Lyme Disease

Identification

1. Indicator Description

This indicator looks at the incidence of Lyme disease in the United States since 1991. Lyme disease is a tick-borne bacterial illness that can cause fever, fatigue, and joint and nervous system complications. It is one of several tick- or mosquito-borne diseases that the Centers for Disease Control and Prevention (CDC) tracks (www.cdc.gov/vitalsigns/vector-borne/index.html; Rosenberg et al., 2018). The spread of Lyme disease is affected by tick prevalence; populations and infection rates among host species; human population patterns, awareness, and behavior; habitat; climate; and other factors. Examining Lyme disease incidence may be useful for understanding the long-term effects of climate change on vector-borne diseases, as shorter-term variations in weather have less of an impact on ticks than on other disease vectors such as mosquitoes. This is the case for several reasons (Ogden et al., 2013):

- Ticks have a relatively long-life cycle, including stages of development that take place in the soil, where temperatures fluctuate less than air temperatures.
- Tick development rates have a delayed response to temperature changes, which minimizes the effects of short-term temperature fluctuations.
- Ticks can take refuge in the soil during periods of extreme heat, cold, drought, or rainfall.
- Ticks are associated with woodland habitats, where microclimates are buffered from temperature extremes that occur in treeless areas.
- Unlike other disease vectors such as mosquitoes, ticks do not have nonparasitic immature feeding stages whose survival is susceptible to short-term changes in weather.

Consequently, in some locations in the United States, Lyme disease incidence would be expected to increase with climate change.

Components of this indicator include:

- Annual incidence of Lyme disease in the United States (Figure 1).
- Change in reported Lyme disease incidence in the Northeast and Upper Midwest (Figure 2).
- Change in incidence and distribution of reported cases of Lyme disease in the Northeast and Upper Midwest (1996 and 2018 maps).

2. Revision History

May 2014:	Indicator published.
June 2015:	Updated indicator with data through 2013.
August 2016:	Updated indicator with data through 2014.
April 2021:	Updated indicator with data through 2018.

Data Sources

3. Data Sources

This indicator is based on annual numbers of confirmed Lyme disease cases, nationally and by state, compiled by CDC's Division of Vector-Borne Diseases. Incidence was calculated using the most recent mid-year population estimates for each year from the U.S. Census Bureau. The 1996 and 2018 comparison maps also came from CDC.

4. Data Availability

All of the data for this indicator are publicly available on CDC and Census Bureau websites.

EPA obtained the data for this indicator from CDC's website. Prior to 2008, CDC compiled only confirmed cases, but in 2008 it also began to track probable (but unconfirmed) cases. CDC's database allows users to query just the confirmed cases, which EPA used for this indicator.

Although data are available for 1990, this indicator starts in 1991 because Lyme disease did not become an official nationally reportable disease until January 1991. In 1990, some states reported Lyme disease incidence using the standardized case definition that went into effect nationwide in 1991, but other states did not.

CDC's national and state-level data are available online. Through the years, these data have been published in CDC's Morbidity and Mortality Weekly Reports (MMWR), which are available at: www.cdc.gov/mmwr/mmwr_nd/index.html. Data from 2009 onward are also available in tabular form at: www.cdc.gov/lyme/stats/tables.html. Beginning in 2016, these data are published on the National Notifiable Disease Surveillance System (NNDSS) Data and Statistics webpage at: https://wonder.cdc.gov/nndss/nndss_annual_tables_menu.asp. Underlying county-level data are not available publicly—or they are combined into multi-year averages before being made publicly available—because of concerns about patient confidentiality. Annual maps of reported cases of Lyme disease, as shown in the 1996/2018 comparison for this indicator, and statistics are also posted online at: www.cdc.gov/lyme/datasurveillance/index.html.

Following CDC's standard practice, incidence has been calculated using population estimates on July 1 of each calendar year. These population estimates are publicly available from the U.S. Census Bureau's Population Estimates Program. Data are available at: www.census.gov/programs-surveys/popest/data/tables.All.html.

Methodology

5. Data Collection

This indicator is based on the annual reported number of Lyme disease cases as compiled by CDC.

State and local health departments report weekly case counts for Lyme disease following CDC's case definitions through the NNDSS. The NNDSS is a public health system for the reporting of individual cases of disease and conditions to state, local, and territorial health departments, which then forward case information to CDC. The provisional state-level data are reported in CDC's MMWR. After all states have verified their data, CDC publishes an annual surveillance summary for Lyme disease and other notifiable diseases.

Health care providers nationwide follow a standardized definition for what constitutes a "confirmed" case of Lyme disease, but this definition has changed over time (see Section 8). The first standardized surveillance case definition was established in 1990 by the Council of State and Territorial Epidemiologists (CSTE). In January 1991, Lyme disease became a nationally notifiable disease in the United States, using the CSTE's 1990 definition. As such, state and local health departments work with health care providers to obtain case reports for Lyme disease based upon the CSTE case definition.

6. Indicator Derivation

Figure 1. Reported Cases of Lyme Disease in the United States, 1991–2018

National incidence of Lyme disease was calculated using the total number of confirmed Lyme disease cases and the national population for each year from 1991 through 2018. EPA calculated incidence by dividing the number of confirmed cases per year by the corresponding population on July 1 in the same calendar year. EPA then multiplied the per-person rate by 100,000 to generate a normalized incidence rate per 100,000 people. This is CDC's standard method of expressing the incidence of Lyme disease.

Figure 2. Change in Reported Lyme Disease Incidence in the Northeast and Upper Midwest, 1991–2018

EPA used ordinary least-squares linear regression to determine the slope of the trend over time for each state. Of the 50 states plus the District of Columbia, 42 have a long-term linear trend in Lyme disease incidence that is statistically significant to a 95-percent level, and 36 have trends that are significant to a 99-percent level. Many of these trends, however, have a very small slope. Taking the regression slope (the annual rate of change) and multiplying it by 27 years (the length of the period of record) to estimate total change, 26 states had a total change of less than 1 case per 100,000 in either direction.

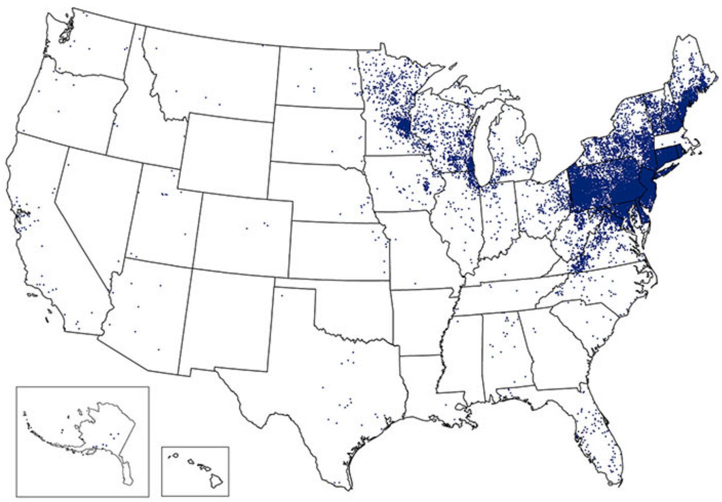
In this analysis, 15 states stand out because they have Lyme disease rates more than 10 times higher than most of the other states, with average rates of more than 10 cases per 100,000 per year during the most recent five years of data. These 15 states are:

- Connecticut
- Delaware
- Maine
- Maryland
- Massachusetts
- Minnesota
- New Hampshire
- New Jersey
- New York
- Pennsylvania
- Rhode Island
- Vermont
- Virginia

- West Virginia
- Wisconsin

Together, these 15 states account for about 95 percent of the nation's reported cases of Lyme disease in 2018, as the map in Figure TD-1 indicates. Note that Massachusetts shows almost no cases in Figure TD-1, but the state has historically had relatively high case numbers, and Lyme disease is still prevalent there. It is just underreported to CDC due to a methodological issue described below.

Figure TD-1. Reported Cases of Lyme Disease in the United States, 2018



Data source: CDC: www.cdc.gov/lyme/stats/maps.html. Accessed January 2021.

Figure 2 shows the total change (annual rate of change [regression slope] multiplied by 27 years) for the states listed above, except Connecticut, Massachusetts, New York, and Rhode Island. These four states have historically had a high incidence of Lyme disease, and they continue to rank among the most impacted states, collectively representing about 19 percent of the nation's reported cases of Lyme disease in 2018. However, these four states have experienced sizable year-to-year variation in surveillance and reporting practices during the period of record, including a few documented methodological changes that have occurred as a result of resource constraints or other factors. Specifically:

- Connecticut and Rhode Island reduced reporting requirements in 2003 and 2004, respectively.

- Starting in 2016, Massachusetts reduced its emphasis on clinician follow-up on positive laboratory reports. Because the CSTE case definition requires clinician follow-up, positive laboratory results without follow-up are not reported to CDC.

- Some counties in New York have switched to estimating Lyme cases instead of direct counting. As of 2016, state totals reported to CDC excluded 30 counties that estimate their cases. Excluding these counties has led to an apparent (but likely false) decrease in CDC's official number of cases for New York over the period of record covered by this indicator.

These four states have been excluded from Figure 2 because the reporting changes described above are sufficient to diminish confidence in any apparent state-level trends. See the footnotes at: https://lymediseaseassociation.org/LDA_Apps/content/Maps/pdf/data_1990to2018detail.pdf for more discussion on the changes in these states, as well as changes in a few other states that have not yet led to apparent irregularities in the data.

Reported Lyme Disease Cases in 1996 and 2018

This comparison uses two maps—one for the year 1996 and one for the year 2018—to illustrate changes in the incidence and distribution of reported cases of Lyme disease in the United States over time. CDC created these maps. Each dot on the maps represents an individual case placed randomly within the patient's county of residence, which may differ from the county of exposure.

Indicator Development

In the course of developing and revising this indicator based on peer review and comments from CDC experts, EPA considered several ways to present the data. For example:

- The incidence of a disease can be tracked with total case counts or with incidence rates that are normalized by population size. EPA chose to display rates for this indicator so as to eliminate state-to-state population differences and changes in population over time as confounding factors. This approach is also consistent with data for EPA's Heat-Related Deaths indicator, which is displayed using incidence rates.

- EPA considered focusing the analysis of reported Lyme disease on a subset of states. One approach was to consider "reference states" as defined by CDC (e.g., www.cdc.gov/mmwr/pdf/ss/ss5710.pdf). Upon clarification from CDC, however, this set of reference states has not been used operationally since CDC's Healthy People 2010 effort, which concluded in 2010, and they do not necessarily represent a consistent baseline from which to track trends. EPA chose to use more objective, data-driven thresholds for selecting states to show readers the change in reported Lyme disease incidence as in Figure 2. However, there is scientific evidence (e.g., Diuk-Wasser et al., 2012; Stromdahl and Hickling, 2012) that notes the geographic differences in *Ixodes scapularis* (the deer tick or blacklegged tick) in North America—and that increases in Lyme disease cases in many states south of 35°N latitude are likely due to non-climate-related expansion of northern *I. scapularis* tick genotypes. Analyzing data for a set of states in the northern part of the range of *I. scapularis* might lead to better understanding of changes in Lyme disease cases as they relate to a warming climate. Thus, future work on this indicator will attempt to reflect the effects of climate change on expansion in the range of *I. scapularis*, increasing abundance of *I. scapularis* where it already occurs, increases in the prevalence of *Borrelia burgdorferi* (the bacteria that actually cause Lyme disease) in host-seeking ticks, and/or updated understanding of other known environmental drivers, such as deer density and changes in landscape, habitat, and biodiversity.

- EPA considered mapping rates or trends by county; however, county-level case totals are only publicly available from CDC in five-year bins, in part because of the very low number of cases reported in many counties.

7. Quality Assurance and Quality Control

Each state has established laws mandating that health providers report cases of various diseases (including Lyme disease) to their health departments. Each state health department verifies its data before sharing them with CDC. The NNDSS is the primary system by which health surveillance data are conveyed to CDC for national-level analyses.

Starting in 1990, CDC launched the National Electronic Telecommunications System for Surveillance (NETSS), replacing mail and phone-based reporting. In 2000, CDC developed the National Electronic Disease Surveillance System (NEDSS) Base System (NBS). This central reporting system sets data and information technology standards for departments that provide data to CDC, ensuring that data are submitted quickly, securely, and in a consistent format.

Using CSTE case definitions, CDC provides state and local health departments and health providers with comprehensive guidance on laboratory diagnosis and case classification criteria, ensuring that all health providers and departments classify Lyme disease cases consistently throughout the United States.

State health officials use various methods to ascertain cases, including passive surveillance initiated by health care providers, laboratory-based surveillance, and “enhanced or active surveillance” (Bacon et al., 2008). State officials check the data and remove duplicate reports before submitting annual totals to CDC.

CDC has undertaken a review of alternative data sources to see how closely they align with the disease counts captured by the NNDSS. These alternative sources include medical claims information from a large insurance database, a survey of clinical laboratories, and a survey that asks individuals whether they have been diagnosed with Lyme disease in the previous year. Results from this review suggest that the NNDSS may be undercounting the true number of cases of Lyme disease (CDC, 2013). A more recent analysis based on insurance data came to a similar conclusion (CDC, 2021). See Section 10 for further discussion about this possible source of uncertainty.

Analysis

8. Comparability Over Time and Space

Lyme disease data collection follows CDC’s case definition to ensure consistency and comparability across the country. The national case definition for Lyme disease has changed several times since Lyme disease became a notifiable disease: in 1996, in 2008, and (less significantly) in 2011 and 2017. Prior to 1996, a confirmed case of Lyme disease required only a skin lesion with the characteristic “bulls-eye” appearance. In 1996, CDC expanded the definition of confirmed cases to include laboratory-confirmed, late-manifestation symptoms such as issues with the musculoskeletal, nervous, and cardiovascular systems. In 2008, the case classifications were expanded again to include suspected and probable cases.

These definition changes necessitate careful comparisons of data from multiple years. While it is not possible to control for the case definition change in 1996, CDC provides the numbers of confirmed cases and suspected and probable cases separately. The granularity of the data enables EPA to use confirmed cases in the incidence rate calculation for all years and exclude the probable cases that have been counted since 2008, ensuring comparability over time.

In addition to the national changes, several state reporting agencies have changed their own data collection and reporting practices at various times. These state-level changes include California in 2005, Connecticut in 2003, the District of Columbia in 2011, Hawaii in 2006, New York in 2007, and Rhode Island in 2004. The extent to which these changes affect overall trends is unknown, but it is worth noting that Connecticut and Rhode Island both have apparent discontinuities in their annual totals around the time of their respective definitional changes, and these two states have statistically insignificant long-term trends, despite other northeastern states having statistically significant increases. Because of these types of state-level uncertainties, Figure 2 only shows state-level trends for 11 states that had relatively consistent reporting practices over time and no obvious irregularities upon inspection of the data. These 11 states all experienced statistically significant ($p < 0.05$) total increases of 10 to 110 cases per 100,000 between 1991 and 2018.

9. Data Limitations

Factors that may have an impact on the confidence, application, or conclusions drawn from this indicator are as follows:

1. For consistency, this indicator includes data for only confirmed cases of Lyme disease. However, changes in diagnosing practices and awareness of the disease over time can affect trends.

2. CDC’s national Lyme disease case definitions have changed multiple times since Lyme disease became a notifiable disease. As discussed in Section 8, it is not possible to control for the case definition change in 1996, which adds some uncertainty to the indicator. Some state agencies have also changed their data collection and reporting practices at various times, as described in Section 8.

3. As described in Section 10, public health experts believe that many cases of Lyme disease are not reported, which means this indicator underestimates the true incidence of the disease (CDC, 2013, 2021). The reporting rate may vary over time and space as a result of differences in funding and emphasis among state surveillance programs. In addition, Lyme disease can be difficult to diagnose. Cases in locations where Lyme disease is not endemic are at particular risk of being unidentified or misdiagnosed.

4. As an indicator of climate change, Lyme disease is limited due to several confounding factors:

    - Pest extermination efforts and public health education may counteract the growth of confirmed cases expected due to warming climates.

    - Importantly, there are several factors driving changes in incidence of Lyme disease other than climate. Several of these factors have not been well-quantified or studied. Possible factors include range expansion of vector ticks, which is not always climate-related; proximity of hosts; changes in deer density; changes in biodiversity; and the effects of landscape changes such as suburbanization, deforestation, and reforestation.

- Pathogen transmission is affected by several factors including geographic distribution, population density, prevalence of infection by zoonotic pathogens, and the pathogen load within individual hosts and vectors (e.g., Cortinas and Kitron, 2006; Lingren et al., 2005; Mills et al., 2010; Raizman et al., 2013).

- Human exposure depends upon socioeconomic and cultural factors, land use, health care access, and living conditions (Gage et al., 2008; Gubler et al., 2001; Hess et al., 2012; Lafferty, 2009; Wilson, 2009).

5. Lyme disease surveillance data capture the county of residence, which is not necessarily the location where an individual was infected.

10. Sources of Uncertainty

The main source of uncertainty for this indicator stems from its dependence on surveillance data. Surveillance data can be subject to underreporting and misclassification. Because Lyme disease is often determined based upon clinical symptoms, lack of symptoms or delayed symptoms may result in overlooked or misclassified cases. Furthermore, surveillance capabilities can vary from state to state, or even from year to year based upon budgeting and personnel.

Although Lyme disease cases are supposed to be reported to the NNDSS, reporting is actually voluntary. As a result, surveillance data for Lyme disease do not provide a comprehensive determination of the U.S. population with Lyme disease. For example, it has been reported that the annual total number of people diagnosed with Lyme disease may be as much as 10 times higher than the surveillance data indicate (CDC, 2013). Another analysis of medical insurance claims for Lyme disease diagnosis and treatment estimated 476,000 cases per year (CDC, 2021)—about 20 times the number of reported confirmed cases in 2018 according to the source data for this indicator. Consequently, this indicator provides an illustration of trends over time, not a measure of the exact number of Lyme disease cases in the United States.

Another issue is that surveillance data are captured by county of residence rather than county of exposure. Reports of Lyme disease may therefore occur in states with no active pathogen populations. For example, a tourist may be infected with Lyme disease while visiting Connecticut (an area with high incidence of Lyme disease) but not be identified as a Lyme disease case until the tourist returns home to Florida (an area where blacklegged ticks cannot survive). This may result in underreporting in areas of high Lyme disease incidence and overreporting in areas of low Lyme disease incidence.

For a discussion of the uncertainties associated with the U.S. Census Bureau's intercensal estimates, see: www.census.gov/programs-surveys/popest/technical-documentation/methodology.html.

11. Sources of Variability

The incidence of Lyme disease is likely to display variability over time and space due to:

- Changes in populations of blacklegged ticks and host species (e.g., deer, mice, birds) over time.
- Spatial distribution of blacklegged ticks and changes in their distribution over time.
- The influence of climate on the activity and seasonality of the blacklegged tick.

- Variability in human population over time and space.

This indicator accounts for these factors by presenting a broad multi-decadal national trend in Figures 1 and 2. EPA has reviewed the statistical significance of these trends (see Section 12).

12. Statistical/Trend Analysis

Based on ordinary least-squares linear regression, the national incidence rate in Figure 1 increases at an average annual rate of +0.18 cases per 100,000 people ($p < 0.001$).

Of the 11 states shaded in Figure 2, all had statistically significant increases in their annual incidence rates from 1991 to 2018 (all p-values substantially less than 0.01), based on ordinary least-squares linear regression. The shading in Figure 2 shows the magnitude of these trends. A broader analysis described in Section 6 found that more than half of the 50 states had significant trends in their annual incidence rates from 1991 to 2018, but most of these states were excluded from Figure 2 because their overall incidence rates have consistently been at least an order of magnitude lower than the rates in the 15 key Northeast and Upper Midwest states where Lyme disease is most prevalent.

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