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Challenges in Predicting Lyme Disease Risk

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Lyme disease is the most common vector-borne disease in the United States, with approximately 30 000 cases reported to the public health system each year.[1] Surveillance for this common disease is not intended to capture every single case, and underreporting is widely acknowledged: from 2005 to 2010, an estimated 300 000 cases were diagnosed each year.[2] The frequency of Lyme disease is likely increasing, as the geographic area with local risk of Lyme disease is expanding. Since the mid-1990s, the number of US counties where the primary tick vector, *Ixodes scapularis*, is documented has increased, as has the number of counties that have a high incidence of human Lyme disease.[3,4] The complex web of factors that define the present distribution of Lyme disease and drive its spread into new areas is not fully understood. Quantitative models can be powerful tools to explain the present distribution and predict when and where Lyme disease cases are likely to occur in the future, information that can aid in targeting efforts to improve awareness of the disease. Bisanzio and coauthors[5] integrate environmental, tick, and Lyme disease case data to predict new detections (first case reported) of Lyme disease at the county level within high-incidence states in the Northeast, Middle Atlantic, and upper Midwest, as well as neighboring states. This effort provides an opportunity to highlight critical gaps in available human and tick data required to model this system accurately.

The validity and public health utility of predictive models are dependent on availability of high-quality input data at spatial scales appropriate for the hypothesis in question, as well as interpretation that incorporates an understanding of the limitations and biases of the data. To account for acarological risk of the disease, Bisanzio and coauthors[5] used the most recently published national data on the county-level distribution of *I scapularis*.[4] Although tick distribution was a significant predictor in their model, it is certainly an underestimate of the tick's actual distribution, owing in part to the lack of any standardized tick surveillance and reporting effort at the time of that study. Tick presence data used in this model were derived from literature review, health department reports, and personal communications and do not represent a systematic sampling effort. Moreover, temporal certainty of when the tick became established in any given county is extremely limited. While Bisanzio and coauthors[5] compensate for poor-quality tick data by incorporating other environmental correlates of tick habitat, they do not account for geographic differences in the density of *Borrelia burgdorferi*–infected host-seeking nymphal ticks, a variable that has been shown to more accurately predict the distribution of reported human Lyme disease than tick presence alone.[6] This omission is attributable to a lack of current and accurate county-level data on this important acarological risk measure. To our knowledge, the only prior systematically collected national county-level data on this measure are model derived and based on a field study[6] funded by the US Centers for Disease Control and Prevention (CDC) conducted across the eastern United States from 2004 to 2007. Over the past decade, high numbers of Lyme disease cases have been reported more broadly than that predicted distribution of host-seeking infected ticks, suggesting a need to update vector presence, abundance, and infection prevalence data.

Human Lyme disease data captured through routine passive public health surveillance are presently the only data source widely available for researchers to use as a surrogate for human disease risk. Multiple biases contribute to these figures and should be accounted for as much as possible in modeling approaches to mitigate their impact and limit overinterpretation of findings. Underreporting is well documented, but "overreporting" of presumably false-positive serologic test results also occurs, particularly in low prior-probability settings.[2,7] In a retrospective review of

reported Lyme disease cases from low-incidence states, approximately 85% were associated with travel-related exposure in high-incidence areas, and the remainder often displayed characteristics potentially indicative of false-positive test results.[7] One can infer that the prior probability of true locally acquired illness is different in a county near the leading edge of Lyme disease expansion, which presumably has an increasing density of infected ticks compared with a county more distant from the leading edge with lower acarological risk. A valid alternative is to use a less precise human disease measure that is in turn less subject to the error associated with single case reports (eg, disease incidence threshold). Bisanzio and coauthors[5] attempt to address this and the absence of acarological risk information by using data from neighboring counties in their diffusion model. Nevertheless, the approach given available data is still likely to yield inaccurate estimates of the risk of local exposure and thus limit the public health utility of the model.

The burden of Lyme disease in the United States is expanding, and current prevention options are insufficient to reverse course.[8] More refined understanding of drivers of Lyme disease will help inform research into the most effective environmental intervention options and improve predictions for further spread. The model by Bisanzio and coauthors[5] and other modeling efforts have highlighted discrete areas where better input data and greater public health context for those data could serve to improve model validity and utility. The CDC is exploring use of alternative data sources to supplement available public health surveillance data to better ascertain the frequency of Lyme disease in the United States. Recognizing that acarological risk changes over time, in 2019 the CDC initiated a national tick and tick-borne pathogen surveillance and reporting program in an effort to provide current, accurate, and publicly available information on the distribution and abundance of host-seeking ticks and the presence and prevalence of their associated human pathogens.[9] Although limited by availability of suitable data, Bisanzio and coauthors[5] also highlight the urgent need for improved clinical and public awareness in areas where Lyme disease is spreading. The CDC is actively working with public health partners in these areas of emergence to address challenges in public and clinical recognition of Lyme disease in the face of rapidly changing disease risk, but even more needs to be done to improve prevention and early and accurate diagnosis. Greater collaboration between academic researchers and public health practitioners can yield improved context in analytic decisions and enhance the public health value of quantitative models.

ARTICLE INFORMATION

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