Received: 21 June 2018 | Revised: 10 August 2018 | Accepted: 26 August 2018

DOI: 10.1111/zph.12525

SHORT COMMUNICATION

WILEY

Impacts of misclassification on Lyme disease surveillance

Heather Rutz[1] | Brenna Hogan[1] | Sarah Hook[2] | Alison Hinckley[2] | Katherine Feldman[1]

[1]Emerging Infections Program, Maryland Department of Health, Baltimore, Maryland

[2]Division of Vector-Borne Diseases, Centers for Disease Control and Prevention, Fort Collins, Colorado

Correspondence
Heather Rutz, Emerging Infections Program Epidemiologist, Center for Zoonotic and Vector-Borne Diseases, Maryland Department of Health, Baltimore, MD.
Email: heather.rutz@maryland.gov

Funding information
National Center for Emerging and Zoonotic Infectious Diseases, Grant/Award Number: CK000203

Abstract

In Maryland, Lyme disease (LD) is the most widely reported tickborne disease. All laboratories and healthcare providers are required to report LD cases to the local health department. Given the large volume of LD reports, the nuances of diagnosing and reporting LD, and the effort required for investigations by local health department staff, surveillance for LD is burdensome and subject to underreporting. To determine the degree to which misclassification occurs in Maryland, we reviewed medical records for a sample of LD reports from 2009. We characterized what proportion of suspected and "not a case" reports could be reclassified as confirmed or probable once additional information was obtained from medical record review, explored the reasons for misclassification, and determined multipliers for a more accurate number of LD cases. We reviewed medical records for reports originally classified as suspected (n = 44) and "not a case" (n = 92). Of these 136 records, 31 (23%) suspected cases and "not a case" reports were reclassified. We calculated multipliers and applied them to the case counts from 2009, and estimate an additional 269 confirmed and probable cases, a 13.3% increase. Reasons for misclassification fell into three general categories: lack of clinical or diagnostic information from the provider; surveillance process errors; and incomplete information provided on laboratory reports. These multipliers can be used to calculate a better approximation of the true number of LD cases in Maryland, but these multipliers only account for underreporting due to misclassification, and do not account for cases that are not reported at all (e.g., LD diagnoses based on erythema migrans alone that are not reported) or for cases that are not investigated. Knowing that misclassification of cases occurs during the existing LD surveillance process underscores the complexities of LD surveillance, which further reinforces the need to find alternative approaches to LD surveillance.

KEYWORDS
Lyme disease, misclassification, multipliers, surveillance

1 | INTRODUCTION

Lyme disease (LD) is the most commonly reported tickborne disease in the United States, and the true number of LD cases could be as much as 10 times higher than what is reported through public health surveillance (Hinckley et al., 2014; Nelson et al., 2015). The reasons that LD is underreported are varied and not entirely understood. One possible contributing factor is that during the public health surveillance process, LD reports are not classified appropriately according to the national case definition as determined by the Council of State and Territorial Epidemiologists (CDC, 2008).

This evaluation was reviewed by the Maryland Department of Health's Institutional Review Board and it was deemed exempt research.

Maryland statutes and regulations (COMAR, 2015; Maryland Code, Health-General, 2018) require healthcare providers to report all LD cases and laboratories to report all positive LD test results to the appropriate local health department. When a LD report is received, local health department staff investigate by requesting additional clinical information from the provider, including onset and diagnosis dates, signs and symptoms, and any additional test results. Local health department staff use these data to classify the report as confirmed, probable, suspected or "not a case" according to the national case definition. Confirmed and probable cases must have clinical data as well as supporting laboratory evidence, although laboratory evidence is not required in LD endemic areas to classify cases with erythema migrans as confirmed (CDC, 2008). Suspected cases are those which have positive two-tier tests or positive IgG Western blot tests only, but clinical data are absent; if additional clinical information were provided, suspected cases could potentially be classified differently. LD reports not classified as confirmed, probable or suspected cases are deemed "not a case." These reports include those for which LD was actually ruled out, those for which reported clinical information was not related to LD, as well as those which lacked enough information to be otherwise classified (i.e., positive first-tier tests only).

To determine the degree to which misclassification occurs in Maryland, the Maryland Emerging Infections Program reviewed medical records for a sample of LD reports from 2009 captured through the public health surveillance process. We calculated multipliers from the suspected and "not a case" reports that were reclassified and applied these to the total number of suspected and "not a case" reported to better estimate the number of LD cases in Maryland in 2009. We also explored the reasons for misclassification of reported LD cases and determined which provider specialties most commonly diagnose LD to identify where to focus education and intervention efforts to improve LD surveillance.

Impacts

- Misclassification of Lyme disease case reports decreased the number of confirmed and probable Lyme disease cases reported for Maryland by 13.3%.
- Reasons for misclassification included: lack of clinical or diagnostic information; surveillance process errors; and incomplete information provided on laboratory reports.
- Clinicians specializing in family medicine, internal medicine and paediatrics were most likely to diagnose cases of Lyme disease. Providers in these specialties should be targeted for education regarding public health reporting or to establish sentinel networks.
- Our results underscore the need to find alternative approaches for Lyme disease surveillance

2 | MATERIAL AND METHODS

As part of efforts described previously (Rutz, Hogan, Hook, Hinckley, & Feldman, 2018), we sampled LD reports submitted to the Maryland Department of Health in 2009. We took a 10% random sample of confirmed, probable and suspected LD cases. In addition, we sampled the following categories of reports that were classified as "not a case": (a) 100% of "not a case" reports submitted by physicians, which contained positive first-tier tests or IgM Western blot tests only and limited, if any, clinical information; and (b) a 10% random sample of "not a case" reports submitted by laboratories that had a positive Western blot test result (>99% were IgM Western blot positive). We did not sample the remaining "not a case" reports which were primarily positive first-tier tests submitted by laboratories with little to no clinical data and were therefore unlikely to have the potential to be reclassified (Table 1).

Given that suspected cases are classified as such due to having positive LD tests in the absence of clinical data, we assumed that these cases had a high potential to be reclassified with additional information as determined through medical record review. We therefore requested and attempted medical record reviews for 100% of the sampled suspected reports. However, given resource availability and our assumption that the "not a case" reports had a lower likelihood of being reclassified, we conducted medical record reviews for 25% of the sampled "not a case" reports submitted by physicians and 50% of the sampled "not a case," Western blot positive reports (Table 1).

With the additional information gained from medical record review, the reports were reclassified, when indicated, according to the 2008 national case definition for LD. We calculated multipliers for suspected and "not a case" LD reports that were reclassified, and we characterized the reasons that LD reports were originally misclassified. The multipliers were used to estimate the actual

TABLE 1 Number of 2009 LD reports in Maryland, by case classification, that were sampled and reviewed

Classification	Reports	Sampled	Underwent Medical Record Review (% of sampled)
Confirmed	1,472	147	*N*/A
Probable	557	56	*N*/A
Suspected	517	52	44 (85)[a]
"Not a case"			
Physician submitted	68	68	17 (25)
Western blot positive	1,514	151	75 (50)
Other	640	0	*N*/A
Total	4,768	474	136

Note. *N*/A: Not applicable.
[a]Eight records not able to be located.

TABLE 2 Multipliers Determined by Final Disposition of Suspected Cases and "Not a case" Reports Following Medical Record Review

	Final Disposition					
	Confirmed or Probable		Suspected		"Not a case"	
Original Classification	Multiplier (95% CI)	No.	Multiplier (95% CI)	No.	Multiplier (95% CI)	No.
Suspected (*n* = 44)	**0.36 (0.22, 0.52)**	**16**	N/A	22	**0.14 (0.05, 0.27)**	**6**
"Not a case," Physician submitted (*n* = 17)	**0.12 (0.02, 0.36)**	**2**	N/A	0	N/A	15
"Not a case," Western blot positive (*n* = 75)	**0.05 (0.02, 0.13)**	**4**	**0.04 (0.01, 0.11)**	**3**	N/A	68

Note. N/A = not applicable; there was no change in classification.
Bolded numbers are for those categories that changed classification.

total number of confirmed and probable cases by applying them to the total number of suspected and "not a case" LD reports for 2009.

In addition, we conducted a survey about practice characteristics and administrative coding practices for the provider listed on all sampled reports (including confirmed and probable cases). Coding practice results are reported elsewhere (Thomas et al., 2018), but this survey allowed us to determine the provider specialties in medical practices that diagnose LD in Maryland patients.

We used Microsoft Office Excel 2007 to characterize administrative codes and used EpiInfo7 for data entry and analysis of medical record review data.

3 | RESULTS

Of 4,768 LD reports received in 2009, our final sample included 474 confirmed, probable, suspected, and "not a case" reports (Table 1). We reviewed 136 medical records, including 44 suspected cases; 75 "not a case," Western blot positive reports; and 17 "not a case," physician submitted reports. All medical records were reviewed on site at the facility. Eight of the 52 suspected medical records were not reviewed as the patient moved out of state and took their records with them, the practice closed, the provider retired or the records were lost.

A total of 292 healthcare practices (accounting for the 474 reports) were surveyed; we obtained responses from 184 (63%) healthcare facilities. The most commonly reported specialty was family medicine, with a total of 80 (43%) facilities having at least one family medicine practitioner. At least one internal medicine specialist was reported at 59 (32%) facilities and at least one paediatrics specialist at 46 (25%) facilities. Few facilities reported having specialists in emergency medicine (*n* = 7, 4%), dermatology (*n* = 9, 5%) or infectious disease (*n* = 9, 5%).

3.1 | Reclassification and calculation of multipliers

Following medical record review, a total of 31 (23%) suspected cases and "not a case" reports were reclassified (Table 2). Half of the originally classified suspected reports changed classification: 36% were reclassified as confirmed or probable, and 14% were reclassified as "not a case". Most "not a case" reports retained their original classification: a total of 9% of "not a case," Western blot positive reports were reclassified to suspected, probable or confirmed cases, and 12% of "not a case," physician submitted reports were reclassified as probable or confirmed cases.

Applying these multipliers to the total case counts of suspected and "not a case" reports from 2009, we estimate that 186 of the suspected cases, seven of the "not a case," physician submitted reports, and 76 of the "not a case," Western blot positive reports should have been classified as confirmed or probable cases. This resulted in an estimated additional 269 confirmed and probable cases in 2009, for an estimated total of 2,298, a 13.3% increase.

3.2 | Reasons for misclassification

Reasons why the 31 suspected cases and "not a case" reports were originally misclassified fell into three general categories: lack of clinical or diagnostic information from the provider during the public health surveillance investigation process (*n* = 19); surveillance process errors (*n* = 8); and incomplete information provided on laboratory reports to local health departments (*n* = 4). Surveillance process errors consisted of surveillance staff overlooking critical information on the case report form, incorrectly interpreting LD test results, or not linking critical testing data reported at different times. Incomplete information on laboratory reports obscured the fact that LD testing had been performed on synovial fluid (which is not included in the case definition for laboratory evidence of infection) because the specimen type was not specified on the laboratory reports sent to the local health departments.

4 | DISCUSSION

Through our efforts, we have characterized practices that are most likely to encounter and report LD cases; determined multipliers to estimate actual confirmed and probable cases for our suspected cases and "not a case" reports; and identified reasons for misclassification of reported suspected cases and "not a case" reports.

Applying our calculated multipliers to the LD reports from 2009 yielded approximately 270 additional confirmed and probable cases, a 13.3% increase, bringing the estimated total to nearly 2,300 cases. Misclassification is just one factor contributing to underreporting of Lyme disease, but our findings support other reports that the disease is underrepresented (Coyle et al., 1996; Hinckley et al., 2014; Matteson, Beckett, O'Fallon, Melton, & Duffy, 1992; Meek, Roberts, Smith, & Cartter, 1996; Naleway, Belongia, Kazmierczak, Greenlee, & Davis, 2002; Nelson et al., 2015; Orloski et al., 1998). While the multipliers from this study could be used to calculate estimates that potentially better approximate the true number of LD cases in Maryland each year, these multipliers account only for underreporting due to misclassification, and do not account for cases that are not reported at all (e.g., LD diagnoses based on erythema migrans alone) or for cases that are not investigated (Rutz, Wee, & Feldman, 2016). In order to calculate more comprehensive multipliers that account for misclassification as well as non-investigated reports, and non-reported cases, alternative investigations or evaluations are required.

Almost two-thirds of the suspected cases and "not a case" reports that changed classification following medical record review did so based on information that should have been communicated by providers during the initial public health investigation. Local health department staff typically make one to four (median two) attempts to obtain additional data from providers during the course of their investigation (Rutz et al., 2016); however providers may find it difficult or cumbersome to report LD, may not be aware of their legal obligation to report or may be unaware that certain variables are critical for public health surveillance purposes. The healthcare facility survey identified family medicine, internal medicine and paediatric practitioners as those specialists who diagnose LD most frequently. Professional medical associations representing these specialties should be targeted for education about LD in general, specifically about public health reporting, and to identify barriers to complete reporting and capture of all relevant information during the initial investigation.

The study was limited in that we did not review all "not a case," Western blot positive reports in our sample, nor did we examine any of the 640 "not a case" reports in the "other" group presented in Table 1. However, only a very small proportion (6%) of the combined "not a case" reports categories that were reviewed changed classification to confirmed or probable cases, indicating that the "not a case" reports likely represent patients who truly do not have LD. Furthermore, there is a possibility that some confirmed or probable cases may have been misclassified as well, due to surveillance process errors, and should be classified as "not a case". However, there may be fewer errors of this type, as there is considerable clinical and testing data from the provider and laboratory that support a LD-confirmed or probable classification. This type of error could lower the multiplier. In addition, the surveillance practices in other states may be different from Maryland's, thus this multiplier may not be generalizable to other jurisdictions.

This study allowed us to better estimate the amount of underreporting of LD due to misclassification in Maryland. That misclassification of cases occurs during the existing LD surveillance process underscores the complexities of LD surveillance, which further reinforces the need to find alternative approaches to LD surveillance. However, with the status quo, training in conducting LD and other infectious disease investigations for surveillance staff could reduce some surveillance process errors. Additionally, targeted education on LD reporting among the types of medical practices identified in this study may reduce underreporting.

ACKNOWLEDGEMENTS

The authors wish to thank Paul Mead for his thoughtful guidance in support of this research. This journal article was supported by the Cooperative Agreement Number CK000203, funded by the Centers for Disease Control and Prevention. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention or the Department of Health and Human Services.

CONFLICT OF INTEREST

The authors have no conflict of interests to declare.

ORCID

Heather Rutz http://orcid.org/0000-0002-4352-0685
Alison Hinckley http://orcid.org/0000-0003-2853-5165

REFERENCES

CDC (2008). *Lyme disease 2008 case definition*. Retrieved from https://wwwn.cdc.gov/NNDSS/script/casedef.aspx?CondYrID=751&DatePub=2008-01-01

COMAR (2015). *Reportable diseases, conditions, outbreaks, and unusual manifestations; submitting clinical materials*. Retrieved from http://www.dsd.state.md.us/comar/getfile.aspx?file=10.06.01.03.htm

Coyle, B., Strickland, G., Liang, Y., Peña, C., McCarter, R., & Israel, E. (1996). The public health impact of Lyme disease in Maryland. *Journal of Infectious Diseases*, *173*, 1260–1262. https://doi.org/10.1093/infdis/173.5.1260

Hinckley, A., Connally, N., Meek, J., Johnson, B., Kemperman, M., Feldman, K., … Mead, P. (2014). Lyme disease testing by large commercial laboratories in the United States. *Clinical Infectious Diseases*, *59*, 676–6781. https://doi.org/10.1093/cid/ciu397

Maryland Code, Health-General (2018). Maryland Code and Court Rules, Health-General, §§ 18–201 and 205, disease prevention. Retrieved from https://govt.westlaw.com/mdc/Document/NF23134A064DB11DE91F5EACF50AC3B69?viewType=FullText&originationContext=documenttoc&transitionType=CategoryPageItem&contextData=(sc.Default)

Matteson, E., Beckett, V., O'Fallon, W., Melton, L., 3rd, & Duffy, J. (1992). Epidemiology of Lyme disease in Olmstead county, MN, 1975–1990. *Journal of Rheumatology*, *19*, 1743–1745.

Meek, J., Roberts, C., Smith, E., Jr., & Cartter, M. (1996). Underreporting of Lyme disease by Connecticut physicians, 1992. *Journal of Public Health Management and Practice*, *2*, 61–65. https://doi.org/10.1097/00124784-199623000-00017

Naleway, A., Belongia, E., Kazmierczak, J., Greenlee, R., & Davis, J. (2002). Lyme disease incidence in Wisconsin: A comparison of state-reported rates and rates from a population-based cohort. *American Journal of Epidemiology*, *155*, 1120–1127. https://doi.org/10.1093/aje/155.12.1120

Nelson, C., Saha, S., Kugeler, J., Delorey, M., Shankar, M., Hinckley, A., & Mead, P. (2015). Incidence of clinician-diagnosed Lyme disease, United States, 2005–2010. *Emerging Infectious Diseases*, *21*, 1625–1631. https://doi.org/10.3201/eid2109.150417

Orloski, K., Campbell, G., Genese, C., Beckley, J., Schriefer, M., Spitalny, K., & Dennis, D. (1998). Emergence of Lyme disease in Hunterdon county, New Jersey, 1993: A case-control study of risk factors and evaluation of reporting patterns. *American Journal of Epidmiology*, *147*, 391–397.

Rutz, H., Hogan, B., Hook, S., Hinckley, A., & Feldman, K. (2018). Exploring an alternative approach to Lyme disease surveillance in Maryland. *Zoonoses Public Health*, *65*, 254–259. https://doi.org/10.1111/zph.12446

Rutz, H., Wee, S. B., & Feldman, K. (2016). Characterizing Lyme disease surveillance in an endemic state. *Zoonoses Public Health*, *65*, 247–253. https://doi.org/10.1111/zph.12275

Thomas, N., Rutz, H., Hook, S., Hinckley, A., Lukacik, G., Backenson, B., … White, J. (2018). Assessing diagnostic coding practices among a sample of healthcare facilities in Lyme disease endemic areas: Maryland and New York – A brief report. *Zoonoses Public Health*, *65*, 275–278. https://doi.org/10.1111/zph.12414

How to cite this article: Rutz H, Hogan B, Hook S, Hinckley A, Feldman K. Impacts of misclassification on Lyme disease surveillance. *Zoonoses Public Health*. 2018;00:1–5. https://doi.org/10.1111/zph.12525