

Economic Burden of Lyme Disease in High-Incidence Areas, United States, 2014–2016

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Sarah Hook, an epidemiologist at CDC in Fort Collins, Colorado. We'll be discussing the economic burden of Lyme disease in the United States.

Welcome, Dr. Hook.

[Sarah Hook] Thanks so much for having me. It's great to be here.

[Sarah Gregory] It doesn't hurt to remind people, what is Lyme disease?

[Sarah Hook] Sure. So I'll start by mentioning that May is Lyme Disease Awareness Month, and so this is the time of year when the ticks that transmit Lyme disease (blacklegged ticks) start becoming active. So we want everyone to be aware of that. But Lyme disease is the most common vector-borne disease in the US. And it's caused by the bacterium *Borrelia burgdorferi*, and this is spread to people, as just mentioned, through the bite of an infected blacklegged tick. And these ticks are most common in the Northeast, mid-Atlantic, and Upper Midwest. And infection with this disease can affect several organ systems and cause a range of symptoms, and often, though not always, it starts with a characteristic rash called erythema migrans.

[Sarah Gregory] Just for new listeners, remind us what a vector-borne disease is.

[Sarah Hook] Sure. So that is the disease that is transmitted by mosquitoes, ticks, fleas, or other arthropods.

[Sarah Gregory] And an arthropod is...?

[Sarah Hook] Sort of a fancy term for an insect or a bug. There are some nuances in there that the entomologists might be upset with me for not mentioning, but yeah, it's basically bug-transmitted illnesses.

[Sarah Gregory] Gotcha. So how many reported cases of Lyme disease are there every year in the United States?

[Sarah Hook] So since the late 90s, the number of reported cases in the US has tripled. So now we're seeing each year approximately 30,000 cases reported to CDC, and these are reported by state health departments or other public health jurisdictions, as I mentioned, where the blacklegged tick most often occurs. So over 90% of these cases are also reported from those same states in the Northeast, mid-Atlantic, and Upper Midwest. But because of underreporting, which we know is a common feature of Lyme disease and other surveillance, we know that this 30,000 per year number does not actually reflect every case of Lyme disease that is diagnosed in the US. And so recent estimates from some folks on our team suggest that there are approximately 476,000 people who are diagnosed by a clinician with Lyme disease each year in the US, so it really is quite a large problem.

[Sarah Gregory] That is actually a stunning number. I didn't even realize that.

How would a person know if they have Lyme disease? You mentioned the rash, but other things? And what if they don't notice the rash?

Economic Burden of Lyme Disease in High-Incidence Areas, United States, 2014–2016

[Sarah Hook] Yeah, I know. That's a good question. So besides the rash, other early symptoms include flu-like symptoms—so, fever, headache, fatigue. And because of the seasonality of ticks, often when you think of flu-like symptoms in the summer or in warmer months, it might be a good idea to think about Lyme disease. Later symptoms, particularly in untreated people, could include additional rashes, arthritis, joint pain, facial palsy, and then potentially even cardiac or neurologic issues. But, again, it's important to interpret these signs and symptoms within the context of likely exposure to these blacklegged ticks or a known recent tick bite. And besides recognizing the signs and symptoms, there are also FDA-cleared laboratory tests that can confirm infection with Lyme disease.

[Sarah Gregory] Okay. I was going to ask that, if there was a test for it. So there is a test, okay. So you mentioned getting treatment. What is the treatment?

[Sarah Hook] So Lyme disease is treated with antibiotics, and the exact treatment regimens are going to vary based on the symptoms experienced and how long the person has been ill. But people treated with appropriate antibiotics in the early stages of Lyme disease usually recover really well.

[Sarah Gregory] Alright. So you mentioned some pretty awful ramifications if people don't get treatment right away. Is there a window for that? I mean, how does this progress and does it always progress? So what happens to people that don't get treatment?

[Sarah Hook] Yeah. So if untreated, the bacteria can disseminate in the body and cause those later signs and symptoms. The neurologic and cardiac manifestations that we mentioned are certainly the more serious ones. Lyme carditis can be a serious result of disseminated disease. And even with these later stages, treatment is very effective. But we just want to underscore the fact that because of these serious manifestations, early diagnosis...well, prevention first, but then early diagnosis and quick treatment with antibiotics is the most important thing to help prevent these later issues.

[Sarah Gregory] I have to ask about this because I actually personally know some people that are doing this or have done it. What do you think of the bee sting treatment that people use as an alternative?

[Sarah Hook] Oh yes, the bee venom injections. Well, I would not be able to recommend those for...I should say I'm not a clinician, but I couldn't recommend that because I don't think any clinical trials have been done evaluating that as an effective treatment. And so, really until we see data showing the effectiveness of it, antibiotics are going to be the most effective way to treat infections.

[Sarah Gregory] Your study is specifically about the economic burden of Lyme. What does that mean? How is a disease calculated economically?

[Sarah Hook] Yes, so we used a cost of illness analysis to estimate this economic burden of Lyme disease in the US. And this type of analysis is a way of measuring medical and other associated costs resulting from a disease, in this case, Lyme disease. And we used an incidence-based design, which means we measure those costs from the onset of disease to the resolution. In this type of study, this is what we did but this is typical of cost of illness studies, costs are typically categorized into three different groups. And those groups are medical costs, and this would be the cost of a doctor's visit, prescription drugs, medical supplies, things like that. The second group would be non-medical costs, and these are things like the cost of traveling for care

Economic Burden of Lyme Disease in High-Incidence Areas, United States, 2014–2016

(the travel-related expenses) or, if you think about possibly additional childcare or home maintenance costs that would be needed because of your illness, that would fall into the category non-medical costs. And the final category is productivity losses, and this is essentially absenteeism from work because of healthcare visits or due to symptoms. We can take those hours lost and apply a cost to them. And so those are the three main types of costs, and that's what we collected in our study.

[Sarah Gregory] Okay. So to help me understand here a little more, from a public health perspective, were these costs...do we look at them actually for individuals or collectively for the US society as a whole? Or both?

[Sarah Hook] This is a great question. I'm glad you brought up. So in these cost of illness studies, it's important to specify whose perspective you are calculating the costs from. You could look at it from the patient's perspective, you could look at it from the healthcare system's perspective. Third party payer insurance, you could look at it from their perspective. Or, as you mentioned, you can total all the costs and look at it...what is the burden to the society as a whole? So in our study, we focused on the cost of the individual or the patient cost, and then also the societal cost. So that is all the cost incurred from those categories just mentioned, no matter who paid for them.

[Sarah Gregory] What time period did you evaluate?

[Sarah Hook] Yeah, so our study was conducted between September 2014 and January 2016. So that's the period where data collection occurred. We collected data from patients from the onset of their disease until they no longer reported incurring costs or after 12 surveys, whichever came first.

[Sarah Gregory] And your study looks at high incidence areas for Lyme disease. Where are these?

[Sarah Hook] So yeah, so in the US most infections, again, occur in the Northeast, the mid-Atlantic, and the Upper Midwest. Some local transmission does also occur in areas of the West Coast, and that's a blacklegged tick. But instead of *Ixodes scapularis* that is most common in the Northeast, mid-Atlantic, and Upper Midwest, on the West Coast you find *Ixodes pacificus* ticks. But for our study, we followed reported cases in four states where Lyme disease is very common, and those states were Connecticut, Maryland, Minnesota, and New York.

[Sarah Gregory] And why did you want to do this study?

[Sarah Hook] So that's a great question, too. So one of our team's priorities here at CDC is to describe the burden (the total burden) of Lyme disease in the US, and there are many facets to this idea of burden. So as I mentioned earlier, to get at disease burden, we recently published those estimates of the number of clinician-diagnosed cases in the US (that nearly 500,000 number). But we embarked upon this current study because we also wanted to describe the economic burden of this disease. And there had been some previous studies on the economic burden of Lyme disease, but these were a little bit outdated or geographically limited or used indirect data sources. So we wanted to be able to provide an updated number to help inform public health action and allocation of resources.

[Sarah Gregory] So how did you go about your study? How did you structure it?

[Sarah Hook] So we started by enrolling patients as soon as they were reported to public health surveillance authorities in those four states I mentioned. And to meet enrollment criteria, participants had to have met the case definition for confirmed or probable Lyme disease. Once they were enrolled, we categorized them into three disease categories. The first was confirmed localized or early disease, the second was confirmed disseminated disease, and then the third was probable disease.

And so, I mentioned those two perspectives that we looked at cost from. And for the patient perspective, we collected cost data from participants, again, from onset until resolution, until they basically no longer reported incurring costs. And we measured this using monthly surveys, and these were taken usually online, but some people took them over the phone with our study coordinators.

So we collected any out-of-pocket medical costs, so any part of that medical cost category that the patients were responsible for. And then we also collected Lyme disease-related non-medical costs, and then productivity losses (or basically their hours absent from work). And so, we summed these up for each participant. We standardized the costs to 2016 US dollars, and then we just calculated the median and mean patient cost per participant. And then we also looked at this by the three disease categories. And so then when we think about the total societal cost, we again summed the medical costs, non-medical costs, and productivity losses, but things were a little bit more involved to get the societal medical costs. And for this aspect of the cost calculation, we requested all billing codes (these are sometimes called CPT codes).

So we requested all codes associated with a participant's illness, and we got those directly from the participant's healthcare provider that they reported to us in surveys. Once we got these billing codes, if the participant had private insurance, we extracted the cost per code from a nationwide insurance claims database. And then if the participant had non-private insurance (so this would be whether uninsured or Medicare or Medicaid), we extracted the cost per code from a Medicaid dataset.

I think what's important to point out here, just to highlight the difference between a total societal cost and a patient out-of-pocket cost, the extracted cost per code really includes the full cost no matter who paid it. So for example, like if the extracted cost of CPT code 99213 for an office visit is \$100, that would represent the \$20 paid by the patient and the remainder paid by the patient's insurance. So again, we added all these up per patient and calculated the median and the mean societal cost per participant overall and then by disease category.

And so then the last big piece of our analysis was extrapolating the median and mean societal cost to the number of clinician-diagnosed cases in the US (so that 476,000 number). And that was so that we could have an aggregate total cost of Lyme disease in the US annually.

[Sarah Gregory] And where did all of this lead you? What did you find to be the economic burden?

[Sarah Hook] Yeah, so what we found was something that's very typical for healthcare cost data, and that was that the range of costs, really any way we looked at it (the patient perspective or the societal perspective), this range that was experienced by patients was very wide. And so that leads to large differences between the median and the mean costs. From the patient perspective, we found that the median cost (or the out-of-pocket cost) was a little over \$200 per participant, while the mean cost was just over \$1,200 per participant. And then for the societal cost, we

found that the median was almost \$700 per participant, and the mean was just over \$2,000 per participant.

So when we extrapolate these...the societal costs per participant, we estimate that the median cost of diagnosed Lyme disease in the US could be around \$345 million dollars, and the mean could be approximately \$968 million dollars per year. And I want to note that those figures are in 2016 US dollars. And so, we also standardized to 2020 US dollars, and that result (our bottom-line result) is that, on average, Lyme disease costs nearly \$1 billion dollars per year in the US. And that is really just a huge financial burden.

[Sarah Gregory] Now that is an astronomical amount of money for one out of many diseases. Could you explain to us, just real quickly, the difference between mean and median?

[Sarah Hook] Sure. So the median cost really reflects the cost that was experienced by most patients, and the mean cost is going to be the average. And so that's why you see that the mean is quite a bit larger, because it takes into account the huge range that we saw. So for example, we had some people who had about \$50 dollars total in their societal cost and some that went up over \$100,000 dollars. And so, the mean will reflect that large range, while the median is going to be more typical of what is experienced by most people.

[Sarah Gregory] Okay, got you. So were there age differences affecting costs?

[Sarah Hook] That's a great question. We used linear regression to look at this question of different variables that might affect the cost in these differences we're seeing. And so, for age, we found that people aged 18 to 65 years had slightly higher costs compared to those under 18. But we didn't see significant differences in those over 65 years old compared to those under 18.

[Sarah Gregory] Maybe that's because they're not out hiking about as much? That's probably a different study, but do you have any ideas on that?

[Sarah Hook] I was trying to think of differences in insurance that may be experienced by these age groups, but I don't have a great answer and can only really say that the differences were pretty slight. But we know that the highest risk groups—so, the groups that carry the largest disease burden—are in children around 8 to 10 years old, and then also in adults in their late 50's and 60's. So I'm not exactly sure, to be honest, what's going on there with age differences.

[Sarah Gregory] And what about gender? Are there gender differences?

[Sarah Hook] We looked at that as well in the regression analysis, but we didn't find significant differences between male and female participants. One difference I would like to highlight, though, is we did find significant differences when we looked at it by disease category. So those with confirmed disseminated disease had costs that were 120% higher than those with confirmed localized or early disease. And then, those with probable disease also had costs that were about 60% higher compared with early or localized disease. Again, that really highlights the importance of prevention and then also early diagnosis and treatment.

[Sarah Gregory] What do you think are the main strengths of your study?

[Sarah Hook] Well, our goal was to get a more comprehensive figure for the cost of Lyme disease. And previous research studies had measured certain cost components, usually just direct medical costs. So our goal really was to design a study where we were able to collect those patient out-of-pocket medical costs, nonmedical costs, and productivity losses. So that is really

one of the main strengths, because for the first time we were able to get information on things like hours missed from work by parents of children with Lyme disease. We were able to collect information on the cost of not just prescription or over-the-counter drugs, but also the cost of things like vitamins or supplements that were taken by patients, which those can get quite expensive. As mentioned, we calculated transportation cost, but that's not just cost to see your doctor, but also cost to the pharmacy, to the laboratory, even cost to see the chiropractor or really anything that was associated with the illness. And those are all expenditures that you wouldn't see if you're just looking at the direct medical cost.

I also think that a strength of our study is our prospective design. And that just means that we followed the patients as close to their illness onset as possible, all the way through to the end. And this really helps attenuate that recall bias by participants when they reported their costs to us, because it is a lot to remember. And if we caught them at the end of their illness, I don't know that we would have as much confidence in the data that we collected if they had to recall all the way back to the beginning. So I think those are the main strengths.

[Sarah Gregory] What about challenges? Were there challenges in conducting this study?

[Sarah Hook] There were, there were. I think the main challenges probably came from the main strengths that I just mentioned. This was a huge, multi-site data collection effort, and it was only possible because of the hard work and diligence on the part of our research team, and those were our partners in Connecticut, Maryland, Minnesota, and New York. And of course we couldn't have done it without our participant's willingness to share detail about their illness. But to get at this level of detail in the cost data, it required a lot of follow-up with not only participants, but also their providers. And so, there were just lots of challenges inherent with that...reminding people to take their surveys and calling busy provider offices over and over and over again to try to get the information we needed. And of course I have to highlight our study coordinators again in these states. They had quite a lot of data entries to do for this study.

Another challenge, and I guess a limitation but also an opportunity for future studies, but as comprehensive as our study was, we had to focus our efforts. And we chose to focus on acute or newly diagnosed cases of Lyme disease. So that means, though, that our results don't include costs for suspected Lyme disease—so for example, the cost of consultation for a tick bite or the cost of diagnostic tests that turn out to be negative. Those costs aren't included here in this nearly \$1 billion dollars per year figure. It also means that our results don't provide a complete picture of costs for nonacute cases—so that is to say those who are experiencing long-term symptoms for more than a year. Both of these are really important facets of the total economic burden, and they would certainly drive up that total societal cost. But as I mentioned, hopefully we can look at these in some future studies.

[Sarah Gregory] And why is knowing the economic burden of a disease important? Besides being depressing...

[Sarah Hook] So for example, with Lyme disease, knowing this large number (\$1 billion), that really underscores the importance of effective prevention. And thankfully, we have some prevention options available for this disease. I want everyone to remember their EPA-registered repellants and to perform tick checks when they come inside, even to shower shortly after being outdoors. But it also highlights the importance of our need for new prevention options. And so, there are a few vaccine and vaccine-like preventive products that are in development right now. And so, knowing this cost really highlights the importance of developing novel prevention

methods. And on that topic of vaccines, we hope that this figure will be useful in a few years when these vaccines are hopefully FDA-cleared. But as many of your listeners probably know, the Advisory Committee on Immunization Practices (or ACIP) often uses results like these (these cost of illness results) to inform their recommendations for use of vaccines in the US. So hopefully this could be helpful for that process in a few years.

[Sarah Gregory] And that's because vaccines are, number one, incredibly expensive and long-term to develop. And also, even if they are safe, they might not really be necessary. So when you have this kind of data to back it up, you show that, yes, it is necessary, cost effective, and takes a huge burden off the overall economic picture, right?

[Sarah Hook] Yeah, exactly. Exactly. And we've actually already begun efforts to look at vaccines in a cost-benefit analysis, and this data...these data points of cost (total societal cost per participant) are really critical to being able to do that type of analysis.

[Sarah Gregory] And recap for us here, what's new about your study (besides the vaccine and data element of it)? What does it add to public health?

[Sarah Hook] Yeah. So what's novel here is really the fact that this study was very, very comprehensive. It's our most comprehensive evaluation of the economic burden of Lyme disease to date. And again, it includes those patient out-of-pocket costs for the first time. So using this data, in terms of what it adds to public health, being able to use it to promote a vaccine if a vaccine is found to be safe and effective is really the number one helpful part of what we've published here. But it also helps to inform allocation of scarce public health resources. So as I mentioned, we have other prevention options. This large number shows us that we should really be focusing on promoting early diagnosis and effective treatment for folks with Lyme disease.

[Sarah Gregory] Dr. Hook, tell us about your background, how you came to be at CDC, and what you like most about your job there...or here?

[Sarah Hook] Yeah. So I came to CDC in 2011, and that's here in Fort Collins where we have the Division of Vector-Borne Diseases. And I actually started in a policy position, but my real interests were in epidemiologic research. So in 2012, I was excited to take a position as research coordinator for TickNET, and TickNET is basically a network of researchers from public health and academia in high-incidence states. And these are researchers all working on Lyme and other tickborne diseases. This is actually the same group that helped pull off this large study, and so I've stayed with TickNET ever since, and I've gotten to move from research coordinator to now getting to lead this network of really amazing people doing really important research on the prevention of Lyme disease. I am really fortunate to get to work with a great group of people here in Fort Collins, and as mentioned, across the country. I think my favorite part of the job is the collaborative aspect of research—so getting to fine-tune research questions with others, develop those analysis plans, working out study logistics, and to be honest, really laughing and/or commiserating together when things don't go as planned in the research. For me, it's really about this amazing group of people I get to work with.

[Sarah Gregory] And finally, we always like to hear what our guests enjoy doing in their non-working time. What are your interests?

[Sarah Hook] Well, I have three little boys (age 1, 3, and 5).

[Sarah Gregory] Oh goodness.

[Sarah Hook] So they keep me pretty busy with fun, fun crazy things. I'm getting pretty good at my truck sound effects, lately. But when I do have some spare time, I enjoy playing the piano and going for runs. I do also like to cook and bake, and it has been fun...the kids are getting big enough to be able to help me in the kitchen. So they seem to be taking some interest in that, especially if they get to lick the bowl and stuff like that. But yeah, those are some of my non-work interests.

[Sarah Gregory] And just out of curiosity, you are Dr. Hook...is that an MD or an epidemiologist? What's your doctorate in?

[Sarah Hook] Yeah. It's in epidemiology. So I recently got that degree in late 2020.

[Sarah Gregory] So you have three tiny children and you just finished up a doctorate degree. That is so impressive.

[Sarah Hook] Well, thank you. Thank you very much. But if you do the math, you'll note that our data collection ended in 2016, and that's when I started both of those endeavors (having children and the PhD). So that's why these results are coming out a little bit late. I suppose I can blame COVID for part of that delay, as well.

[Sarah Gregory] Well, yes. That's not an uncommon predicament these days.

Well, thank you for taking the time out of your obviously busy life to talk to me today, Dr. Hook.

[Sarah Hook] Thank you. It was my pleasure. This was really fun, I appreciate it so much.

[Sarah Gregory] And thanks for joining me out there. You can read the June 2022 article, *Economic Burden of Reported Lyme Disease in High-Incidence Areas, United States, 2014–2016*, online at [cdc.gov/eid](https://www.cdc.gov/eid).

I'm Sarah Gregory for *Emerging Infectious Diseases*.

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