic area, which includes New York, New Jersey and Pennsylvania, had the highest number of cases at 17,846 [5]. Pennsylvania was responsible for 57% of these cases at 10,208-7,920 of which were confirmed and 2,288 were probable [5]. The total number of confirmed cases in Pennsylvania from the years 2000 through 2016 was 87,852 [17] (See appendix B). However, the unconfirmed occurrence of Lyme disease is far greater [17].

Due to this data, Pennsylvania is commonly referred to as "ground zero" for the disease because it has consistently displayed the highest number of cases over the years for a variety of reasons. In fact, the total number of confirmed cases in Pennsylvania from 2000 through 2018 is 106,718 [17]. Due to the occurrence of unconfirmed cases, "Reports of Lyme Disease" [17] actually estimates a total of 1,067,180 true cases total throughout Pennsylvania.

Contributing factors

Of the 900 worldwide species of ticks, Pennsylvania is home to at least 25 different species. One of these 25 species is the Blacklegged tick. The Blacklegged tick commonly feeds on mice, chipmunks, birds, raccoons, black bear and white-tailed deer [7]. The two most common reservoirs for Lyme disease are white-footed mice and white-tailed deer [1]. All of these animals are commonly reside throughout Pennsylvania.

According to a 2019 report by the Quality Deer Management Association, "Pennsylvania antlered deer harvest increased from 137,580 in 2015 to 163,750 in 2017, a year when 23 of every 100 hunters in the state took a buck" [18]. In fact, Pennsylvania is the only state to annually harvest 300,000 white-tailed deer [18]. The white-footed mouse is known as the "most successful mammal in Pennsylvania" [19], because it can thrive in the climate and habitats provided in the state. The high population of both these animals make Pennsylvania a breeding ground for the Blacklegged tick.

Pennsylvania is the only state that is known for its 17 million acres forest coverage [20]. This commonwealth is covered with more than 60 percent of its area in deep forests [20], with urban trees and community woodlots in between (See appendix C). In fact, the name Pennsylvania translates in Latin to "Penn's Woods" [20]. This geographical uniqueness contributes to the vast population of wildlife hosts for the Blacklegged tick to survive on and the landscape for it to survive in.

Appendix A

The following figure was taken from the Centers for Disease Control and Prevention under the article titled Lyme Disease Maps: Most Recent Year [35].

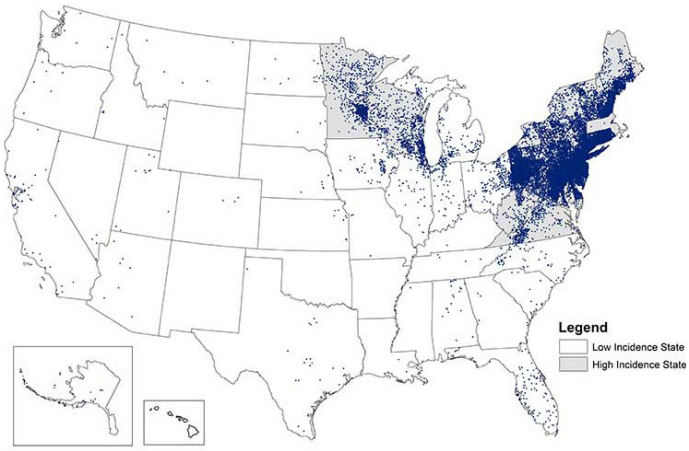

Figure 1: Each dot represents one confirmed case within that county of residence [35].

Appendix B

The following figure was taken from the *Pennsylvania Task Force Report on Lyme Disease in Pennsylvania* [34].

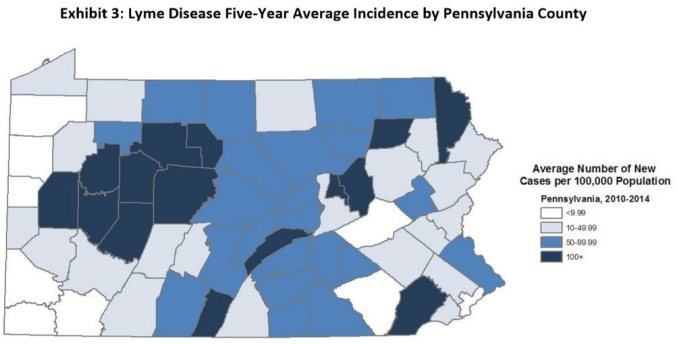

Figure 2: Lyme disease prevalence in Pennsylvania counties from 2010-2014 [34].

Appendix C

Each figure was taken from the Northern Research Station-Forest Inventory and Analysis research bulletin titiled *Pennsylvania's Forest 2004* [37].

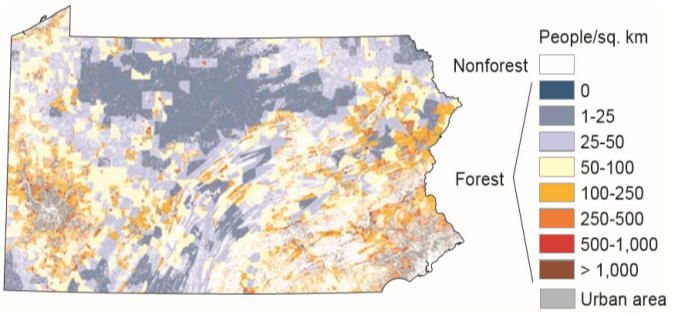

Figure 3: Each dot represents one confirmed case within that county of residence [35].

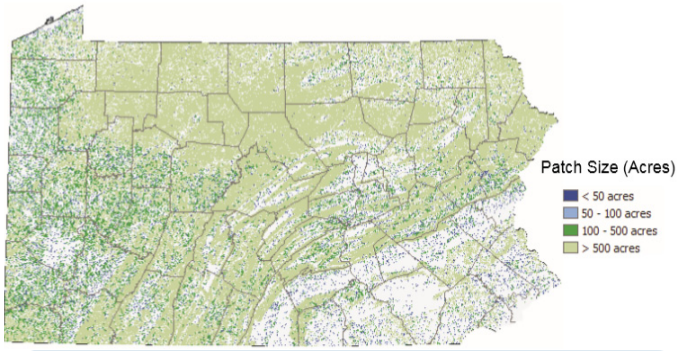

Figure 3a: Average forest patch size, Pennsylvania, 2000 [37].

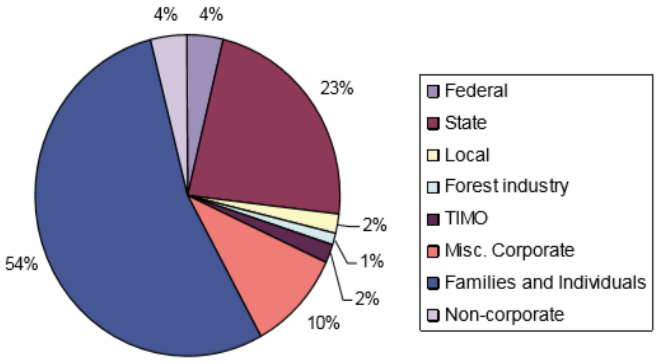

Figure 3b: Forest ownership in Pennsylvania, 2004 [37].

Findings

In 2003, a study was released that analyzed the ticks in Pennsylvania to test for the presence of both *Anaplasma pagocytophilum* and *B. burgdorferi*, through both PCR and DNA sequencing [21]. Ticks were collected in Northwestern and Southeastern Pennsylvania. In respects to *B. burgdorferi*, 162 of 263 ticks collected in the Northwest and 25 of 191 ticks collected in the Southeast were all confirmed positive [21]. In April 2014, another research article was released that determined the prevalence of *B. burgdorferi* across Pennsylvania. From 2012 through 2014, 1,855 adults *I. scapularis* ticks were collected across the 67 statewide counties [22]. All 67 counties confirmed the presence of *I. scapularis* positive with *B. burgdorferi*.

From 2014 into 2015, seasonal activity of *I. scapularis* was studied over the course of one year in the mid-western part of Pennsylvania. This location was chosen due to lack of research of that area prior. Larvae, nymphs and adult ticks were all analyzed. Seasonal activity of larvae and nymphs were similar in the Midwest as in the Northeast [23]. Pre- and post-winter density of adult ticks were comparable and not significantly different [23] across the Midwest as in the Northeast.

A study was done over the course of six years on the white-footed mice population in Pennypack Ecological Restoration Trust located in Huntingdon, Pennsylvania. This study was done to prove a hypothesis that if the population of mice was high, then that would correlate with a high incidence of Lyme disease [24]. Following the mark-recapture method, any mice caught were studied, released and potentially recaptured again. Seasonal changes were also analyzed. The population of mice fluctuated over the years. However, cases of disease reported by the CDC did not fluctuate in correspondence to the changes in mice population [24]. Additionally, the seasonal weather pattern data showed that "incidence of Lyme disease decreases as rainfall in the autumn and winter increase" [24]. Overall, this data found rejects the hypothesis that disease incidence correlates to mice population [24].

Although Lyme is responsible for causing hundreds of thousands of people annually to become sick, this does not mean every diagnosis is lethal. In fact, Lyme disease being noted as cause of death is rare [10]. To come to this conclusion, the National Center for Health Statistics (NCHS) reviewed records from 1999 through 2003 that were shared by the International Classification of Diseases (ICD) [10]. The year 1999 was chosen because that was the first year in which Lyme was listed under a unique code as a potential cause of death on death certifications [10]. During these four years, Lyme contributed to the death of 119 records from 25 states [10].

Limitations

Routine surveillance is a huge limitation when it comes to studying tick-borne diseases and their caseload. As mentioned previously, the number of predicted unconfirmed cases expands much greater than the confirmed cases. The chief for the CDC epidemiology and surveillance committee, Dr. Paul Mead, explains that the "routine surveillance only gives us part of the picture and that the true number of illnesses is much greater" [25]. Due to this, the urgency of this public health crisis is difficult to bring attention to when the numbers are not representing truly how impactful this disease can become.

There was limited data collected in the Clark [24] study regarding mice population in Pennypack and not enough years were covered. This is a huge limitation seen across the board in many of these studies analyzed. Also, it is important to note that multiple host populations must be studied, not just one individual host. *I. scapularis* has two primary hosts – the white-footed mouse and the white-tailed deer. It is unrealistic to compare disease incidence to one host species without considering the population of the other host species during the same time-period. Implementing this restriction does not make for true results. For example, if there was a fluctuation in deer population during that time period, this may have also influenced the number of ticks available to spread disease.

Conclusion

There are several efforts that have been implemented by the task force of Pennsylvania to educate the public regarding Lyme disease. All these efforts, and more, can be found in the text titled "Lyme Disease in Pennsylvania", reported by the Task Force on Lyme Disease and Related Tick-Borne Diseases-Pursuant to Act 83 of 2014. These efforts include education and awareness, prevention and surveillance [26]:

- Education & Awareness: National campaigns, curriculum/programming in a few schools, advocacy groups (PA Lyme Resource Network, etc.) focused on community-based work, some school-based and community-based program successes. Tick-borne and other chronic infections research and practice – Drexel University College of Medicine Conference March 2015

- Prevention: CDC signage posted in PA State Parks and State Forest Districts in spring 2015, 2015 PADOH community outreach campaign, ongoing community outreach conducted by the Chester County Department of Health and Philadelphia Department of Public Health.

- Surveillance: Existing infrastructure for human TBD surveillance by PADOH and tick surveillance by PADEP. Entomology departments at East Stroudsburg University, Indiana University, Shippensburg University, Penn State and other colleges in PA also have the capacity to support tick field surveys.

A study was done from 2013 through 2015 that focused on the number of *I. scapularis* ticks present on white-tailed deer that were harvested across Pennsylvania. Of the 9,912 deer harvested, 66.9% of their ticks were Blacklegged ticks. This high percentage reconfirms that *I. scapularis* is the most prevalent tick across that state and is commonly found on deer [27]. Utilization of PCR analysis and DNA extraction from these collected ticks plays a critical role in determining the presence of the bacterium [21]. According to Courtney et al. [21], "this approach provides a rapid means for assessing the risk of Lyme disease… residing in the areas sampled." Also determined through this study was that it is extremely likely that the confirmed cases do not come close to the actual cases present in the area [21].

Regarding the April 2015 article that determined the prevalence rates of *B. burgdorferi* across the 67 counties of Pennsylvania, Hutchinson et al. [22] concluded their findings "substantiate that Lyme disease risk is high throughout Pennsylvania." In terms of the seasonality study written by Simmons et al. [23], it was concluded that the population of *I. scapularis* in mid-western Pennsylvania is similar to southeastern New York State and generously contributes to the high Lyme disease risk in the Northeast section of the United States [23].

As mentioned previously, Lyme rarely plays a role in direct cause of death. For those who did die while having been di-

agnosed with this disease, the underlying cause is due to "the disease or injury which initiated the chain of morbid events leading directly to death" or "any other significant condition which contributed to the fatal outcome, but was not related to the disease or condition directly causing death" [10]. Of the 119 deaths mentioned previously, Lyme was "coded as an underlying or multiple cause of death" [10], which means the symptoms that are a result of this disease can be detrimental.

Disease transmission

As mentioned previously, a tick must bite its host to transmit disease. With this bite, it is the tick's saliva that carries the bacterial pathogen during blood feeding [28]. However, not only does the tick need saliva for the transmission process, but it also undergoes something called Saliva-Assisted Transmission (SAT) [28]. Through SAT, ticks can maintain homeostasis while feeding [28]. Ever since it has been discovered, this concept has aided researchers in the development of vaccination [28].

Preventative measures

There are multiple preventative measures that have been utilized to prevent contracting Lyme in both humans and domestic animals. Vaccines are a common preventative method against Lyme disease in animals, but further research studies are needed in use on humans [4]. Ultimately, to prevent humans from being exposed to the disease, doctors recommend the following three methods:

- Remove and destroy the tick immediately following discovery on the skin
- Spend less time in wooded or grassy areas
- Cover any exposed skin with clothing when outdoors

Pertaining to domestic animals, there are quite a few simple preventative measures recommended. First, the most important method of prevention is keeping your pet from being exposed. However, this is not always easy, being that many dogs spend most of their lives outdoors. Avoiding walking your dog through woody, sandy and grassy areas may help [16]. Another important preventative measure was mentioned above vaccination. The Nobivac Lyme vaccine is a product of Merck. It targets the two key outer surface proteins, Osps, at the cellular level [29]. These proteins play a huge role in disease transmission [29]. Nobivac induces borreliacidal antibodies by forming a complex at these two proteins along the cell membrane [29]. In turn, it kills *B. burgdorferi* [29].

Another form of prevention against ticks is the use of a reliable flea and tick preventative medication. These medications come in oral and topical forms, and must be prescribed by a veterinarian.

Finally, one other preventative measure that has been suggested is through deer population control. Since white-tailed deer play such a significant role in transmitting the disease, it has been assumed that reduction in deer population will reduce case load. A research article on this theory was published back in 2016, but states that it is "poorly understood" [30]. Although complete elimination of the species has resulted in a substantial reduction in Blacklegged ticks, wiping out this species is unrealistic and the reduction in population "yielded mixed results" [30]. In turn, Kugeler et al. [30] determined that there is "insufficient evidence to recommend deer population reduction as a Lyme disease prevention measure, except in specific ecologic circumstances" [30].

Control and treatment

Overall, tick treatment and control options are few and far between. Many are expensive or require ecological interventions that may interfere negatively with natural agriculture or wildlife through acaricide spraying [31]. Acaricides play a role in killing ticks. An alternative to tick control that may be detrimental to nature are the use of tick tubes cotton treated formulations of acaricides located within cardboard tubes as a means of providing nesting material for tick hosts [31].

Since *B. burgdorferi* is a bacterial pathogen, the use of antibiotics as a treatment method in both humans and dogs has been successful. However, the sooner treatment starts, the greater chance of a full recovery [32]. There are two methods of administering antibiotics through oral and intravenous routes. Oral antibiotics are the standard treatment of choice if a patient is suffering from "early-stage Lyme disease" [32]. Oral medications are normally administered for 14-21 days; these include doxycycline, for use in adults and children older than 8 years old, and amoxicillin or cefuroxime, for use in younger children, adults, pregnant or breast-feeding women [32]. Regarding intravenous medications, these are used when the disease has started to directly affect the central nervous system and are administered for 14-28 days full recovery may take a bit longer [32]. Even after receiving a course of antibiotics, 10-20 % of people remain sick [33]. Any symptoms that do not dissipate after treatment are termed "post-Lyme disease syndrome" [32]; there is no full recovery after that point.

Funding and current research

Unfortunately, Lyme disease research has always been severely underfunded. In 2019 alone, the National Institutes of Health (NIH) spent $23 million on Lyme disease research and an additional $56 million on studying all tickborne diseases [33]. In 2018, a report was written to emphasis the exponential threat tickborne diseases are making in our lives it mentions that cases of Lyme disease has tripled since the 1990s and also mentions what effects the disease has on our health, animal habitats and other ecologic shifts it has made [33]. This further proved the need for continued research into tickborne diseases.

Scientist in individual laboratories require funding from the "NIH and CDC for diagnostic and treatment research" [33]. Due to the persistence of scientists' call for help, the CDC's budget on Lyme has grew from $10.7 million to $12 million the first increase seen in the past five years [33]. $6 million was funded through the National Institute of Allergy and Infectious Diseases (NIAID) and prioritizing vaccinations was at the top of their list [33]. Previously, a vaccine used for humans was 80% effective [33]. However, in 2002, it was pulled from the market due to safety concerns [33].

Asides from vaccination, others are putting their research into both pesticides and tick-filling funguses [33]. Finally, understanding just how *B. burgdorferi* persists in treated patients has been the key focus in other foundations [33].

Summary

This literature review analyzed important key points about Lyme disease. In 2018, the United States faced over 30,000 reported cases. However, researchers believe the unreported cases reach well over six figures. Pennsylvania alone accounted for 30% of these cases. Pennsylvania is known as the "ground zero"

of Lyme disease due to its high prevalence within the state. Some factors that are responsible for this high prevalence include forest coverage, climate and wildlife population, to name a few.

When infected with Lyme disease, it can have serious implications to one's health. Humans have a limited number of preventative measures they can undergo. Although these measures are simple, they are not always ideal depending on their lifestyle. Pertaining to domestic animals, there are plenty more preventative options that are commonly used. To date, only domestic animals have safe and effective vaccinations available for their owners to use on them as a preventative measure. Acaricides used in the environment is a popular control option utilized, but it can have an unintended negative impact on nature. Oral and intravenous antibiotics must be administered as a treatment option. However, many patients may suffer from a chronic condition and never fully recover even after undergoing serious treatment [38,39].

Finally, researchers have invested millions of dollars every year to help aid their studies in tickborne diseases. Although they are severely underfunded, they rely heavily on money from well known corporations to help with this research. Lyme is an ongoing disease that will never be eliminated. Its detrimental effects it can take on an individual is life changing and it is a disease that must be taken seriously.

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