BMJ Open

Obstacles to diagnosis and treatment of Lyme disease: A qualitative study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-021367
Article Type:	Research
Date Submitted by the Author:	08-Jan-2018
Complete List of Authors:	Hirsch, Annemarie; Geisinger, Department of Epidemiology and Health Services Research Herman, Rachel; Gettysburg College Rebman, Alison; Johns Hopkins School of Medicine, Department of Medicine, Division of Rheumatology Moon, Katherine; Johns Hopkins University Bloomberg School of Public Health, Department of Environmental Health and Engineering Aucott, John; Johns Hopkins School of Medicine, Department of Medicine, Division of Rheumatology Heaney, Christopher; Johns Hopkins University Bloomberg School of Public Health, Department of Environmental Health and Engineering; Johns Hopkins University Bloomberg School of Public Health, Department of Epidemiology Schwartz, BS; Geisinger, Department of Epidemiology and Health Services Research; Johns Hopkins University Bloomberg School of Public Health, Department of Environmental Health and Engineering
Keywords:	QUALITATIVE RESEARCH, SOCIAL MEDICINE, Patient delay, Lyme disease

Obstacles to diagnosis and treatment of Lyme disease: A qualitative study

Annemarie G. Hirsch[1], PhD, MPH; Rachel J. Herman[2]; Alison Rebman[3], MPH; Katherine Moon[4], PhD; John Aucott[3], MD; Christopher Heaney[4,5], PhD; Brian S. Schwartz[1,4], MD, MS

1. Department of Epidemiology and Health Services Research, Geisinger
2. Gettysburg College
3. Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine
4. Department of Environmental Health and Engineering, Johns Hopkins University Bloomberg School of Public Health
5. Department of Epidemiology, Johns Hopkins University Bloomberg School of Public Health

Corresponding author:
Annemarie Hirsch, PhD, MPH
Assistant Professor
Department of Epidemiology and Health Services Research
Geisinger
Danville, PA 17822
aghirsch@geisinger.edu
267-626-8810

Abstract

Objective For most individuals with Lyme disease, prompt treatment leads to rapid resolution of infection. However, severe complications can occur if treatment is delayed. Our objective was to identify themes around belated diagnosis or treatment of Lyme disease using the General Model of Total Patient Delay (GMTPD).

Design We conducted a qualitative interview study using in-depth telephone interviews.

Setting Participants were patients from a large, integrated health system in the state of Pennsylvania.

Participants There were 26 participants. Participants had to have a diagnosis of Lyme disease between 2014 and 2017 and a positive IgG Western blot. We used a stratified purposeful sampling design to identify patients with and without late Lyme disease manifestations. To ensure variation in care experiences, we oversampled patients diagnosed outside of primary care.

Outcome measures We asked participants about their experience from first Lyme disease symptoms to treatment. We applied an iterative coding process to identify key themes and then synthesized codes into higher order codes representing the GMTPD stages: appraisal delay (symptom to recognition of illness); illness delay (inferring illness to deciding to seek help); behavioral delay (deciding to seek help to the act of seeking help); scheduling delay (seeking help to attending an appointment); and treatment delay (attending appointment to treatment).

Results Appraisal delay themes included symptom misattribution; intermittent symptoms; and misperceptions about the necessity of a bull’s-eye rash. Health insurance status was a driver of illness and behavioral delay. Scheduling delay was not noted by participants, in part, because 10 of 26 patients went to urgent care or emergency department settings. Misdiagnoses were more common in these settings, contributing to treatment delay.

Conclusion Our study identified potentially modifiable risk factors for belated treatment. Targeting these risk factors may minimize time to treatment and reduce the occurrence of preventable complications.

Strengths and limitations of this study

- To our knowledge, this is the first study to examine which factors account for belated treatment of Lyme disease.
- Through the lens of the General Model of Total Patient Delay, a widely used model that describes the decisional processes and potential delays prior to treatment, we identified distinct phases between onset of first Lyme disease symptoms and Lyme disease treatment.
- This study was conducted in a well-defined sample of participants who had both a Lyme disease diagnosis and a positive IgG Western blot.
- The objective of this study was not to quantify the extent to which factors contribute to belated Lyme disease treatment and thus future studies will be required to determine the degree to which the potential risk factors increase the risk of belated treatment.
- This study was conduct among patients from a single integrated health system that includes 44 community practice sites and 12 hospital campuses across a large geographic region.

Funding: This work was supported by the Steve & Alexandra Cohen Foundation. The Steve and Alexandra Cohen Foundation did not participate in data collection, analysis, or the writing of this manuscript.

Competing interests: None declared

Data sharing: Interview guide and codebook available by request to corresponding author.

Lyme disease is a tick-borne infectious disease that is on the rise in the Northeast, Mid-Atlantic, and Upper Midwest regions of the United States (Nelson et al., 2015). Delays in diagnosis or treatment (hereafter referred to as belated treatment) of Lyme disease can lead to preventable complications, representing later stages of the disease when the infection disseminates, including neurologic manifestations, cardiac abnormalities, and arthritis (Mead, 2015). While little is known about the prevalence of belated treatment in Lyme disease, the observation that 32% of Lyme disease cases are diagnosed with arthritis, 12% with neurologic conditions, and 1-2% with carditis (Mead, 2015) suggests that belated treatment may occur in as many as 40% of cases. To date, the study of time to treatment has largely focused on cancer and cardiovascular events (Scott, Walter, Webster, Sutton, & Emery, 2012). No study has examined which factors account for belated treatment of Lyme disease, despite the benefits of prompt treatment of this disease.

The General Model of Total Patient Delay (GMTPD) (Andersen, Cacioppo, & Roberts, 1995) is a widely used, five-stage model that describes the decisional processes and potential delays prior to treatment (Scott et al., 2012). Appraisal delay is the time between when a person first notices an unexplained symptom until the person concludes he/she is ill. Appraisal has generally been found to be the key determinant in delay in seeking help (Scott et al., 2012). Illness delay is the time between inferring illness and deciding to seek help; behavioral delay represents the time between deciding an illness requires medical care and acting; scheduling delay is the time between deciding to seek help and attending an appointment; and treatment delay is the time between the first appointment with a health care provider and onset of treatment (Andersen et al., 1995). While this model has been widely applied to cancer and myocardial infarction, it has not been applied to Lyme disease. Thus, the primary drivers of belated treatment in Lyme disease remain unknown.

To identify themes around belated treatment, as well as to evaluate the application of the GMTPD to Lyme disease, we interviewed 26 patients with a diagnosis of Lyme disease to gain insight into their experiences between onset of Lyme disease symptoms and treatment. Such understanding is critical to informing strategies that would reduce time to diagnosis and treatment and prevent late stage Lyme disease.

METHODS

We conducted a qualitative study using in-depth telephone interviews of Geisinger patients with a Lyme disease diagnosis to understand what happens between the onset of Lyme disease symptoms and treatment. We analyzed interview findings through the GMTPD framework. This study was approved by the Geisinger Institutional Review Board.

Study setting and sample

We identified study participants using the electronic health record (EHR) from Geisinger, an integrated health system servicing more than 45 counties in Pennsylvania and New Jersey, both high-incidence states for Lyme disease (Centers for Disease Control and Prevention [CDC], 2017). Patients were eligible if they were at least 18 years of age; had an International Classification of Disease code (ICD-9: 088.81 or ICD-10: A69.20) for Lyme disease associated with at least one clinical encounter between 2014 and 2017; and an IgG Western blot meeting CDC criteria of five or more positive bands (CDC, 2015). We used a stratified purposeful sampling design to identify patients with and without late Lyme disease manifestations: Lyme arthritis (ICD-9: 711.8x; ICD-10: M01.X0); facial palsy (ICD-9: 351.0, 352.9; ICD-10: G51.0; G52.9); meningoencephalitis (ICD-9: 320.7; ICD-10: G01); or myocarditis (ICD-9: 422.0; ICD-10: I41). To ensure variation in care experiences, we oversampled patients diagnosed outside of primary care. We first sent letters to notify 93 patients (47 with late manifestations and 46 without) that they were eligible for the study. Two weeks later we telephoned patients to schedule a telephone interview. Participants who completed an interview received a $50 gift card. Recruitment continued until data saturation, the point at which no new information seemed to emerge during coding (Corbin & Strauss, 2008).

Data collection

We conducted in-depth, semi-structured, open-ended telephone interviews between August and September 2017, each lasting approximately 30 minutes. Telephone interviews allowed for capture of patient experiences across the large geographic area served by Geisinger. An experienced interviewer (first author AGH) obtained verbal consent and asked participants to talk about their experience with Lyme disease, from symptom onset to treatment. The interviewer was a researcher employed by the health system that treated participants for Lyme disease. To address any potential concerns participants might have had in describing their care experiences to a health system employee, the interviewer informed participants that their responses would not impact the care received at Geisinger and would be kept confidential. The interviewer then used an interview guide to follow-up on the account that included questions in six primary areas: Lyme disease knowledge; pre-treatment symptoms;

care-seeking behavior; diagnosis process; treatment process; and post-treatment symptoms. All interviews were audio-recorded and transcribed verbatim. No additional field notes were recorded. We did not return transcripts to participants for comment or correction.

Analysis

We applied a deductive content analysis of interview transcripts, based on the GMTPD (Elo & Kyngäs, 2008). We applied an iterative coding process to identify themes corresponding to the six primary areas as well as emergent themes. After the first five interviews, one of two coders reviewed the transcripts to develop a preliminary coding framework. A second coder then applied the framework to the same five interviews. The coding team (2 members) discussed findings and reached consensus on an updated coding scheme, revising the scheme as new themes emerged. The coding team also updated the interview guide to incorporate questions around emergent themes for future interviews. In the final phase of analysis, the coders developed higher order categories representing the five delay stages of the GMTPD. Analysis was conducted using Atlas.ti.7.

RESULTS

Out of the 93 patients to whom we sent a letter, we telephoned 56 patients and reached 33. Of these, 26 (79%) agreed to be interviewed. We stopped recruitment calls after reaching saturation. While the interviewers were intended to be one-on-one, two patients had a spouse with them in the room during the interview. In one case, a spouse joined the call. However, analysis was confined to the information presented by the 26 patients.

Slightly more than half of participants were female; 30% had a history of being on Medical Assistance (a surrogate for low family socioeconomic status); and participants ranged in age from 22 to 70 years (**Table 1**). Half of the participants first sought care for Lyme disease from a primary care provider and 38.5% first went to an urgent care center or emergency department.

Ten participants reported that they had a rash, three of whom described the rash as a bull's-eye. Four of the participants who reported a rash sought care because of the rash. The remaining did not seek care until other symptoms (e.g., fatigue, joint pain) appeared. Two of the four participants who saw a doctor because of the rash were initially misdiagnosed. Eleven participants reported having joint pain, though patients did not specify whether the joint pain was diagnosed as Lyme arthritis. Eight patients reported having Bell's palsy, two patients reported carditis, and one patient reported a diagnosis of Lyme meningitis.

A number of themes emerged regarding seeking care for Lyme disease symptoms. We classified these themes into one of the five GMTPD stages (**Table 2**). Participants reported seeking care both within and external to Geisinger for their initial Lyme disease symptoms, but we did not ask in which health care system delays occurred.

GMTPD Stages

Appraisal delay

Participants consistently reported an appraisal delay, a gap between their first symptom and recognition that they were ill (**Table 2**). Some participants attributed this gap to the inconsistent nature of their symptoms. One participant explained,

> "I was just having occasional joint achiness where it kind of felt like I slept funny on my elbow. It would be sore for a day or two and then it would go away."

Patients also misattributed symptoms to minor injuries, pre-existing conditions, or the flu. One participant noted, "I also have fibromyalgia, so it's kind of hard to differentiate."

Patients ruled out Lyme disease in the absence of the bull's-eye rash perceived to be characteristic of Lyme disease, delaying medical attention even in the presence of a rash. One participant explained,

> "And then I got a like this rash on my legs, on my arms, on my back. It was really bad. And I didn't even know about Lyme disease at that time… I mean I knew that you'd get a bull's-eye rash. And it wasn't that, so I went to the doctor probably about… at least three weeks later."

Illness delay/behavioral delay

Generally, once patients decided to seek medical care (illness delay), they acted on the decision (behavioral delay). One of the 26 participants noted a gap of five or six days between deciding he needed medical care and seeking care due to health insurance:

> "Every hour or so I would take my temperature and it was just going up and up... And I didn't have insurance. And I thought I have to make it to Monday, because Monday is when my insurance was going to kick in. I said I have got to

> survive until Monday. I mean I would have went that Wednesday or Thursday that I was so sick. I had called somebody I know that's a nurse and she said, 'I don't want you to die on me but get in your bed and don't frickin' move,… until Monday if you can make it.' So, I, I took the words she said to heart and just kind of didn't move the entire weekend."

While no other patients articulated this gap between deciding to seek care and acting on it, health insurance was the most commonly occurring theme regarding the delay in deciding whether to seek medical attention for their symptoms (**Table 2**).

Scheduling delay

Scheduling delay did not emerge as a problem for any of the participants. Ten of the 26 participants initially sought care for symptoms at an urgent care or emergency department setting. Some of these patients noted that they decided to seek medical attention at these establishments because of the weekend and evening hours.

Treatment delay

When present, delays between the first appointment with a health care provider about Lyme disease symptoms and treatment were generally reported to be the result of a misdiagnosis (e.g., cellulitis). Nine of the 26 participants (34.6%) reported that they were not diagnosed with Lyme disease at their first contact with a medical professional regarding Lyme disease symptoms. Seven of these nine participants (77.8%) reported a misdiagnosis that occurred at an urgent care or emergency department setting, representing 70% of patients who first sought care in these settings (**Table 2**). One participant described this experience,

> "No, they [emergency department] didn't do any blood tests... Kind of examined and kind of listened to me. It was very busy that night. I know there was 1 or 2 doctors on and they had a bunch of drunks they were taking care of and things, so I think they may have missed the boat. …the nurse tells my wife, 'You know I think you got to watch because,' I think she said, 'I think there's more here than what it appears.' But that was it, and then they discharged me."

Non-GMTPD themes

Role of family

In multiple stages of the GMTPD, the involvement of family prompted action leading to treatment of Lyme disease. Most commonly, family members prompted patients to call the doctor (reducing illness/behavioral delay). For example:

> "I could no longer read the computer screen. I couldn't read the paper. And she (my wife) said, 'That's it, we're done playing around.' And I ended up at the doctors."

Another example was:

> "She (my sister) said to me, 'That (rash) doesn't look right.' And I said, 'Eh, it'll go away in a couple of days.' So, she told my mom, and my mom called me and said, 'I'm coming up to look at it. I think we should go to the doctor.' I said, 'Ma, it'll be fine.' She said, 'No, I think we should go.' So…, my sister calls and gets an appointment."

Family also played a role in reducing the treatment delay phase, after the patient saw a medical professional. In one instance, a patient was hospitalized for what was originally diagnosed as pain medication dependency. It was not until a family member demanded a transfer to a different hospital that Lyme disease was diagnosed.

> "So, I was there [at the hospital] for three or four days and all of the sudden I developed Bell's palsy. And they did a CAT scan and they determined it was not a stroke. I laid there five more days where they did nothing. My sister and mother came to visit. They would not have recognized me. My face was swollen and droopy. So my sister had me transferred to another hospital. Within hours I was diagnosed with neurological Lyme."

Consequences of delays

The original interview guide did not include questions regarding the impact of Lyme disease on work absenteeism/presentism or changes in productivity at work or home. However, the detrimental impact of Lyme disease on the ability to work and fulfill caregiving roles emerged as a common theme among participants.

> "I couldn't function, and I'm a care-taker for my mother, although she's a good 92 now…She took care of me, but I could not function. I lived on the sofa or in bed. That's how tired I was. If I tried to a do a little bit of anything, I would have to get back down, because I couldn't handle it."

Another person described a change in his work productivity before getting treated for Lyme disease.

> "I'd never sit down at work ever. I have my own machine shop. And I like nobody ever sees me sit. …like it came to the point where I was sitting and then actually at lunchtime and stuff I would actually lay on the bench."

For some of these patients, the impact on work and caregiving persisted after treatment.

> “Yeah, yeah, I was off [work] for quite a while between them actually finally determining it was Lyme disease and the treatment and then the post check-up after the treatment to make sure I was fine. Yeah, I was probably off for at least two months, if not more.”

A second patient explained:

> “I own my own business, I’ve been in business since 1990. It is definitely not the same. I have a hard time spelling words. I mean you got to go in, you got to sell yourself, you got to get all the work and, it’s just tough anymore. I just don’t have the, it’s hard to put things together, you know what I mean, like on the fly. Like with words and everything. You seem to lose that edge and I don’t know how to explain it. You know and everybody says, ‘Oh you got old,’ but it just like changed instantly.”

DISCUSSION

We conducted the first study, to our knowledge, to explore the experiences associated with the time between onset of symptoms and treatment of Lyme disease, with a specific focus on identifying themes related to belated treatment. Our study identified barriers to timely treatment that have been observed in other disease areas, as well as barriers specific to Lyme disease. We identified potential knowledge gaps in Lyme disease among patients and medical professionals, including misperceptions about the necessity of a bull’s-eye rash. Understanding the conditions that participants perceive contribute to treatment delays can inform strategies that promote prompt treatment of Lyme disease, preventing dissemination of infection and the resulting disease complications.

Application of the GMTPD to Lyme disease was very instructive and showed that Lyme disease generally conformed to the model. The appraisal stage emerged as a distinct and dominant phase, as has been observed when this model has been applied to other diseases (Scott et al., 2012; Smith, Pope, & Botha, 2005; Evans, Ziebland, & McPherson, 2006). We identified three appraisal delay themes: symptom misattribution, intermittent symptoms, and lack of bull's-eye rash. Both the intermittent nature of symptoms as well as the symptom misattribution to less serious or pre-existing conditions has been reported to account for appraisal delays in various cancers, particularly when the early symptoms were commonly occurring non-specific symptoms (e.g. fatigue) (Evans, Chapple, Salisbury, Corrie, & Ziebland, 2014; Brouha, Tromp, Hordijk, Winnubst, & de Leeuw, 2005). Specific to Lyme disease, respondents misattributed the joint pain of Lyme disease to other conditions with joint pain, such as rheumatoid arthritis and fibromyalgia.

Appraisal delays also resulted from a misunderstanding of the characteristic Lyme disease rash, erythema migrans. Specifically, participants reported that they did not suspect Lyme disease if they did not have a rash with central clearing, referred to as a bull's-eye rash. Approximately 20 to 30% of people with Lyme disease do not present with erythema migrans and among those who do have the rash, only 19% have the stereotypical bull's-eye appearance (Tibbles & Edlow, 2007). The impact of the belief in the necessity of central clearing on belated treatment is compounded by the diagnostic challenges associated with Lyme disease in the absence of the rash. One study reported that 54% of patients with Lyme disease who did not have erythema migrans were initially misdiagnosed compared to 23% of patients who did have erythema migrans (Aucott et al., 2009). Our findings highlight an important knowledge gap among patients regarding the skin manifestations of Lyme disease. Patient education campaigns that address this issue could reduce the time between infection and treatment.

The illness and behavioral delay stages appeared to be most influenced by health insurance status. Our findings are consistent with delays attributed to lack of health insurance observed in other disease areas. A lack of insurance has been associated with longer pre-hospital delays in myocardial infarction (Nguyen, Saczynski, Gore, & Goldberg, 2010; Smolderen et al., 2010) and with care-seeking behavior in cancer (Rauscher et al., 2010). It is unknown whether the belated treatment due to lack of health insurance translate into an increased risk of late Lyme disease among the uninsured.

Scheduling delay was not a major contributor to belated treatment in our study, as nearly half of patients we interviewed sought care at emergency departments or urgent care centers, medical settings that typically offer same-day, evening, and weekend appointments. While the availability of urgent care clinics and emergency departments appeared to minimize scheduling delays, the patients who first sought care at these locations reported more occurrences of misdiagnoses. Thus, the time saved in the scheduling delay stage by seeking care in one of these settings could be outweighed by the treatment delays resulting from misdiagnoses in these settings. The number of urgent care settings have dramatically increased over the last decade, but little is known regarding the quality of care for Lyme disease in these settings (Yee, Lechner, & Boukus, 2013).

Family interventions were identified to decrease the time to treatment in Lyme disease, consistent with the role of family and friends in belated treatment for cancer and cardiovascular disease (Perkins-Porras, Whitehead, Strike, & Steptoe, 2009; Barr, McKinley, O'Brien, & Herkes, 2006). Smith and colleagues (2005) reported that, for many patients with cancer, friends and family helped with the process of illness attribution (Smith et al., 2005) by observing or discussing vague symptoms with patients, ultimately making the connection between symptoms and illness that had gone unrecognized by the patient. The extent to which family structure, marital status, and social support play a role in Lyme disease diagnosis and treatment has not been studied.

The impact of Lyme disease on work and caregiving activities emerged as a salient theme for participants, impacting patients prior to treatment and, in some cases, even after treatment. While costs occurring after a Lyme disease diagnosis have been studied (Adrion, Aucott, Lemke, & Weiner, 2015), these studies do not account for the time between infection and treatment of disease, likely underestimating costs. Specifically, little is known about the indirect costs resulting from lost productivity (Zhang et al., 2006). A comprehensive study of indirect and direct costs of Lyme disease before and after treatment would give a more complete picture of the individual and population-level burden of this disease.

To our knowledge, this is the first study to evaluate the application of GMTPD to Lyme disease. Through the lens of this model we identified distinct phases between onset of first Lyme disease symptoms and Lyme disease treatment. Our study was conducted in a well-defined sample of participants with a positive IgG Western blot, a lab result present only at least six to eight weeks after Lyme disease infection. Our study had limitations. First, while our patients described interactions with health systems beyond Geisinger, all participants were tested for Lyme disease at Geisinger. However, with more than 44 Geisinger community practice sites and 12 hospital campuses across a large geographic region, there is likely a great deal of diversity in Lyme disease diagnosis and treatment experiences within the health system. Second, the objective of this study was not to quantify the extent to which each delay phase contributed to belated treatment in Lyme disease. We identified several explanations for belated treatment of Lyme disease that are intervenable and can be targeted to minimize time to treatment and reduce the burden of Lyme disease on patients and society. To prioritize resources around secondary prevention strategies in Lyme disease, a quantitative study is needed to both determine how much each phase contributes to belated treatment and to quantify the degree to which factors increase risk of belated treatment.

Author contribution: AH, AR, KM, JA, CH, and BS participated in the design of the study; AH conducted data collection; AH and RH conducted data analysis; all authors participated in the writing of the manuscript.

References

Adrion, E. R., Aucott, J., Lemke, K. W., & Weiner, J. P. (2015). Health care costs, utilization and patterns of care following Lyme disease. *PloS One, 10*(2).

Andersen, B. L., Cacioppo, J. T., & Roberts, D. C. (1995). Delay in seeking a cancer diagnosis: Delay stages and psychophysiological comparison processes. *British Journal of Social Psychology, 34*(1), 33-52.

Aucott, J., Morrison, C., Munoz, B., Rowe, P. C., Schwarzwalder, A., & West, S. K. (2009). Diagnostic challenges of early Lyme disease: Lessons from a community case series. *BMC Infectious Diseases, 9*(1), 79.

Barr, J., McKinley, S., O'Brien, E., & Herkes, G. (2006). Patient recognition of and response to symptoms of TIA or stroke. *Neuroepidemiology, 26*(3), 168-175.

Brouha, X. D., Tromp, D. M., Hordijk, G., Winnubst, J. A., & de Leeuw, R. J. (2005). Oral and pharyngeal cancer: Analysis of patient delay at different tumor stages. *Head & Neck, 27*(11), 939-945.

Centers for Disease Control and Prevention. Lyme Disease: Data and statistics. (2017). Retrieved from https://www.cdc.gov/lyme/stats/index.html

Centers for Disease Control and Prevention. Lyme Disease: Understanding the Immunoblot Test. (2015). Retrieved from https://www.cdc.gov/lyme/diagnosistesting/labtest/twostep/westernblot/index.html

Corbin, J., & Strauss, A. (2008). Basics of qualitative research: Techniques and procedures for developing grounded theory (3rd ed.). Thousand Oaks, CA: Sage Publications Inc.

Elo, S., & Kyngäs, H. (2008). The qualitative content analysis process. *Journal of Advanced Nursing, 62*(1), 107-115.

Evans, J., Ziebland, S., & McPherson, A. (2006). Minimizing delays in ovarian cancer diagnosis: An expansion of Andersen's model of ‘total patient delay’. *Family Practice, 24*(1), 48-55.

Evans, J., Chapple, A., Salisbury, H., Corrie, P., & Ziebland, S. (2014). "It can't be very important because it comes and goes" – patients' accounts of intermittent symptoms preceding a pancreatic cancer diagnosis: A qualitative study. *BMJ Open, 4*(2).

Mead, P. S. (2015). Epidemiology of Lyme disease. *Infectious Disease Clinics of North America, 29*(2), 187-210.

Nelson, C. A., Saha, S., Kugeler, K. J., Delorey, M. J., Shankar, M. B., Hinckley, A. F., & Mead, P. S. (2015). Incidence of clinician-diagnosed Lyme disease. *Emerging Infectious Diseases, 21*(9), 1625-1631.

Nguyen, H. L., Saczynski, J. S., Gore, J. M., & Goldberg, R. J. (2010). Age and sex differences in duration of prehospital delay in patients with acute myocardial infarction: A systematic review. *Circulation.Cardiovascular Quality and Outcomes, 3*(1), 82-92.

Perkins-Porras, L., Whitehead, D. L., Strike, P. C., & Steptoe, A. (2009). Pre-hospital delay in patients with acute coronary syndrome: Factors associated with patient decision time and home-to-hospital delay. *European Journal of Cardiovascular Nursing, 8*(1), 26-33.

Rauscher, G. H., Ferrans, C. E., Kaiser, K., Campbell, R. T., Calhoun, E. E., & Warnecke, R. B. (2010). Misconceptions about breast lumps and delayed medical presentation in urban breast cancer patients. *Cancer Epidemiology, Biomarkers & Prevention, 19*(3), 640-647.

Scott, S., Walter, F., Webster, A., Sutton, S., & Emery, J. (2012). The model of pathways to treatment: Conceptualization and integration with existing theory. *British Journal of Health Psychology, 18*(1), 45-65.

Smith, L. K., Pope, C., & Botha, J. L. (2005). Patients' help-seeking experiences and delay in cancer presentation: A qualitative synthesis. *The Lancet, 366*(9488), 825-831.

Smolderen, K. G., Spertus, J. A., Nallamothu, B. K., Krumholz, H. M., Tang, F., Ross, J. S., Chan, P. S. (2010). Health care insurance, financial concerns in accessing care, and delays to hospital presentation in acute myocardial infarction. *Jama, 303*(14), 1392-1400.

Tibbles, C. D., & Edlow, J. A. (2007). Does this patient have erythema migrans? *Jama, 297*(23), 2617-2627.

Yee, T., Lechner, A. E., & Boukus, E. R. (2013). The surge in urgent care centers: Emergency department alternative or costly convenience. *Research Brief, (26), 1-6.*

Zhang, X., Meltzer, M. I., Pena, C. A., Hopkins, A. B., Wroth, L., & Fix, A. D. (2006). Economic impact of Lyme disease. *Emerging Infectious Diseases, 12*(4), 653-660.

Table 1. Characteristics and Lyme disease symptoms, signs, and diagnosis patterns of participants (n = 26)	
Age, years, n (%)	
18-39	9 (34.6)
40-64	11 (42.3)
65+	6 (23.1)
Female, n (%)	14 (53.8)
Race/ethnicity, n (%)	
White, non-Hispanic	26 (100)
Ever received Medical Assistance, n (%)	8 (30.1)
Rash, n (%)	
"Bulls-eye" rash	3 (11.5)
Other rash	7 (26.9)
No rash	16 (61.5)
First symptom recalled[1], n (%)	
Joint pain/swelling	7 (26.9)
Rash	4 (15.4)
Fatigue	4 (15.4)
Headache	3 (11.5)
Other	9 (34.6)
Symptom that triggered first contact with medical provider, n (%)	
Joint pain	9 (34.6)
Rash	4 (44.4)
Fatigue	3 (11.5)
Bell's palsy	2 (7.7)
Other	8 (30.7)
Self-reported Lyme-related diagnoses, n (%)	
Joint pain (diagnosis of Lyme arthritis not specified)	10 (38.5)
Bell's Palsy	8 (30.7)
Carditis	2 (7.7)
Meningitis	1 (3.8)
First medical care provider contacted, n (%)	
Urgent care/emergency department	10 (38.5)
Primary care provider	13 (50.0)
Other	3 (11.5)
Misdiagnosed by medical provider, n (%)	9 (34.6)
Medical care provider who misdiagnosed[2], n (% of misdiagnoses)	
Urgent care/emergency department (both)	7 (77.8)
Primary care provider	4 (44.4)

1. Total greater than 26 because one participant reported pain and rash occurred at the same time.
2. Total greater than 9 because two patients were misdiagnosed by both emergency department and primary care physician.

Table 2. Participant quotes regarding the General Model of Total Patient Delay stages

Stage / domain	Quotes from participants during in-depth interviews
Appraisal	
Intermittent symptoms	• I never really had more than one spot at the same time, I never had like my feet hurt, my shoulders hurt. I never had like my elbows hurt and my knee hurt. Normally it was one spot at a time. And it just rotated, like I said one spot hurt, then like it could disease be weeks later, another spot would hurt, and then it'd go back to the other spot." • It was mostly my knees and my legs, a little bit in my arms every now and then, but it wasn't consistent like it was in my legs.
Misattribution	• I got a new computer, and I thought that it was not positioned correctly and because I was just on the computer pretty much all day and maybe through I strained by neck. • I was just kind of dealing with it because I thought maybe I slept on it [elbow] wrong or something. • My joints hurt, but I have rheumatoid arthritis, so I never associated it with LYME DISEASE, because I've had rheumatoid arthritis for many years, and I thought I was just getting another flare, so all the symptoms for my joint pain, I just associated with my rheumatoid condition.
Rash pattern	• I didn't think of Lyme, because it was it wasn't a bull's eye at all. • And it started growing and growing and, interestingly enough, it didn't assume the kind of quintessential bull's eye pattern. I always jokingly refer to it as a political boundary. It looked more like a map of the world, it was very, while it was roughly circular in shape, it was very jutted in and out it looked more like Antarctica on my arm. • Because you know we're in the kind of live in the country, you hear about it and knew a couple people that had had it, but they had all you know had gotten the typical symptoms of you know, the red bulls-eye.
Illness/behavioral delay	
Health insurance	• So, I mean I just did as good as I could [to get the tick out]… but I wasn't sure that I got it all and I didn't have insurance at the point, so I didn't bother to go to the doctor. So, I just let it go, figured I wait and see, stupid idea. • I didn't have insurance. That was one of the main things. And, like I said, I was young, and I was just starting a new job, so I didn't have a lot of money. So, I was like, I don't know how I'll pay for that.
Treatment delay	
Emergency department and urgent care settings	• I saw my primary care physician about two weeks later [after emergency department visit.] And that's when she told me that I had the Lyme disease and then she said they [emergency department] had suspected it while I was in the emergency room, and nothing was ever given to me then. The test was done in the ER. Because I remember she [primary care physician] was mad that nobody there had contacted me and she said they, you know,,could've gotten me started sooner on the medication." • I went up to the ER and they told disease me I had bursitis. Either bursitis or tendonitis. And told me that I'm to check back if I have any more issues. Well, it was still excruciating I went back before the week was up. That's when they told me I had the opposite, either bursitis or tendonitis. One of them. One or the other was, they thought the issue was, well it never went away. My doctor was out on vacation and I had called the office and… I said when she gets back, I need to see her ASAP. So, she had called and she got a hold of me and went back down into the office and as soon as she came in, she told me right away, I bet you have Lyme disease.

Standards for Reporting Qualitative Research (SRQR) Checklist

Topic	**Item**	**Author Response**
S1 Title	Concise description of the nature and topic of the study. Identifying the study as qualitative or indicating the approach or data collection methods is recommended.	Page 1, Title page: The title identifies the study as qualitative: “Obstacles to diagnosis and treatment of Lyme disease: A qualitative study”
S2 Abstract	Summary of key elements using the abstract format of the intended publication.	Page 2, Abstract: The abstract adheres to journal specifications.
S3 Problem formulation	Description and significance of the problem/phenomenon studied: review of relevant theory and empirical work; problem statement.	Page 4: Paragraph 1 describes the risks associated with late diagnosis and treatment of Lyme disease. Paragraph 2 describes the application of the General Model of Total Patient Delay to the study of delayed treatment.
S4 Purpose or research question	Purpose of the study and specific objectives or questions.	Page 5: Paragraph 1 states that the objective of the paper is “to identify themes around belated treatment, as well as to evaluate the application of the General Model of Total Patient Delay to Lyme disease…”
S5 Qualitative approach and research paradigm	Qualitative approach and guiding theory; identifying the research paradigm is also recommended.	Page 5: Paragraph 2 states that the interview findings were analyzed through the theory of General Model of Total Patient Delay. Page 6: Paragraph 1 states, “We applied a deductive content analysis of interview transcripts based on the General Model of Total Patient Delay.”
S6 Researchers’ characteristics and reflexivity	Researchers’ characteristics that may influence the research; potential or actual interaction between researchers’ characteristics and the research questions, approach, methods, results, and/or transferability.	Page 6: Paragraph 2 states: “The interviewer is a researcher employed by the health system that treated participants for Lyme disease. To address any concerns participants might have had in describing their care experiences to a health system employee, the interviewer informed participants that their responses would not impact the care received at Geisinger and would be kept confidential.”
S7 Context	Setting/site and salient contextual factors.	Page 5: The section “Study setting and sample” describes the study setting. Page 6: Paragraph 2 states: We conducted in-depth, semi-structured, open-ended telephone interviews… Telephone interviews allowed for capture of patient experiences across the large geographic area served by Geisinger.”
S8 Sampling strategy	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary; rationale.	Pages 5-6: The “Study setting and sample” section describes the sample, how they were selected, criteria for selection, rationale for selection, and explains that recruitment continued until data saturation.
S9 Ethical issues pertaining to human subjects	Documentation of approval by an appropriate ethics review board.	Page 5: First paragraph in the “Methods” section states that the study was approved by the Geisinger Institutional Review Board.
S10 Data collection methods	Types of data collected; details of data collection procedures; rationale	Page 6: The “Data Collection” section describes the methods for data collection, including the use

		of telephone interviews; the types of questions asked; and the timeframe of the interviews. Page 7: The “Analysis” section describes the application of deductive content analysis; the coding process; and the use of the General Model of Total Patient Delay to develop higher-order codes.
S11 Data collection instruments	Description of instruments	Page 6: The “Data Collection” section describes six categories of questions included in the interview guide. Page 7: The “Analysis” section notes: “The coding team also updated the interview guide to incorporate questions around emergent themes for future interviews.”
S12 Units of study	Number and relevant characteristics of participants	Pages 7-8: The first three paragraphs of the “Results” section describe the study participants. Table 1: Characteristics and Lyme disease symptoms, signs, and diagnosis patterns of participants
S13 Data processing	Methods for processing data prior to and during analysis.	Page 7: The “Data Collection” section notes that all interviews were audio-recorded and transcribed verbatim.
S14 Data analysis	Process by which inferences , themes, etc., were identified and developed.	Page 7: The “Analysis” section describes the data analysis process, including the identification of themes and the application of the General Model of Total Patient Delay.
S15 Techniques to enhance trustworthiness	Techniques to enhance trustworthiness and credibility of data analysis.	Page 7: The “Analysis” section describes the use of two coders and the requirement of consensus on the coding framework, coding, and identification of emergent themes.
S16 Synthesis and interpretation	Main findings	Pages 7-13: “Results are presented on these pages as well as in Tables 1 and 2.
S17 Links to empirical data	Evidence (e.g. quotes) to substantiate findings.	Pages 8-13: Quotes are embedded in the “Results” section and presented in Table 2.
S18 Integration with prior work, implications, transferability, and contributions to the field.	Short summary of main findings; explanation of how findings and conclusions…connect to earlier scholarship; unique contribution.	Pages 13-17: The “Discussion” section summarizes the main findings, links the findings to prior works, and describes the contribution of this manuscript to the field.
S19 Limitations	Trustworthiness and limitations of findings	Pages 16 and 17 describe the limitations of the study.
S20 Conflicts of interest	Potential sources of influence	Page 3: No competing interests were declared by authors.
S21 Funding	Sources of funding	Page 3: This work was supported by the Steve & Alexandra Cohen Foundation. The Steve and Alexandra Cohen Foundation did not participate in data collection, analysis, or the writing of this manuscript.

BMJ Open

Obstacles to diagnosis and treatment of Lyme disease in the U.S.: A qualitative study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-021367.R1
Article Type:	Research
Date Submitted by the Author:	08-Mar-2018
Complete List of Authors:	Hirsch, Annemarie; Geisinger, Department of Epidemiology and Health Services Research Herman, Rachel; Gettysburg College Rebman, Alison; Johns Hopkins School of Medicine, Department of Medicine, Division of Rheumatology Moon, Katherine; Johns Hopkins University Bloomberg School of Public Health, Department of Environmental Health and Engineering Aucott, John; Johns Hopkins School of Medicine, Department of Medicine, Division of Rheumatology Heaney, Christopher; Johns Hopkins University Bloomberg School of Public Health, Department of Environmental Health and Engineering; Johns Hopkins University Bloomberg School of Public Health, Department of Epidemiology Schwartz, BS; Geisinger, Department of Epidemiology and Health Services Research; Johns Hopkins University Bloomberg School of Public Health, Department of Environmental Health and Engineering
Primary Subject Heading:	Qualitative research
Secondary Subject Heading:	Infectious diseases
Keywords:	QUALITATIVE RESEARCH, SOCIAL MEDICINE, Patient delay, Lyme disease

Obstacles to diagnosis and treatment of Lyme disease in the U.S.: A qualitative study

Annemarie G. Hirsch[1], PhD, MPH; Rachel J. Herman[2]; Alison Rebman[3], MPH; Katherine Moon[4], PhD; John Aucott[3], MD; Christopher Heaney[4,5], PhD; Brian S. Schwartz[1,4], MD, MS

1. Department of Epidemiology and Health Services Research, Geisinger
2. Gettysburg College
3. Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine
4. Department of Environmental Health and Engineering, Johns Hopkins University Bloomberg School of Public Health
5. Department of Epidemiology, Johns Hopkins University Bloomberg School of Public Health

Corresponding author:
Annemarie Hirsch, PhD, MPH
Assistant Professor
Department of Epidemiology and Health Services Research
Geisinger
Danville, PA 17822
aghirsch@geisinger.edu
267-626-8810

Abstract

Objective For many individuals with Lyme disease, prompt treatment leads to rapid resolution of infection. However, severe complications can occur if treatment is delayed. Our objective was to identify themes around belated diagnosis or treatment of Lyme disease using the General Model of Total Patient Delay (GMTPD).

Design We conducted a qualitative interview study using in-depth telephone interviews.

Setting Participants were patients from a large, integrated health system in the state of Pennsylvania.

Participants There were 26 participants. Participants had to have a diagnosis of Lyme disease between 2014 and 2017 and a positive IgG Western blot. We used a stratified purposeful sampling design to identify patients with and without late Lyme disease manifestations. To ensure variation in care experiences, we oversampled patients diagnosed outside of primary care.

Outcome measures We asked participants about their experience from first Lyme disease symptoms to treatment. We applied an iterative coding process to identify key themes and then synthesized codes into higher order codes representing the GMTPD stages: appraisal delay (symptom to recognition of illness); illness delay (inferring illness to deciding to seek help); behavioral delay (deciding to seek help to the act of seeking help); scheduling delay (seeking help to attending an appointment); and treatment delay (attending appointment to treatment).

Results Appraisal delay themes included symptom misattribution; intermittent symptoms; and misperceptions about the necessity of a bull's-eye rash. Health insurance status was a driver of illness and behavioral delay. Scheduling delay was not noted by participants, in part, because 10 of 26 patients went to urgent care or emergency department settings. Misdiagnoses were more common in these settings, contributing to treatment delay.

Conclusion Our study identified potentially modifiable risk factors for belated treatment. Targeting these risk factors may minimize time to treatment and reduce the occurrence of preventable complications.

Strengths and limitations of this study

- To our knowledge, this is the first study to examine which factors account for belated treatment of Lyme disease.
- Through the lens of the General Model of Total Patient Delay, a widely used model that describes the decisional processes and potential delays prior to treatment, we identified distinct phases between onset of first Lyme disease symptoms and Lyme disease treatment.
- This study was conducted in a well-defined sample of participants who had both a Lyme disease diagnosis and a positive IgG Western blot.
- The study was conducted in a health system in the U.S. Some findings may not be generalizable to other countries due to differences in factors such as healthcare cost and access.
- While our eligibility criteria were highly specific for Lyme disease, requiring a positive IgG Western blot may have excluded patients who received care in the first few weeks of infection, when the test is expected to be negative.

Funding: This work was supported by the Steve & Alexandra Cohen Foundation. The Steve and Alexandra Cohen Foundation did not participate in data collection, analysis, or the writing of this manuscript.

Competing interests: None declared

Data sharing: Interview guide and codebook available by request to corresponding author.

Lyme disease is a tick-borne infectious disease that is on the rise in the Northeast, Mid-Atlantic, and Upper Midwest regions of the United States (Nelson et al., 2015). Delays in diagnosis or treatment (hereafter referred to as belated treatment) of Lyme disease can lead to preventable complications, representing later stages of the disease when the infection disseminates, including neurologic manifestations, cardiac abnormalities, and arthritis (Mead, 2015). While little is known about the prevalence of belated treatment in Lyme disease, the observation that 32% of Lyme disease cases are diagnosed with arthritis, 12% with neurologic conditions, and 1-2% with carditis (Mead, 2015) suggests that belated treatment may occur in as many as 40% of cases. To date, the study of time to treatment has largely focused on cancer and cardiovascular events (Scott, Walter, Webster, Sutton, & Emery, 2012). No study has examined which factors account for belated treatment of Lyme disease, despite the benefits of prompt treatment of this disease.

The General Model of Total Patient Delay (GMTPD) (Andersen, Cacioppo, & Roberts, 1995) is a widely used, five-stage model that describes the decisional processes and potential delays prior to treatment (Scott et al., 2012). Appraisal delay is the time between when a person first notices an unexplained symptom until the person concludes he/she is ill. Appraisal has generally been found to be the key determinant in delay in seeking help (Scott et al., 2012). Illness delay is the time between inferring illness and deciding to seek help; behavioral delay represents the time between deciding an illness requires medical care and acting; scheduling delay is the time between deciding to seek help and attending an appointment; and treatment delay is the time between the first appointment with a health care provider and onset of treatment (Andersen et al., 1995). While this model has been widely applied to cancer and myocardial infarction, it has not been applied to Lyme disease. Thus, the primary drivers of belated treatment in Lyme disease remain unknown.

To identify themes around belated treatment, as well as to evaluate the application of the GMTPD to Lyme disease, we interviewed 26 patients with a diagnosis of Lyme disease to gain insight into their experiences between onset of Lyme disease symptoms and treatment. Such understanding is critical to informing strategies that would reduce time to diagnosis and treatment and prevent late stage Lyme disease.

METHODS

We conducted a qualitative study using in-depth telephone interviews of Geisinger patients with a Lyme disease diagnosis to understand what happens between the onset of Lyme disease symptoms and treatment. We analyzed interview findings through the GMTPD framework. This study was approved by the Geisinger Institutional Review Board.

Study setting and sample

We identified study participants using the electronic health record (EHR) from Geisinger, an integrated health system servicing more than 45 counties in Pennsylvania and New Jersey, both high-incidence states for Lyme disease (Centers for Disease Control and Prevention [CDC], 2017). Patients were eligible if they were at least 18 years of age; had an International Classification of Disease code (ICD-9: 088.81 or ICD-10: A69.20) for Lyme disease associated with at least one clinical encounter between 2014 and 2017; and an IgG Western blot meeting CDC criteria of five or more positive bands (CDC, 2015). We used a stratified purposeful sampling design to identify patients with and without late Lyme disease manifestations: Lyme arthritis (ICD-9: 711.8x; ICD-10: M01.X0); facial palsy (ICD-9: 351.0, 352.9; ICD-10: G51.0; G52.9); meningoencephalitis (ICD-9: 320.7; ICD-10: G01); or myocarditis (ICD-9: 422.0; ICD-10: I41). To ensure variation in care experiences, we oversampled patients diagnosed outside of primary care. We first sent letters to notify 93 patients (47 with late manifestations and 46 without) that they were eligible for the study. Two weeks later we telephoned patients to schedule a telephone interview. Participants who completed an interview received a $50 gift card. Recruitment continued until data saturation, the point at which no new information seemed to emerge during coding (Corbin & Strauss, 2008).

Data collection

We conducted in-depth, semi-structured, open-ended telephone interviews between August and September 2017, each lasting approximately 30 minutes. Telephone interviews allowed for capture of patient experiences across the large geographic area served by Geisinger. Geisinger's Institutional Review Board waived the requirement of written consent after determining that the study posed no more than minimal risk of harm to participants. An experienced interviewer (first author AGH) obtained verbal consent and asked participants to talk about their experience with Lyme disease, from symptom onset to treatment. The interviewer was a researcher employed by the health system that treated participants for Lyme disease. To address any potential concerns participants might have had in describing their care experiences to a health system employee, the interviewer informed participants that their responses would not impact the care received at Geisinger and would be kept confidential. The

interviewer then used an interview guide to follow-up on the account that included questions in six primary areas: Lyme disease knowledge; pre-treatment symptoms; care-seeking behavior; diagnosis process; treatment process; and post-treatment symptoms. All interviews were audio-recorded and transcribed verbatim. No additional field notes were recorded. We did not return transcripts to participants for comment or correction.

Analysis

We applied a deductive content analysis of interview transcripts, based on the GMTPD (Elo & Kyngäs, 2008). We applied an iterative coding process to identify themes corresponding to the six primary areas as well as emergent themes. After the first five interviews, one of two coders reviewed the transcripts to develop a preliminary coding framework. A second coder then applied the framework to the same five interviews. The coding team (2 members) discussed findings and reached consensus on an updated coding scheme, revising the scheme as new themes emerged. The coding team also updated the interview guide to incorporate questions around emergent themes for future interviews. In the final phase of analysis, the coders developed higher order categories representing the five delay stages of the GMTPD. Analysis was conducted using Atlas.ti.7.

Patient and Public Involvement

Patients were not involved in the development of the research question, the design, recruitment, or conduct of this study. Results of this study will be disseminated to study participants via letter and disseminated to patients via health system print newsletters and social media outlets.

RESULTS

Out of the 93 patients to whom we sent a letter, we telephoned 56 patients and reached 33. Of these, 26 (79%) agreed to be interviewed. We stopped recruitment calls after reaching saturation. While the interviewers were intended to be one-on-one, two patients had a spouse with them in the room during the interview. In one case, a spouse joined the call. However, analysis was confined to the information presented by the 26 patients.

Slightly more than half of participants were female; 30% had a history of being on Medical Assistance (a surrogate for low family socioeconomic status) (Casey J.A., Pollak, J., Glymour M.M., Mayeda E.R., Hirsch A.G., & Schwartz B.S., 2018); and participants ranged in age from 22 to 70 years (**Table 1**). Half of the participants first sought care for Lyme disease from a primary care provider and 38.5% first went to an urgent care center or emergency department.

Ten participants reported that they had a rash, three of whom described the rash as a bull's-eye. Four of the participants who reported a rash sought care because of the rash. The remaining did not seek care until other symptoms (e.g., fatigue, joint pain) appeared. Two of the four participants who saw a doctor because of the rash were initially misdiagnosed. Eleven participants reported having joint pain, though patients did not specify whether the joint pain was diagnosed as Lyme arthritis. Eight patients reported having Bell's palsy, two patients reported carditis, and one patient reported a diagnosis of Lyme meningitis.

A number of themes emerged regarding seeking care for Lyme disease symptoms. We classified these themes into one of the five GMTPD stages (**Table 2**).

Participants reported seeking care both within and external to Geisinger for their initial Lyme disease symptoms, but we did not ask in which health care system delays occurred.

GMTPD Stages

Appraisal delay

Participants consistently reported an appraisal delay, a gap between their first symptom and recognition that they were ill (**Table 2**). Some participants attributed this gap to the inconsistent nature of their symptoms. One participant explained,

> "I was just having occasional joint achiness where it kind of felt like I slept funny on my elbow. It would be sore for a day or two and then it would go away."

Patients also misattributed symptoms to minor injuries, pre-existing conditions, or the flu. One participant noted, "I also have fibromyalgia, so it's kind of hard to differentiate."

Patients ruled out Lyme disease in the absence of the bull's-eye rash perceived to be characteristic of Lyme disease, delaying medical attention even in the presence of a rash. One participant explained,

> "And then I got a like this rash on my legs, on my arms, on my back. It was really bad. And I didn't even know about Lyme disease at that time… I mean I knew that you'd get a bull's-eye rash. And it wasn't that, so I went to the doctor probably about… at least three weeks later."

Illness delay/behavioral delay

Generally, once patients decided to seek medical care (illness delay), they acted on the decision (behavioral delay). One of the 26 participants noted a gap of five or six days between deciding he needed medical care and seeking care due to health insurance:

> "Every hour or so I would take my temperature and it was just going up and up... And I didn't have insurance. And I thought I have to make it to Monday, because Monday is when my insurance was going to kick in. I said I have got to survive until Monday. I mean I would have went that Wednesday or Thursday that I was so sick. I had called somebody I know that's a nurse and she said, 'I don't want you to die on me but get in your bed and don't frickin' move,… until Monday if you can make it.' So, I, I took the words she said to heart and just kind of didn't move the entire weekend."

While no other patients articulated this gap between deciding to seek care and acting on it, health insurance was the most commonly occurring theme regarding the delay in deciding whether to seek medical attention for their symptoms (**Table 2**).

Scheduling delay

Scheduling delay did not emerge as a problem for any of the participants. Ten of the 26 participants initially sought care for symptoms at an urgent care or emergency department setting. Some of these patients noted that they decided to seek medical attention at these establishments because of the weekend and evening hours.

Treatment delay

When present, delays between the first appointment with a health care provider about Lyme disease symptoms and treatment were generally reported to be the result of a misdiagnosis (e.g., cellulitis). Nine of the 26 participants (34.6%) reported that they were not diagnosed with Lyme disease at their first contact with a medical professional regarding Lyme disease symptoms. Seven of these nine participants (77.8%) reported a misdiagnosis that occurred at an urgent care or emergency department setting, representing 70% of patients who first sought care in these settings (**Table 2**). One participant described this experience,

> "No, they [emergency department] didn't do any blood tests... Kind of examined and kind of listened to me. It was very busy that night. I know there was 1 or 2 doctors on and they had a bunch of drunks they were taking care of and things, so I think they may have missed the boat. …the nurse tells my wife, 'You know I think you got to watch because,' I think she said, 'I think there's more here than what it appears.' But that was it, and then they discharged me."

Non-GMTPD themes

Role of family

In multiple stages of the GMTPD, the involvement of family prompted action leading to treatment of Lyme disease. Most commonly, family members prompted patients to call the doctor (reducing illness/behavioral delay). For example:

> "I could no longer read the computer screen. I couldn't read the paper. And she (my wife) said, 'That's it, we're done playing around.' And I ended up at the doctors."

Another example was:

> "She (my sister) said to me, 'That (rash) doesn't look right.' And I said, 'Eh, it'll go away in a couple of days.' So, she told my mom, and my mom called me and said, 'I'm coming up to look at it. I think we should go to the doctor.' I said,

> 'Ma, it'll be fine.' She said, 'No, I think we should go.' So…, my sister calls and gets an appointment."

Family also played a role in reducing the treatment delay phase, after the patient saw a medical professional. In one instance, a patient was hospitalized for what was originally diagnosed as pain medication dependency. It was not until a family member demanded a transfer to a different hospital that Lyme disease was diagnosed.

> "So, I was there [at the hospital] for three or four days and all of the sudden I developed Bell's palsy. And they did a CAT scan and they determined it was not a stroke. I laid there five more days where they did nothing. My sister and mother came to visit. They would not have recognized me. My face was swollen and droopy. So my sister had me transferred to another hospital. Within hours I was diagnosed with neurological Lyme."

Consequences of delays

The original interview guide did not include questions regarding the impact of Lyme disease on work absenteeism/presenteeism or changes in productivity at work or home. However, the detrimental impact of Lyme disease on the ability to work and fulfill caregiving roles emerged as a common theme among participants.

> "I couldn't function, and I'm a care-taker for my mother, although she's a good 92 now…She took care of me, but I could not function. I lived on the sofa or in bed. That's how tired I was. If I tried to a do a little bit of anything, I would have to get back down, because I couldn't handle it."

Another person described a change in his work productivity before getting treated for Lyme disease.

> "I'd never sit down at work ever. I have my own machine shop. And I like nobody ever sees me sit. …like it came to the point where I was sitting and then actually at lunchtime and stuff I would actually lay on the bench."

For some of these patients, the impact on work and caregiving persisted after treatment.

> "Yeah, yeah, I was off [work] for quite a while between them actually finally determining it was Lyme disease and the treatment and then the post check-up after the treatment to make sure I was fine. Yeah, I was probably off for at least two months, if not more."

A second patient explained:

> "I own my own business, I've been in business since 1990. It is definitely not the same. I have a hard time spelling words. I mean you got to go in, you got to sell yourself, you got to get all the work and, it's just tough anymore. I just don't have the, it's hard to put things together, you know what I mean, like on the fly. Like with words and everything. You seem to lose that edge and I don't know how to explain it. You know and everybody says, 'Oh you got old,' but it just like changed instantly."

DISCUSSION

We conducted the first study, to our knowledge, to explore the experiences associated with the time between onset of symptoms and treatment of Lyme disease, with a specific focus on identifying themes related to belated treatment. Our study identified barriers to timely treatment that have been observed in other disease areas, as well as barriers specific to Lyme disease. We identified potential knowledge gaps in Lyme disease among patients and medical professionals, including misperceptions about the necessity of a bull's-eye rash. Understanding the conditions that participants perceive contribute to treatment delays can inform strategies that promote prompt treatment of Lyme disease, preventing dissemination of infection and the resulting disease complications.

Application of the GMTPD to Lyme disease was very instructive and showed that Lyme disease generally conformed to the model. The appraisal stage emerged as a distinct and dominant phase, as has been observed when this model has been applied to other diseases (Scott et al., 2012; Smith, Pope, & Botha, 2005; Evans, Ziebland, & McPherson, 2006). We identified three appraisal delay themes: symptom misattribution, intermittent symptoms, and lack of bull's-eye rash. Both the intermittent nature of symptoms as well as the symptom misattribution to less serious or pre-existing conditions has been reported to account for appraisal delays in various cancers, particularly when the early symptoms were commonly occurring non-specific symptoms (e.g. fatigue) (Evans, Chapple, Salisbury, Corrie, & Ziebland, 2014; Brouha, Tromp, Hordijk, Winnubst, & de Leeuw, 2005). Specific to Lyme disease, respondents misattributed the joint pain of Lyme disease to other conditions with joint pain, such as rheumatoid arthritis and fibromyalgia.

Appraisal delays also resulted from a misunderstanding of the characteristic Lyme disease rash, erythema migrans. Specifically, participants reported that they did not suspect Lyme disease if they did not have a rash with central clearing, referred to as a bull's-eye rash. Approximately 20 to 30% of people with Lyme disease do not present with erythema migrans and among those who do have the rash, only 19% have the stereotypical bull's-eye appearance (Tibbles & Edlow, 2007). The impact of the belief in the necessity of central clearing on belated treatment is compounded by the diagnostic challenges associated with Lyme disease in the absence of the rash. One study reported that 54% of patients with Lyme disease who did not have erythema migrans were initially misdiagnosed compared to 23% of patients who did have erythema migrans (Aucott et al., 2009). Our findings highlight an important knowledge gap among patients regarding the skin manifestations of Lyme disease. Patient education campaigns that address this issue could reduce the time between infection and treatment.

The illness and behavioral delay stages appeared to be most influenced by health insurance status. Our findings are consistent with delays attributed to lack of health insurance observed in other disease areas. A lack of insurance has been associated with longer pre-hospital delays in myocardial infarction (Nguyen, Saczynski, Gore, & Goldberg, 2010; Smolderen et al., 2010) and with care-seeking behavior in cancer (Rauscher et al., 2010). It is unknown whether the belated treatment due to lack of health insurance translate into an increased risk of late Lyme disease among the uninsured.

Scheduling delay was not a major contributor to belated treatment in our study, as nearly half of patients we interviewed sought care at emergency departments or urgent care centers, medical settings that typically offer same-day, evening, and weekend appointments. While the availability of urgent care clinics and emergency departments appeared to minimize scheduling delays, the patients who first sought care at these locations reported more occurrences of misdiagnoses. Thus, the time saved in the scheduling delay stage by seeking care in one of these settings could be outweighed by the treatment delays resulting from misdiagnoses in these settings. The number of urgent care settings have dramatically increased over the last decade, but little is known regarding the quality of care for Lyme disease in these settings (Yee, Lechner, & Boukus, 2013).

Family interventions were identified to decrease the time to treatment in Lyme disease, consistent with the role of family and friends in belated treatment for cancer and cardiovascular disease (Perkins-Porras, Whitehead, Strike, & Steptoe, 2009; Barr, McKinley, O'Brien, & Herkes, 2006). Smith and colleagues (2005) reported that, for many patients with cancer, friends and family helped with the process of illness attribution (Smith et al., 2005) by observing or discussing vague symptoms with patients, ultimately making the connection between symptoms and illness that had gone unrecognized by the patient. The extent to which family structure, marital status, and social support play a role in Lyme disease diagnosis and treatment has not been studied.

The impact of Lyme disease on work and caregiving activities emerged as a salient theme for participants, impacting patients prior to treatment and, in some cases, even after treatment. While costs occurring after a Lyme disease diagnosis have been studied (Adrion, Aucott, Lemke, & Weiner, 2015), these studies do not account for the time between infection and treatment of disease, likely underestimating costs. Prior studies that focused on productivity loss and activity limitations in Lyme disease have been confined to individuals reporting symptoms persisting for more than six months

(Johnson, Aylward, Stricker, 2011; Johnson, Wilcox, Mankoff, & Stricker, 2014). A comprehensive study of indirect and direct costs across the full spectrum of Lyme disease, before and after treatment, would give a more complete picture of the individual and population-level burden of this disease.

To our knowledge, this is the first study to evaluate the application of GMTPD to Lyme disease. Through the lens of this model we identified distinct phases between onset of first Lyme disease symptoms and Lyme disease treatment. Our study was conducted in a well-defined sample of participants with a positive IgG Western blot, a lab result present only at least six to eight weeks after Lyme disease infection. Our study had limitations. First, while our eligibility criteria was highly specific for Lyme disease, requiring a positive IgG Western blot may have excluded patients who received care in the first few weeks of infection, when the test is expected to be negative (CDC, 2015). Second, while our patients described interactions with health systems beyond Geisinger, all participants were tested for Lyme disease at Geisinger. With more than 44 Geisinger community practice sites and 12 hospital campuses across a large geographic region, there is likely a great deal of diversity in Lyme disease diagnosis and treatment experiences within the health system. However, these findings may not be generalizable to other countries due to differences in factors such as healthcare cost and access. Finally, the objective of this study was not to quantify the extent to which each delay phase contributed to belated treatment in Lyme disease. We identified several explanations for belated treatment of Lyme disease that are intervenable and can be targeted to minimize time to treatment and reduce the burden of Lyme disease on patients and society. To prioritize resources around secondary prevention strategies in Lyme disease, a large quantitative study on patients across the full spectrum of Lyme disease is needed to both determine how much each phase contributes to belated treatment and to quantify the degree to which factors increase risk of belated treatment.

Author contribution: AH, AR, KM, JA, CH, and BS participated in the design of the study; AH conducted data collection; AH and RH conducted data analysis; all authors participated in the writing of the manuscript.

References

Adrion, E. R., Aucott, J., Lemke, K. W., & Weiner, J. P. (2015). Health care costs, utilization and patterns of care following Lyme disease. *PloS One, 10*(2).

Andersen, B. L., Cacioppo, J. T., & Roberts, D. C. (1995). Delay in seeking a cancer diagnosis: Delay stages and psychophysiological comparison processes. *British Journal of Social Psychology, 34*(1), 33-52.

Aucott, J., Morrison, C., Munoz, B., Rowe, P. C., Schwarzwalder, A., & West, S. K. (2009). Diagnostic challenges of early Lyme disease: Lessons from a community case series. *BMC Infectious Diseases, 9*(1), 79.

Barr, J., McKinley, S., O'Brien, E., & Herkes, G. (2006). Patient recognition of and response to symptoms of TIA or stroke. *Neuroepidemiology, 26*(3), 168-175.

Brouha, X. D., Tromp, D. M., Hordijk, G., Winnubst, J. A., & de Leeuw, R. J. (2005). Oral and pharyngeal cancer: Analysis of patient delay at different tumor stages. *Head & Neck, 27*(11), 939-945.

Casey, J.A., Pollak J., Glymour M.M., Mayeda E.R., Hirsch A.G., Schwartz B.S. (2018). Measures of SES for electronic health record-based research. AJPM. 54(3), 430-439.

Centers for Disease Control and Prevention. Lyme Disease: Data and statistics. (2017). Retrieved from https://www.cdc.gov/lyme/stats/index.html

Centers for Disease Control and Prevention. Lyme Disease: Understanding the Immunoblot Test. (2015). Retrieved from https://www.cdc.gov/lyme/diagnosistesting/labtest/twostep/westernblot/index.html

Corbin, J., & Strauss, A. (2008). Basics of qualitative research: Techniques and procedures for developing grounded theory (3rd ed.). Thousand Oaks, CA: Sage Publications Inc.

Elo, S., & Kyngäs, H. (2008). The qualitative content analysis process. *Journal of Advanced Nursing, 62*(1), 107-115.

Evans, J., Ziebland, S., & McPherson, A. (2006). Minimizing delays in ovarian cancer diagnosis: An expansion of Andersen's model of 'total patient delay'. *Family Practice, 24*(1), 48-55.

Evans, J., Chapple, A., Salisbury, H., Corrie, P., & Ziebland, S. (2014). "It can't be very important because it comes and goes" – patients' accounts of intermittent symptoms preceding a pancreatic cancer diagnosis: A qualitative study. *BMJ Open, 4*(2).

Johnson, L., Aylward, A., Stricker R.B. (2011). Healthcare access and burden of care for patients with Lyme disease: A large United States survey. *Health Policy*, 102, 64-71.

Johnson, L., Wilcox, S., Mankoff, J., Stricker R.B. (2014). Severity of chronic Lyme disease compared to other chronic conditions: a quality of life survey. *PeerJ*. DOI 10.7717/peerj.322.

Mead, P. S. (2015). Epidemiology of Lyme disease. *Infectious Disease Clinics of North America, 29*(2), 187-210.

Nelson, C. A., Saha, S., Kugeler, K. J., Delorey, M. J., Shankar, M. B., Hinckley, A. F., & Mead, P. S. (2015). Incidence of clinician-diagnosed Lyme disease. *Emerging Infectious Diseases, 21*(9), 1625-1631.

Nguyen, H. L., Saczynski, J. S., Gore, J. M., & Goldberg, R. J. (2010). Age and sex differences in duration of prehospital delay in patients with acute myocardial infarction: A systematic review. *Circulation.Cardiovascular Quality and Outcomes, 3*(1), 82-92.

Perkins-Porras, L., Whitehead, D. L., Strike, P. C., & Steptoe, A. (2009). Pre-hospital delay in patients with acute coronary syndrome: Factors associated with patient decision time and home-to-hospital delay. *European Journal of Cardiovascular Nursing, 8*(1), 26-33.

Rauscher, G. H., Ferrans, C. E., Kaiser, K., Campbell, R. T., Calhoun, E. E., & Warnecke, R. B. (2010). Misconceptions about breast lumps and delayed medical presentation in urban breast cancer patients. *Cancer Epidemiology, Biomarkers & Prevention, 19*(3), 640-647.

Scott, S., Walter, F., Webster, A., Sutton, S., & Emery, J. (2012). The model of pathways to treatment: Conceptualization and integration with existing theory. *British Journal of Health Psychology, 18*(1), 45-65.

Smith, L. K., Pope, C., & Botha, J. L. (2005). Patients' help-seeking experiences and delay in cancer presentation: A qualitative synthesis. *The Lancet, 366*(9488), 825-831.

Smolderen, K. G., Spertus, J. A., Nallamothu, B. K., Krumholz, H. M., Tang, F., Ross, J. S., Chan, P. S. (2010). Health care insurance, financial concerns in accessing care, and delays to hospital presentation in acute myocardial infarction. *Jama, 303*(14), 1392-1400.

Tibbles, C. D., & Edlow, J. A. (2007). Does this patient have erythema migrans? *Jama, 297*(23), 2617-2627.

Yee, T., Lechner, A. E., & Boukus, E. R. (2013). The surge in urgent care centers: Emergency department alternative or costly convenience. *Research Brief, (26), 1-6.*

Table 1. Characteristics and Lyme disease symptoms, signs, and diagnosis patterns of participants (n = 26)	
Age, years, n (%)	
18-39	9 (34.6)
40-64	11 (42.3)
65+	6 (23.1)
Female, n (%)	14 (53.8)
Race/ethnicity, n (%)	
White, non-Hispanic	26 (100)
Ever received Medical Assistance, n (%)	8 (30.1)
Rash, n (%)	
“Bulls-eye” rash	3 (11.5)
Other rash	7 (26.9)
No rash	16 (61.5)
First symptom recalled[1], n (%)	
Joint pain/**swelling**	8 (30.8)
Rash	4 (15.4)
Fatigue	4 (15.4)
Headache	3 (11.5)
Other[2]	8 (30.8)
Symptom that triggered first contact with medical provider, n (%)	
Joint pain	9 (34.6)
Rash	4 (44.4)
Fatigue	3 (11.5)
Bell’s palsy	2 (7.7)
Other	8 (30.7)
Self-reported Lyme-related diagnoses, n (%)	
Joint pain (diagnosis of Lyme arthritis not specified)	10 (38.5)
Bell’s Palsy	8 (30.7)
Carditis	2 (7.7)
Meningitis	1 (3.8)
First medical care provider contacted, n (%)	
Urgent care/emergency department	10 (38.5)
Primary care provider	13 (50.0)
Other	3 (11.5)
Misdiagnosed by medical provider, n (%)	9 (34.6)
Medical care provider who misdiagnosed[3], n (% of misdiagnoses)	
Urgent care/emergency department (both)	7 (77.8)
Primary care provider	4 (44.4)

1. Total greater than 26 because one participant reported pain and rash occurred at the same time.
2. Other symptoms: vomiting; shortness of breath; aches/pains, not specific to joints (3); Bell’s palsy; tick bite; no symptoms
3. Total greater than 9 because two patients were misdiagnosed by both emergency department and primary care physician.

Table 2. Participant quotes regarding the General Model of Total Patient Delay stages

Stage / domain	Quotes from participants during in-depth interviews
Appraisal	
Intermittent symptoms	• I never really had more than one spot at the same time, I never had like my feet hurt, my shoulders hurt. I never had like my elbows hurt and my knee hurt. Normally it was one spot at a time. And it just rotated, like I said one spot hurt, then like it could disease be weeks later, another spot would hurt, and then it'd go back to the other spot." • It was mostly my knees and my legs, a little bit in my arms every now and then, but it wasn't consistent like it was in my legs.
Misattribution	• I got a new computer, and I thought that it was not positioned correctly and because I was just on the computer pretty much all day and maybe through I strained by neck. • I was just kind of dealing with it because I thought maybe I slept on it [elbow] wrong or something. • My joints hurt, but I have rheumatoid arthritis, so I never associated it with LYME DISEASE, because I've had rheumatoid arthritis for many years, and I thought I was just getting another flare, so all the symptoms for my joint pain, I just associated with my rheumatoid condition.
Rash pattern	• I didn't think of Lyme, because it was it wasn't a bull's eye at all. • And it started growing and growing and, interestingly enough, it didn't assume the kind of quintessential bull's eye pattern. I always jokingly refer to it as a political boundary. It looked more like a map of the world, it was very, while it was roughly circular in shape, it was very jutted in and out it looked more like Antarctica on my arm. • Because you know we're in the kind of live in the country, you hear about it and knew a couple people that had had it, but they had all you know had gotten the typical symptoms of you know, the red bulls-eye.
Illness/behavioral delay	
Health insurance	• So, I mean I just did as good as I could [to get the tick out]… but I wasn't sure that I got it all and I didn't have insurance at the point, so I didn't bother to go to the doctor. So, I just let it go, figured I wait and see, stupid idea. • I didn't have insurance. That was one of the main things. And, like I said, I was young, and I was just starting a new job, so I didn't have a lot of money. So, I was like, I don't know how I'll pay for that.
Treatment delay	
Emergency department and urgent care settings	• I saw my primary care physician about two weeks later [after emergency department visit.] And that's when she told me that I had the Lyme disease and then she said they [emergency department] had suspected it while I was in the emergency room, and nothing was ever given to me then. The test was done in the ER. Because I remember she [primary care physician] was mad that nobody there had contacted me and she said they, you know,,could've gotten me started sooner on the medication." • I went up to the ER and they told me I had bursitis. Either bursitis or tendonitis. And told me that I'm to check back if I have any more issues. Well, it was still excruciating I went back before the week was up. That's when they told me I had the opposite, either bursitis or tendonitis. One of them. One or the other was, they thought the issue was, well it never went away. My doctor was out on vacation and I had called the office and… I said when she gets back, I need to see her ASAP. So, she had called and she got a hold of me and went back down into the office and as soon as she came in, she told me right away, I bet you have Lyme disease.

Standards for Reporting Qualitative Research (SRQR) Checklist

Topic	Item	Author Response
S1 Title	Concise description of the nature and topic of the study. Identifying the study as qualitative or indicating the approach or data collection methods is recommended.	Page 1, Title page: The title identifies the study as qualitative: "Obstacles to diagnosis and treatment of Lyme disease: A qualitative study"
S2 Abstract	Summary of key elements using the abstract format of the intended publication.	Page 2, Abstract: The abstract adheres to journal specifications.
S3 Problem formulation	Description and significance of the problem/phenomenon studied: review of relevant theory and empirical work; problem statement.	Page 4: Paragraph 1 describes the risks associated with late diagnosis and treatment of Lyme disease. Paragraph 2 describes the application of the General Model of Total Patient Delay to the study of delayed treatment.
S4 Purpose or research question	Purpose of the study and specific objectives or questions.	Page 5: Paragraph 1 states that the objective of the paper is "to identify themes around belated treatment, as well as to evaluate the application of the General Model of Total Patient Delay to Lyme disease…"
S5 Qualitative approach and research paradigm	Qualitative approach and guiding theory; identifying the research paradigm is also recommended.	Page 5: Paragraph 2 states that the interview findings were analyzed through the theory of General Model of Total Patient Delay. Page 6: Paragraph 1 states, "We applied a deductive content analysis of interview transcripts based on the General Model of Total Patient Delay."
S6 Researchers' characteristics and reflexivity	Researchers' characteristics that may influence the research; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability.	Page 6: Paragraph 2 states: "The interviewer is a researcher employed by the health system that treated participants for Lyme disease. To address any concerns participants might have had in describing their care experiences to a health system employee, the interviewer informed participants that their responses would not impact the care received at Geisinger and would be kept confidential."
S7 Context	Setting/site and salient contextual factors.	Page 5: The section "Study setting and sample" describes the study setting. Page 6: Paragraph 2 states: We conducted in-depth, semi-structured, open-ended telephone interviews… Telephone interviews allowed for capture of patient experiences across the large geographic area served by Geisinger."
S8 Sampling strategy	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary; rationale.	Pages 5-6: The "Study setting and sample" section describes the sample, how they were selected, criteria for selection, rationale for selection, and explains that recruitment continued until data saturation.
S9 Ethical issues pertaining to human subjects	Documentation of approval by an appropriate ethics review board.	Page 5: First paragraph in the "Methods" section states that the study was approved by the Geisinger Institutional Review Board.
S10 Data collection methods	Types of data collected; details of data collection procedures; rationale	Page 6: The "Data Collection" section describes the methods for data collection, including the use

		of telephone interviews; the types of questions asked; and the timeframe of the interviews. Page 7: The "Analysis" section describes the application of deductive content analysis; the coding process; and the use of the General Model of Total Patient Delay to develop higher-order codes.
S11 Data collection instruments	Description of instruments	Page 6: The "Data Collection" section describes six categories of questions included in the interview guide. Page 7: The "Analysis" section notes: "The coding team also updated the interview guide to incorporate questions around emergent themes for future interviews."
S12 Units of study	Number and relevant characteristics of participants	Pages 7-8: The first three paragraphs of the "Results" section describe the study participants. Table 1: Characteristics and Lyme disease symptoms, signs, and diagnosis patterns of participants
S13 Data processing	Methods for processing data prior to and during analysis.	Page 7: The "Data Collection" section notes that all interviews were audio-recorded and transcribed verbatim.
S14 Data analysis	Process by which inferences , themes, etc., were identified and developed.	Page 7: The "Analysis" section describes the data analysis process, including the identification of themes and the application of the General Model of Total Patient Delay.
S15 Techniques to enhance trustworthiness	Techniques to enhance trustworthiness and credibility of data analysis.	Page 7: The "Analysis" section describes the use of two coders and the requirement of consensus on the coding framework, coding, and identification of emergent themes.
S16 Synthesis and interpretation	Main findings	Pages 7-13: "Results are presented on these pages as well as in Tables 1 and 2.
S17 Links to empirical data	Evidence (e.g. quotes) to substantiate findings.	Pages 8-13: Quotes are embedded in the "Results" section and presented in Table 2.
S18 Integration with prior work, implications, transferability, and contributions to the field.	Short summary of main findings; explanation of how findings and conclusions…connect to earlier scholarship; unique contribution.	Pages 13-17: The "Discussion" section summarizes the main findings, links the findings to prior works, and describes the contribution of this manuscript to the field.
S19 Limitations	Trustworthiness and limitations of findings	Pages 16 and 17 describe the limitations of the study.
S20 Conflicts of interest	Potential sources of influence	Page 3: No competing interests were declared by authors.
S21 Funding	Sources of funding	Page 3: This work was supported by the Steve & Alexandra Cohen Foundation. The Steve and Alexandra Cohen Foundation did not participate in data collection, analysis, or the writing of this manuscript.

BMJ Open

Obstacles to diagnosis and treatment of Lyme disease in the U.S.: A qualitative study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-021367.R2
Article Type:	Research
Date Submitted by the Author:	26-Apr-2018
Complete List of Authors:	Hirsch, Annemarie; Geisinger, Department of Epidemiology and Health Services Research Herman, Rachel; Gettysburg College Rebman, Alison; Johns Hopkins School of Medicine, Department of Medicine, Division of Rheumatology Moon, Katherine; Johns Hopkins University Bloomberg School of Public Health, Department of Environmental Health and Engineering Aucott, John; Johns Hopkins School of Medicine, Department of Medicine, Division of Rheumatology Heaney, Christopher; Johns Hopkins University Bloomberg School of Public Health, Department of Environmental Health and Engineering; Johns Hopkins University Bloomberg School of Public Health, Department of Epidemiology Schwartz, BS; Geisinger, Department of Epidemiology and Health Services Research; Johns Hopkins University Bloomberg School of Public Health, Department of Environmental Health and Engineering
Primary Subject Heading:	Qualitative research
Secondary Subject Heading:	Infectious diseases
Keywords:	QUALITATIVE RESEARCH, SOCIAL MEDICINE, Patient delay, Lyme disease

Obstacles to diagnosis and treatment of Lyme disease in the U.S.: A qualitative study

Annemarie G. Hirsch[1], PhD, MPH; Rachel J. Herman[2]; Alison Rebman[3], MPH; Katherine Moon[4], PhD; John Aucott[3], MD; Christopher Heaney[4,5], PhD; Brian S. Schwartz[1,4], MD, MS

1. Department of Epidemiology and Health Services Research, Geisinger, Danville, United States
2. Gettysburg College, Gettysburg, United States
3. Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, United States
4. Department of Environmental Health and Engineering, Johns Hopkins University Bloomberg School of Public Health, Baltimore, United States
5. Department of Epidemiology, Johns Hopkins University Bloomberg School of Public Health, Baltimore, United States

Corresponding author:
Annemarie Hirsch, PhD, MPH
Assistant Professor
Department of Epidemiology and Health Services Research
Geisinger
Danville, PA 17822
aghirsch@geisinger.edu
267-626-8810

Word Count: 3,705

ABSTRACT

Objective For many individuals with Lyme disease, prompt treatment leads to rapid resolution of infection. However, severe complications can occur if treatment is delayed. Our objective was to identify themes around belated diagnosis or treatment of Lyme disease using the General Model of Total Patient Delay (GMTPD).

Design We conducted a qualitative interview study using in-depth telephone interviews.

Setting Participants were patients from a large, integrated health system in the state of Pennsylvania, USA.

Participants There were 26 participants. Participants had to have a diagnosis of Lyme disease between 2014 and 2017 and a positive IgG Western blot. We used a stratified purposeful sampling design to identify patients with and without late Lyme disease manifestations. To ensure variation in care experiences, we oversampled patients diagnosed outside of primary care.

Outcome measures We asked participants about their experience from first Lyme disease symptoms to treatment. We applied an iterative coding process to identify key themes and then synthesized codes into higher order codes representing the GMTPD stages: appraisal delay (symptom to recognition of illness); illness delay (inferring illness to deciding to seek help); behavioral delay (deciding to seek help to the act of seeking help); scheduling delay (seeking help to attending an appointment); and treatment delay (attending appointment to treatment).

Results Appraisal delay themes included symptom misattribution; intermittent symptoms; and misperceptions about the necessity of a bull's-eye rash. Health insurance status was a driver of illness and behavioral delay. Scheduling delay was not noted by participants, in part, because 10 of 26 patients went to urgent care or emergency department settings. Misdiagnoses were more common in these settings, contributing to treatment delay.

Conclusion Our study identified potentially modifiable risk factors for belated treatment. Targeting these risk factors may minimize time to treatment and reduce the occurrence of preventable complications.

Strengths and limitations of this study

- To our knowledge, this is the first study to examine which factors account for belated treatment of Lyme disease.
- Through the lens of the General Model of Total Patient Delay, a widely used model that describes the decisional processes and potential delays prior to treatment, we identified distinct phases between onset of first Lyme disease symptoms and Lyme disease treatment.
- This study was conducted in a well-defined sample of participants who had both a Lyme disease diagnosis and a positive IgG Western blot.
- The study was conducted in a health system in the U.S. Some findings may not be generalizable to other countries due to differences in factors such as healthcare cost and access.
- While our eligibility criteria were highly specific for Lyme disease, requiring a positive IgG Western blot may have excluded patients who received care in the first few weeks of infection, when the test is expected to be negative.

Funding: This work was supported by the Steve & Alexandra Cohen Foundation. The Steve and Alexandra Cohen Foundation did not participate in data collection, analysis, or the writing of this manuscript.

Competing interests: None declared

Data sharing: Interview guide and codebook available by request to corresponding author.

INTRODUCTION

Lyme disease is a tick-borne infectious disease that is on the rise in the Northeast, Mid-Atlantic, and Upper Midwest regions of the United States.[1] Delays in diagnosis or treatment (hereafter referred to as belated treatment) of Lyme disease can lead to preventable complications, representing later stages of the disease when the infection disseminates, including neurologic manifestations, cardiac abnormalities, and arthritis.[2] While little is known about the prevalence of belated treatment in Lyme disease, the observation that 32% of Lyme disease cases are diagnosed with arthritis, 12% with neurologic conditions, and 1-2% with carditis,[2] suggests that belated treatment may occur in as many as 40% of cases. To date, the study of time to treatment has largely focused on cancer and cardiovascular events.[3] No study has examined which factors account for belated treatment of Lyme disease, despite the benefits of prompt treatment of this disease.

The General Model of Total Patient Delay (GMTPD)[4] is a widely used, five-stage model that describes the decisional processes and potential delays prior to treatment.[3] Appraisal delay is the time between when a person first notices an unexplained symptom until the person concludes he/she is ill. Appraisal has generally been found to be the key determinant in delay in seeking help.[3] Illness delay is the time between inferring illness and deciding to seek help; behavioral delay represents the time between deciding an illness requires medical care and acting; scheduling delay is the time between deciding to seek help and attending an appointment; and treatment delay is the time between the first appointment with a health care provider and onset of treatment.[4] While this model has been widely applied to cancer and myocardial infarction, it has not been applied to Lyme disease. Thus, the primary drivers of belated treatment in Lyme disease remain unknown.

To identify themes around belated treatment, as well as to evaluate the application of the GMTPD to Lyme disease, we interviewed 26 patients with a diagnosis of Lyme disease to gain insight into their experiences between onset of Lyme disease symptoms and treatment. Such understanding is critical to informing strategies that would reduce time to diagnosis and treatment and prevent late stage Lyme disease.

METHODS

We conducted a qualitative study using in-depth telephone interviews of Geisinger patients with a Lyme disease diagnosis to understand what happens between the onset of Lyme disease symptoms and treatment. We analyzed interview findings through the GMTPD framework. This study was approved by the Geisinger Institutional Review Board.

Study setting and sample

We identified study participants using the electronic health record (EHR) from Geisinger, an integrated health system servicing more than 45 counties in Pennsylvania and New Jersey, USA, both high-incidence states for Lyme disease.[5] Patients were eligible if they were at least 18 years of age; had an International Classification of Disease code (ICD-9: 088.81 or ICD-10: A69.20) for Lyme disease associated with at least one clinical encounter between 2014 and 2017; and an IgG Western blot meeting CDC criteria of five or more positive bands.[6] We used a stratified purposeful sampling design to identify patients with and without late Lyme disease manifestations: Lyme arthritis (ICD-9: 711.8x; ICD-10: M01.X0); facial palsy (ICD-9: 351.0, 352.9; ICD-10: G51.0; G52.9); meningoencephalitis (ICD-9: 320.7; ICD-10: G01); or myocarditis (ICD-9: 422.0; ICD-10: I41). To ensure variation in care experiences, we oversampled patients diagnosed outside of primary care. We first sent letters to notify 93 patients (47 with late manifestations and 46 without) that they were eligible for the study. Two weeks later we telephoned patients to schedule a telephone interview. Participants who completed an interview received a $50 gift card. Recruitment continued until data saturation, the point at which no new information seemed to emerge during coding.[7]

Data collection

We conducted in-depth, semi-structured, open-ended telephone interviews between August and September 2017, each lasting approximately 30 minutes. Telephone interviews allowed for capture of patient experiences across the large geographic area served by Geisinger. Geisinger's Institutional Review Board waived the requirement of written consent after determining that the study posed no more than minimal risk of harm to participants. An experienced interviewer (first author AGH) obtained verbal consent and asked participants to talk about their experience with Lyme disease, from symptom onset to treatment. The interviewer was a researcher employed by the health system that treated participants for Lyme disease. To address any potential concerns participants might have had in describing their care experiences to a health system employee, the interviewer informed participants that their responses would not impact the care received at Geisinger and would be kept confidential. The

interviewer then used an interview guide to follow-up on the account that included questions in six primary areas: Lyme disease knowledge; pre-treatment symptoms; care-seeking behavior; diagnosis process; treatment process; and post-treatment symptoms. All interviews were audio-recorded and transcribed verbatim. No additional field notes were recorded. We did not return transcripts to participants for comment or correction.

Analysis

We applied a deductive content analysis of interview transcripts, based on the GMTPD.[8] We applied an iterative coding process to identify themes corresponding to the six primary areas as well as emergent themes. After the first five interviews, one of two coders reviewed the transcripts to develop a preliminary coding framework. A second coder then applied the framework to the same five interviews. The coding team (2 members) discussed findings and reached consensus on an updated coding scheme, revising the scheme as new themes emerged. The coding team also updated the interview guide to incorporate questions around emergent themes for future interviews. In the final phase of analysis, the coders developed higher order categories representing the five delay stages of the GMTPD. Analysis was conducted using Atlas.ti.7.

Patient and Public Involvement

Patients were not involved in the development of the research question, the design, recruitment, or conduct of this study. Results of this study will be disseminated to study participants via letter and disseminated to patients via health system print newsletters and social media outlets.

RESULTS

Out of the 93 patients to whom we sent a letter, we telephoned 56 patients and reached 33. Of these, 26 (79%) agreed to be interviewed. We stopped recruitment calls after reaching saturation. While the interviewers were intended to be one-on-one, two patients had a spouse with them in the room during the interview. In one case, a spouse joined the call. However, analysis was confined to the information presented by the 26 patients.

Slightly more than half of participants were female; 30% had a history of being on Medical Assistance (a surrogate for low family socioeconomic status);[9] and participants ranged in age from 22 to 70 years (**Table 1**). Half of the participants first sought care for Lyme disease from a primary care provider and 38.5% first went to an urgent care center or emergency department.

Ten participants reported that they had a rash, three of whom described the rash as a bull's-eye. Five of the participants who reported a rash sought care because of the rash. The remaining did not seek care until other symptoms (e.g., fatigue, joint pain) appeared. Two of the five participants who saw a doctor because of the rash were initially misdiagnosed. Eleven participants reported having joint pain, though patients did not specify whether the joint pain was diagnosed as Lyme arthritis. Eight patients reported having Bell's palsy, two patients reported carditis, and one patient reported a diagnosis of Lyme meningitis.

Table 1. Characteristics and Lyme disease symptoms and diagnosis patterns of participants (n = 26)	
Age, years, n (%)	
18-39	9 (34.6)
40-64	11 (42.3)
65+	6 (23.1)
Female, n (%)	14 (53.8)
Race/ethnicity, n (%)	
White, non-Hispanic	26 (100)
Ever received Medical Assistance, n (%)	8 (30.1)
Rash, n (%)	
"Bulls-eye" rash	3 (11.5)
Other rash	7 (26.9)
No rash	16 (61.5)
First symptom recalled[1], n (%)	
Joint pain/**swelling**	8 (30.8)
Rash	4 (15.4)
Fatigue	4 (15.4)
Headache	3 (11.5)
Other[2]	8 (30.8)
Symptom that triggered first contact with medical provider, n (%)	
Joint pain	9 (34.6)
Rash	5 (19.2)
Fatigue	3 (11.5)
Bell's palsy	2 (7.7)
Other[3]	7 (26.9)
Self-reported Lyme-related diagnoses, n (%)	
Joint pain (diagnosis of Lyme arthritis not specified)	10 (38.5)
Bell's Palsy	8 (30.7)
Carditis	2 (7.7)
Meningitis	1 (3.8)
First medical care provider contacted, n (%)	
Urgent care/emergency department	10 (38.5)
Primary care provider	13 (50.0)
Other	3 (11.5)
Misdiagnosed by medical provider, n (%)	9 (34.6)
Medical care provider who misdiagnosed[4], n (% of misdiagnoses)	
Urgent care/emergency department (both)	7 (77.8)
Primary care provider	4 (44.4)

1. Total greater than 26 because one participant reported pain and rash occurred at the same time.
2. Other symptoms: vomiting; shortness of breath; aches/pains, not specific to joints (3); Bell's palsy; tick bite; none reported
3. Other symptoms: Vision change (2); incidental finding (2); stiff neck; vomiting; dizziness
4. Total greater than 9 because two patients were misdiagnosed by both emergency department and primary care physician.

A number of themes emerged regarding seeking care for Lyme disease symptoms. We classified these themes into one of the five GMTPD stages (**Table 2**). Participants reported seeking care both within and external to Geisinger for their initial

Lyme disease symptoms, but we did not ask in which health care system delays occurred.

Table 2. Participant quotes regarding the General Model of Total Patient Delay stages

Stage / domain	Quotes from participants during in-depth interviews
Appraisal	
Intermittent symptoms	• I never really had more than one spot at the same time, I never had like my feet hurt, my shoulders hurt. I never had like my elbows hurt and my knee hurt. Normally it was one spot at a time. And it just rotated, like I said one spot hurt, then like it could disease be weeks later, another spot would hurt, and then it'd go back to the other spot. • It was mostly my knees and my legs, a little bit in my arms every now and then, but it wasn't consistent like it was in my legs.
Misattribution	• I got a new computer, and I thought that it was not positioned correctly and because I was just on the computer pretty much all day and maybe through I strained by neck. • I was just kind of dealing with it because I thought maybe I slept on it [elbow] wrong or something. • My joints hurt, but I have rheumatoid arthritis, so I never associated it with LYME DISEASE, because I've had rheumatoid arthritis for many years, and I thought I was just getting another flare, so all the symptoms for my joint pain, I just associated with my rheumatoid condition.
Rash pattern	• I didn't think of Lyme, because it was it wasn't a bull's eye at all. • And it started growing and growing and, interestingly enough, it didn't assume the kind of quintessential bull's eye pattern. I always jokingly refer to it as a political boundary. It looked more like a map of the world, it was very, while it was roughly circular in shape, it was very jutted… looked more like Antarctica on my arm. • Because you know we're in the kind of live in the country, you hear about it and knew a couple people that had had it, but they had all you know had gotten the typical symptoms of you know, the red bulls-eye.
Illness/behavioral delay	
Health insurance	• So, I mean I just did as good as I could [to get the tick out]… but I wasn't sure that I got it all and I didn't have insurance at the point, so I didn't bother to go to the doctor. So, I just let it go, figured I wait and see, stupid idea. • I didn't have insurance. That was one of the main things. And, like I said, I was young, and I was just starting a new job, so I didn't have a lot of money. So, I was like, I don't know how I'll pay for that.
Treatment delay	
Emergency department and urgent care settings	• I saw my primary care physician about two weeks later [after emergency department visit.] And that's when she told me that I had the Lyme disease and then she said they [emergency department] had suspected it while I was in the emergency room, and nothing was ever given to me then. The test was done in the ER. Because I remember she [primary care physician] was mad that nobody there had contacted me and she said they, you know, could've gotten me started sooner on the medication." • I went up to the ER and they told me I had bursitis. Either bursitis or tendonitis. And told me that I'm to check back if I have any more issues. Well, it was still excruciating I went back before the week was up. That's when they told me I had the opposite, either bursitis or tendonitis. One of them. One or the other was, they thought the issue was, well it never went away. My doctor was out on vacation and I had called the office and… I said when she gets back, I need to see her ASAP. So, she had called and she got a hold of me and went back down into the office and as soon as she came in, she told me right away, I bet you have Lyme disease.

GMTPD Stages

Appraisal delay

Participants consistently reported an appraisal delay, a gap between their first symptom and recognition that they were ill (**Table 2**). Some participants attributed this gap to the inconsistent nature of their symptoms. One participant explained,

> "I was just having occasional joint achiness where it kind of felt like I slept funny on my elbow. It would be sore for a day or two and then it would go away."

Patients also misattributed symptoms to minor injuries, pre-existing conditions, or the flu. One participant noted, "I also have fibromyalgia, so it's kind of hard to differentiate."

Patients ruled out Lyme disease in the absence of the bull's-eye rash perceived to be characteristic of Lyme disease, delaying medical attention even in the presence of a rash. One participant explained,

> "And then I got a like this rash on my legs, on my arms, on my back. It was really bad. And I didn't even know about Lyme disease at that time… I mean I knew that you'd get a bull's-eye rash. And it wasn't that, so I went to the doctor probably about… at least three weeks later."

Illness delay/behavioral delay

Generally, once patients decided to seek medical care (illness delay), they acted on the decision (behavioral delay). One of the 26 participants noted a gap of five or six days between deciding he needed medical care and seeking care due to health insurance:

> "Every hour or so I would take my temperature and it was just going up and up... And I didn't have insurance. And I thought I have to make it to Monday, because Monday is when my insurance was going to kick in. I said I have got to survive until Monday. I mean I would have went that Wednesday or Thursday that I was so sick. I had called somebody I know that's a nurse and she said, 'I don't want you to die on me but get in your bed and don't frickin' move,… until Monday if you can make it.' So, I, I took the words she said to heart and just kind of didn't move the entire weekend."

While no other patients articulated this gap between deciding to seek care and acting on it, health insurance was the most commonly occurring theme regarding the delay in deciding whether to seek medical attention for their symptoms (**Table 2**).

Scheduling delay

Scheduling delay did not emerge as a problem for any of the participants. Ten of the 26 participants initially sought care for symptoms at an urgent care or emergency department setting. Some of these patients noted that they decided to seek medical attention at these establishments because of the weekend and evening hours.

Treatment delay

When present, delays between the first appointment with a health care provider about Lyme disease symptoms and treatment were generally reported to be the result of a misdiagnosis (e.g., cellulitis). Nine of the 26 participants (34.6%) reported that they were not diagnosed with Lyme disease at their first contact with a medical professional regarding Lyme disease symptoms. Seven of these nine participants (77.8%) reported a misdiagnosis that occurred at an urgent care or emergency department setting, representing 70% of patients who first sought care in these settings (**Table 2**). One participant described this experience,

> "No, they [emergency department] didn't do any blood tests... Kind of examined and kind of listened to me. It was very busy that night. I know there was 1 or 2 doctors on and they had a bunch of drunks they were taking care of and things, so I think they may have missed the boat. …the nurse tells my wife, 'You know I think you got to watch because,' I think she said, 'I think there's more here than what it appears.' But that was it, and then they discharged me."

Non-GMTPD themes

Role of family

In multiple stages of the GMTPD, the involvement of family prompted action leading to treatment of Lyme disease. Most commonly, family members prompted patients to call the doctor (reducing illness/behavioral delay). For example:

> "I could no longer read the computer screen. I couldn't read the paper. And she (my wife) said, 'That's it, we're done playing around.' And I ended up at the doctors."

Another example was:

> "She (my sister) said to me, 'That (rash) doesn't look right.' And I said, 'Eh, it'll go away in a couple of days.' So, she told my mom, and my mom called me and said, 'I'm coming up to look at it. I think we should go to the doctor.' I said,

> 'Ma, it'll be fine.' She said, 'No, I think we should go.' So…, my sister calls and gets an appointment."

Family also played a role in reducing the treatment delay phase, after the patient saw a medical professional. In one instance, a patient was hospitalized for what was originally diagnosed as pain medication dependency. It was not until a family member demanded a transfer to a different hospital that Lyme disease was diagnosed.

> "So, I was there [at the hospital] for three or four days and all of the sudden I developed Bell's palsy. And they did a CAT scan and they determined it was not a stroke. I laid there five more days where they did nothing. My sister and mother came to visit. They would not have recognized me. My face was swollen and droopy. So my sister had me transferred to another hospital. Within hours I was diagnosed with neurological Lyme."

Consequences of delays

The original interview guide did not include questions regarding the impact of Lyme disease on work absenteeism/presenteeism or changes in productivity at work or home. However, the detrimental impact of Lyme disease on the ability to work and fulfill caregiving roles emerged as a common theme among participants.

> "I couldn't function, and I'm a care-taker for my mother, although she's a good 92 now…She took care of me, but I could not function. I lived on the sofa or in bed. That's how tired I was. If I tried to a do a little bit of anything, I would have to get back down, because I couldn't handle it."

Another person described a change in his work productivity before getting treated for Lyme disease.

> "I'd never sit down at work ever. I have my own machine shop. And I like nobody ever sees me sit. …like it came to the point where I was sitting and then actually at lunchtime and stuff I would actually lay on the bench."

For some of these patients, the impact on work and caregiving persisted after treatment.

> "Yeah, yeah, I was off [work] for quite a while between them actually finally determining it was Lyme disease and the treatment and then the post check-up after the treatment to make sure I was fine. Yeah, I was probably off for at least two months, if not more."

A second patient explained:

> "I own my own business, I've been in business since 1990. It is definitely not the same. I have a hard time spelling words. I mean you got to go in, you got to sell yourself, you got to get all the work and, it's just tough anymore. I just don't have the, it's hard to put things together, you know what I mean, like on the fly. Like with words and everything. You seem to lose that edge and I don't know how to explain it. You know and everybody says, 'Oh you got old,' but it just like changed instantly."

DISCUSSION

We conducted the first study, to our knowledge, to explore the experiences associated with the time between onset of symptoms and treatment of Lyme disease, with a specific focus on identifying themes related to belated treatment. Our study identified barriers to timely treatment that have been observed in other disease areas, as well as barriers specific to Lyme disease. We identified potential knowledge gaps in Lyme disease among patients and medical professionals, including misperceptions about the necessity of a bull's-eye rash. Understanding the conditions that participants perceive contribute to treatment delays can inform strategies that promote prompt treatment of Lyme disease, preventing dissemination of infection and the resulting disease complications.

Application of the GMTPD to Lyme disease was very instructive and showed that Lyme disease generally conformed to the model. The appraisal stage emerged as a distinct and dominant phase, as has been observed when this model has been applied to other diseases.[3,10,11] We identified three appraisal delay themes: symptom misattribution, intermittent symptoms, and lack of bull's-eye rash. Both the intermittent nature of symptoms as well as the symptom misattribution to less serious or pre-existing conditions has been reported to account for appraisal delays in various cancers, particularly when the early symptoms were commonly occurring non-specific symptoms (e.g. fatigue).[12,13] Specific to Lyme disease, respondents misattributed the joint pain of Lyme disease to other conditions with joint pain, such as rheumatoid arthritis and fibromyalgia.

Appraisal delays also resulted from a misunderstanding of the characteristic Lyme disease rash, erythema migrans. Specifically, participants reported that they did not suspect Lyme disease if they did not have a rash with central clearing, referred to as a bull's-eye rash. Approximately 20 to 30% of people with Lyme disease do not present with erythema migrans and among those who do have the rash, only 19% have the stereotypical bull's-eye appearance.[14] The impact of the belief in the necessity of central clearing on belated treatment is compounded by the diagnostic challenges associated with Lyme disease in the absence of the rash. One study reported that 54% of patients with Lyme disease who did not have erythema migrans were initially misdiagnosed compared to 23% of patients who did have erythema migrans.[15] Our findings highlight an important knowledge gap among patients regarding the skin manifestations of Lyme disease. Patient education campaigns that address this issue could reduce the time between infection and treatment.

The illness and behavioral delay stages appeared to be most influenced by health insurance status. Our findings are consistent with delays attributed to lack of health insurance observed in other disease areas. A lack of insurance has been associated with longer pre-hospital delays in myocardial infarction[16,17] and with care-seeking behavior in cancer.[18] It is unknown whether the belated treatment due to lack of health insurance translate into an increased risk of late Lyme disease among the uninsured.

Scheduling delay was not a major contributor to belated treatment in our study, as nearly half of patients we interviewed sought care at emergency departments or urgent care centers, medical settings that typically offer same-day, evening, and weekend appointments. While the availability of urgent care clinics and emergency departments appeared to minimize scheduling delays, the patients who first sought care at these locations reported more occurrences of misdiagnoses. Thus, the time saved in the scheduling delay stage by seeking care in one of these settings could be outweighed by the treatment delays resulting from misdiagnoses in these settings. The number of urgent care settings have dramatically increased over the last decade, but little is known regarding the quality of care for Lyme disease in these settings.[19]

Family interventions were identified to decrease the time to treatment in Lyme disease, consistent with the role of family and friends in belated treatment for cancer and cardiovascular disease.[20,21] Smith and colleagues[10] reported that, for many patients with cancer, friends and family helped with the process of illness attribution by observing or discussing vague symptoms with patients, ultimately making the connection between symptoms and illness that had gone unrecognized by the patient. The extent to which family structure, marital status, and social support play a role in Lyme disease diagnosis and treatment has not been studied.

The impact of Lyme disease on work and caregiving activities emerged as a salient theme for participants, impacting patients prior to treatment and, in some cases, even after treatment. While costs occurring after a Lyme disease diagnosis have been studied,[22] these studies do not account for the time between infection and treatment of disease, likely underestimating costs. Prior studies that focused on productivity loss and activity limitations in Lyme disease have been confined to individuals reporting symptoms persisting for more than six months.[23,24] A comprehensive study of indirect and direct costs across the full spectrum of Lyme disease, before and after treatment, would give a more complete picture of the individual and population-level burden of this disease.

To our knowledge, this is the first study to evaluate the application of GMTPD to Lyme disease. Through the lens of this model we identified distinct phases between onset of first Lyme disease symptoms and Lyme disease treatment. Our study was conducted in a well-defined sample of participants with a positive IgG Western blot, a lab result present only at least six to eight weeks after Lyme disease infection. Our study had limitations. First, while our eligibility criteria was highly specific for Lyme disease, requiring a positive IgG Western blot, patients may have been excluded as a result of false-negative test results that can occur at all stages disease, but most commonly among patients tested in the first few weeks of infection, when the test is expected to be negative.[6,25,26] Second, while our patients described interactions with health systems beyond Geisinger, all participants were tested for Lyme disease at Geisinger. With more than 44 Geisinger community practice sites and 12 hospital campuses across a large geographic region, there is likely a great deal of diversity in Lyme disease diagnosis and treatment experiences within the health system. However, these findings may not be generalizable to other countries due to differences in factors such as healthcare cost and access. Finally, the objective of this study was not to quantify the extent to which each delay phase contributed to belated treatment in Lyme disease. We identified several explanations for belated treatment of Lyme disease that are intervenable and can be targeted to minimize time to treatment and reduce the burden of Lyme disease on patients and society. To prioritize resources around secondary prevention strategies in Lyme disease, a large quantitative study on patients across the full spectrum of Lyme disease is needed to both determine how much each phase contributes to belated treatment and to quantify the degree to which factors increase risk of belated treatment.

Author contribution: AH, AR, KM, JA, CH, and BS participated in the design of the study; AH conducted data collection; AH and RH conducted data analysis; all authors participated in the writing of the manuscript.

REFERENCES

1 Nelson CA, Saha S, Kugeler KJ, et al. Incidence of Clinician-Diagnosed Lyme Disease, United States, 2005-2010. *Emerg Infect Dis* 2015;21:1625-1631. doi:10.3201/eid2109.150417

2 Mead PS. Epidemiology of Lyme disease. *Infect Dis Clin North Am* 2015;29:187-210. doi:10.1016/j.idc.2015.02.010

3 Scott SE, Walter FM, Webster A, et al. The model of pathways to treatment: conceptualization and integration with existing theory. *Br J Health Psychol* 2012;18:45-65. doi:10.1111/j.2044-8287.2012.02077.x

4 Andersen BL, Cacioppo JT. Delay in seeking a cancer diagnosis: delay stages and psychophysiological comparison processes. *Br J Soc Psychol* 1995;34:33-52.

5 Centers for Disease Control and Prevention. Lyme Disease: Data and statistics. 2016. https://www.cdc.gov/lyme/stats/index.html (accessed Oct 2017).

6 Centers for Disease Control and Prevention. Lyme Disease: Understanding the Immunoblot Test. 2015. https://www.cdc.gov/lyme/diagnosistesting/labtest/twostep/westernblot/index.html (accessed Oct 2017).

7 Corbin J, Strauss A. Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory (3rd ed.). Thousand Oaks, CA: Sage 2008.

8 Elo S, Kyngäs H. The qualitative content analysis process. *J Adv Nurs* 2008;62:107-115. doi:10.1111/j.1365-2648.2007.04569.x

9 Casey JA, Pollak J, Glymour MM, et al. Measures of SES for Electronic Health Record-based Research. *Am J Prev Med* 2018;54:430-439. doi:10.1016/j.amepre.2017.10.004

10 Smith LK, Pope C, Botha JL. Patients' help-seeking experiences and delay in cancer presentation: a qualitative synthesis. *Lancet* 2005;366:825-831. doi:10.1016/S0140-6736(05)67030-4

11 Evans J, Ziebland S, McPherson A. Minimizing delays in ovarian cancer diagnosis: an expansion of Andersen's model of ‘total patient delay’. *Fam Pract* 2007;24:48-55. doi:10.1093/fampra/cml063

12 Evans J, Chapple A, Salisbury H, et al. "It can't be very important because it comes and goes"--patients' accounts of intermittent symptoms preceding a pancreatic cancer diagnosis: a qualitative study. *BMJ Open* 2014;4:e004215. doi:10.1136/bmjopen-2013-004215

13 Brouha XD, Tromp DM, Hordijk GJ, et al. Oral and pharyngeal cancer: analysis of patient delay at different tumor stages. *Head Neck* 2005;27:939-945. doi:10.1002/hed.20270

14 Tibbles CD, Edlow JA. Does this patient have erythema migrans? *JAMA* 2007;297:2617-2627. doi:10.1001/jama.297.23.2617

15 Aucott J, Morrison C, Munoz B, et al. Diagnostic challenges of early Lyme disease: lessons from a community case series. *BMC Infect Dis* 2009;9:79. doi:10.1186/1471-2334-9-79

16 Nguyen HL, Saczynski JS, Gore JM, et al. Age and sex differences in duration of prehospital delay in patients with acute myocardial infarction: a systematic review. *Circ Cardiovasc Qual Outcomes* 2010;3:82-92. doi:10.1161/CIRCOUTCOMES.109.884361

17 Smolderen KG, Spertus JA, Nallamothu BK, et al. Health care insurance, financial concerns in accessing care, and delays to hospital presentation in acute myocardial infarction. *JAMA* 2010;303:1392-1400. doi:10.1001/jama.2010.409

18 Rauscher GH, Ferrans CE, Kaiser K, et al. Misconceptions about breast lumps and delayed medical presentation in urban breast cancer patients. *Cancer Epidemiol Biomarkers Prev* 2010;19:640-647. doi:10.1158/1055-9965.EPI-09-0997

19 Yee T, Lechner AE, Boukus ER. The surge in urgent care centers: emergency department alternative or costly convenience. *Res Brief* 2013;(26),1-6.

20 Perkins-Porras L, Whitehead DL, Strike PC, et al. Pre-hospital delay in patients with acute coronary syndrome: factors associated with patient decision time and home-to-hospital delay. *Eur J Cardiovasc Nurs* 2009;8:26-33. doi:10.1016/j.ejcnurse.2008.05.001

21 Barr J, McKinley S, O'Brien E, et al. Patient recognition of and response to symptoms of TIA or stroke. *Neuroepidemiology* 2006;26:168-175. doi:10.1159/000091659

22 Adrion ER, Aucott J, Lemke KW, et al. Health care costs, utilization and patterns of care following Lyme disease. *PloS One* 2015;10:e0116767. doi:10.1371/journal.pone.0116767

23 Johnson L, Aylward A, Stricker RB. Healthcare access and burden of care for patients with Lyme disease: A large United States survey. *Health Policy* 2011;102,64-71. doi:10.1016/j.healthpol.2011.05.007

24 Johnson L, Wilcox S, Mankoff J, et al. Severity of chronic Lyme disease compared to other chronic conditions: a quality of life survey. *PeerJ* 2014;2:e322. doi:10.7717/peerj.322

25 Cook MJ, Puri BK. Commercial test kits for detection of Lyme borreliosis: a meta-analysis of test accuracy. *Int J Gen Med* 2016;9:427-440. doi:10.2147/IJGM.S122313

26 Waddell LA, Greig J, Mascarenhas M. The Accuracy of Diagnostic Tests for Lyme Disease in Humans, A systematic Review and Meta-Analysis of North American Research. *PLoS One* 2016;11:e0168613. doi:10.1371/journal.pone.0168613

Standards for Reporting Qualitative Research (SRQR) Checklist

Topic	Item	Author Response
S1 Title	Concise description of the nature and topic of the study. Identifying the study as qualitative or indicating the approach or data collection methods is recommended.	Page 1, Title page: The title identifies the study as qualitative: “Obstacles to diagnosis and treatment of Lyme disease: A qualitative study”
S2 Abstract	Summary of key elements using the abstract format of the intended publication.	Page 2, Abstract: The abstract adheres to journal specifications.
S3 Problem formulation	Description and significance of the problem/phenomenon studied: review of relevant theory and empirical work; problem statement.	Page 4: Paragraph 1 describes the risks associated with late diagnosis and treatment of Lyme disease. Paragraph 2 describes the application of the General Model of Total Patient Delay to the study of delayed treatment.
S4 Purpose or research question	Purpose of the study and specific objectives or questions.	Page 5: Paragraph 1 states that the objective of the paper is “to identify themes around belated treatment, as well as to evaluate the application of the General Model of Total Patient Delay to Lyme disease…”
S5 Qualitative approach and research paradigm	Qualitative approach and guiding theory; identifying the research paradigm is also recommended.	Page 5: Paragraph 2 states that the interview findings were analyzed through the theory of General Model of Total Patient Delay. Page 6: Paragraph 1 states, “We applied a deductive content analysis of interview transcripts based on the General Model of Total Patient Delay.”
S6 Researchers’ characteristics and reflexivity	Researchers’ characteristics that may influence the research; potential or actual interaction between researchers’ characteristics and the research questions, approach, methods, results, and/or transferability.	Page 6: Paragraph 2 states: “The interviewer is a researcher employed by the health system that treated participants for Lyme disease. To address any concerns participants might have had in describing their care experiences to a health system employee, the interviewer informed participants that their responses would not impact the care received at Geisinger and would be kept confidential.”
S7 Context	Setting/site and salient contextual factors.	Page 5: The section “Study setting and sample” describes the study setting. Page 6: Paragraph 2 states: We conducted in-depth, semi-structured, open-ended telephone interviews… Telephone interviews allowed for capture of patient experiences across the large geographic area served by Geisinger.”
S8 Sampling strategy	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary; rationale.	Pages 5-6: The “Study setting and sample” section describes the sample, how they were selected, criteria for selection, rationale for selection, and explains that recruitment continued until data saturation.
S9 Ethical issues pertaining to human subjects	Documentation of approval by an appropriate ethics review board.	Page 5: First paragraph in the “Methods” section states that the study was approved by the Geisinger Institutional Review Board.
S10 Data collection methods	Types of data collected; details of data collection procedures; rationale	Page 6: The “Data Collection” section describes the methods for data collection, including the use

		of telephone interviews; the types of questions asked; and the timeframe of the interviews. Page 7: The “Analysis” section describes the application of deductive content analysis; the coding process; and the use of the General Model of Total Patient Delay to develop higher-order codes.
S11 Data collection instruments	Description of instruments	Page 6: The “Data Collection” section describes six categories of questions included in the interview guide. Page 7: The “Analysis” section notes: “The coding team also updated the interview guide to incorporate questions around emergent themes for future interviews.”
S12 Units of study	Number and relevant characteristics of participants	Pages 7-8: The first three paragraphs of the “Results” section describe the study participants. Table 1: Characteristics and Lyme disease symptoms, signs, and diagnosis patterns of participants
S13 Data processing	Methods for processing data prior to and during analysis.	Page 7: The “Data Collection” section notes that all interviews were audio-recorded and transcribed verbatim.
S14 Data analysis	Process by which inferences , themes, etc., were identified and developed.	Page 7: The “Analysis” section describes the data analysis process, including the identification of themes and the application of the General Model of Total Patient Delay.
S15 Techniques to enhance trustworthiness	Techniques to enhance trustworthiness and credibility of data analysis.	Page 7: The “Analysis” section describes the use of two coders and the requirement of consensus on the coding framework, coding, and identification of emergent themes.
S16 Synthesis and interpretation	Main findings	Pages 7-13: “Results are presented on these pages as well as in Tables 1 and 2.
S17 Links to empirical data	Evidence (e.g. quotes) to substantiate findings.	Pages 8-13: Quotes are embedded in the “Results” section and presented in Table 2.
S18 Integration with prior work, implications, transferability, and contributions to the field.	Short summary of main findings; explanation of how findings and conclusions…connect to earlier scholarship; unique contribution.	Pages 13-17: The “Discussion” section summarizes the main findings, links the findings to prior works, and describes the contribution of this manuscript to the field.
S19 Limitations	Trustworthiness and limitations of findings	Pages 16 and 17 describe the limitations of the study.
S20 Conflicts of interest	Potential sources of influence	Page 3: No competing interests were declared by authors.
S21 Funding	Sources of funding	Page 3: This work was supported by the Steve & Alexandra Cohen Foundation. The Steve and Alexandra Cohen Foundation did not participate in data collection, analysis, or the writing of this manuscript.

BMJ Open

Obstacles to diagnosis and treatment of Lyme disease in the U.S.: A qualitative study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-021367.R3
Article Type:	Research
Date Submitted by the Author:	04-May-2018
Complete List of Authors:	Hirsch, Annemarie; Geisinger, Department of Epidemiology and Health Services Research Herman, Rachel; Gettysburg College Rebman, Alison; Johns Hopkins School of Medicine, Department of Medicine, Division of Rheumatology Moon, Katherine; Johns Hopkins University Bloomberg School of Public Health, Department of Environmental Health and Engineering Aucott, John; Johns Hopkins School of Medicine, Department of Medicine, Division of Rheumatology Heaney, Christopher; Johns Hopkins University Bloomberg School of Public Health, Department of Environmental Health and Engineering; Johns Hopkins University Bloomberg School of Public Health, Department of Epidemiology Schwartz, BS; Geisinger, Department of Epidemiology and Health Services Research; Johns Hopkins University Bloomberg School of Public Health, Department of Environmental Health and Engineering
Primary Subject Heading:	Qualitative research
Secondary Subject Heading:	Infectious diseases
Keywords:	QUALITATIVE RESEARCH, SOCIAL MEDICINE, Patient delay, Lyme disease

Obstacles to diagnosis and treatment of Lyme disease in the U.S.: A qualitative study

Annemarie G. Hirsch[1], PhD, MPH; Rachel J. Herman[2]; Alison Rebman[3], MPH; Katherine Moon[4], PhD; John Aucott[3], MD; Christopher Heaney[4,5], PhD; Brian S. Schwartz[1,4], MD, MS

1. Department of Epidemiology and Health Services Research, Geisinger, Danville, United States
2. Gettysburg College, Gettysburg, United States
3. Department of Medicine, Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, United States
4. Department of Environmental Health and Engineering, Johns Hopkins University Bloomberg School of Public Health, Baltimore, United States
5. Department of Epidemiology, Johns Hopkins University Bloomberg School of Public Health, Baltimore, United States

Corresponding author:
Annemarie Hirsch, PhD, MPH
Assistant Professor
Department of Epidemiology and Health Services Research
Geisinger
Danville, PA 17822
aghirsch@geisinger.edu
267-626-8810

Word Count: 3,705

ABSTRACT

Objective For many individuals with Lyme disease, prompt treatment leads to rapid resolution of infection. However, severe complications can occur if treatment is delayed. Our objective was to identify themes around belated diagnosis or treatment of Lyme disease using the General Model of Total Patient Delay (GMTPD).

Design We conducted a qualitative interview study using in-depth telephone interviews.

Setting Participants were patients from a large, integrated health system in the state of Pennsylvania, USA.

Participants There were 26 participants. Participants had to have a diagnosis of Lyme disease between 2014 and 2017 and a positive IgG Western blot. We used a stratified purposeful sampling design to identify patients with and without late Lyme disease manifestations. To ensure variation in care experiences, we oversampled patients diagnosed outside of primary care.

Outcome measures We asked participants about their experience from first Lyme disease symptoms to treatment. We applied an iterative coding process to identify key themes and then synthesized codes into higher order codes representing the GMTPD stages: appraisal delay (symptom to recognition of illness); illness delay (inferring illness to deciding to seek help); behavioral delay (deciding to seek help to the act of seeking help); scheduling delay (seeking help to attending an appointment); and treatment delay (attending appointment to treatment).

Results Appraisal delay themes included symptom misattribution; intermittent symptoms; and misperceptions about the necessity of a bull’s-eye rash. Health insurance status was a driver of illness and behavioral delay. Scheduling delay was not noted by participants, in part, because 10 of 26 patients went to urgent care or emergency department settings. Misdiagnoses were more common in these settings, contributing to treatment delay.

Conclusion Our study identified potentially modifiable risk factors for belated treatment. Targeting these risk factors may minimize time to treatment and reduce the occurrence of preventable complications.

Strengths and limitations of this study

- To our knowledge, this is the first study to examine which factors account for belated treatment of Lyme disease.
- Through the lens of the General Model of Total Patient Delay, a widely used model that describes the decisional processes and potential delays prior to treatment, we identified distinct phases between onset of first Lyme disease symptoms and Lyme disease treatment.
- This study was conducted in a well-defined sample of participants who had both a Lyme disease diagnosis and a positive IgG Western blot.
- The study was conducted in a health system in the U.S. Some findings may not be generalizable to other countries due to differences in factors such as healthcare cost and access.
- While our eligibility criteria were highly specific for Lyme disease, requiring a positive IgG Western blot may have excluded patients who received care in the first few weeks of infection, when the test is expected to be negative.

Funding: This work was supported by the Steve & Alexandra Cohen Foundation. The Steve and Alexandra Cohen Foundation did not participate in data collection, analysis, or the writing of this manuscript.

Competing interests: None declared

Data sharing: Interview guide and codebook available by request to corresponding author.

INTRODUCTION

Lyme disease is a tick-borne infectious disease that is on the rise in the Northeast, Mid-Atlantic, and Upper Midwest regions of the United States.[1] Delays in diagnosis or treatment (hereafter referred to as belated treatment) of Lyme disease can lead to preventable complications, representing later stages of the disease when the infection disseminates, including neurologic manifestations, cardiac abnormalities, and arthritis.[2] While little is known about the prevalence of belated treatment in Lyme disease, the observation that 32% of Lyme disease cases are diagnosed with arthritis, 12% with neurologic conditions, and 1-2% with carditis,[2] suggests that belated treatment may occur in as many as 40% of cases. To date, the study of time to treatment has largely focused on cancer and cardiovascular events.[3] No study has examined which factors account for belated treatment of Lyme disease, despite the benefits of prompt treatment of this disease.

The General Model of Total Patient Delay (GMTPD)[4] is a widely used, five-stage model that describes the decisional processes and potential delays prior to treatment.[3] Appraisal delay is the time between when a person first notices an unexplained symptom until the person concludes he/she is ill. Appraisal has generally been found to be the key determinant in delay in seeking help.[3] Illness delay is the time between inferring illness and deciding to seek help; behavioral delay represents the time between deciding an illness requires medical care and acting; scheduling delay is the time between deciding to seek help and attending an appointment; and treatment delay is the time between the first appointment with a health care provider and onset of treatment.[4] While this model has been widely applied to cancer and myocardial infarction, it has not been applied to Lyme disease. Thus, the primary drivers of belated treatment in Lyme disease remain unknown.

To identify themes around belated treatment, as well as to evaluate the application of the GMTPD to Lyme disease, we interviewed 26 patients with a diagnosis of Lyme disease to gain insight into their experiences between onset of Lyme disease symptoms and treatment. Such understanding is critical to informing strategies that would reduce time to diagnosis and treatment and prevent late stage Lyme disease.

METHODS

We conducted a qualitative study using in-depth telephone interviews of Geisinger patients with a Lyme disease diagnosis to understand what happens between the onset of Lyme disease symptoms and treatment. We analyzed interview findings through the GMTPD framework. This study was approved by the Geisinger Institutional Review Board.

Study setting and sample

We identified study participants using the electronic health record (EHR) from Geisinger, an integrated health system servicing more than 45 counties in Pennsylvania and New Jersey, USA, both high-incidence states for Lyme disease.[5] Patients were eligible if they were at least 18 years of age; had an International Classification of Disease code (ICD-9: 088.81 or ICD-10: A69.20) for Lyme disease associated with at least one clinical encounter between 2014 and 2017; and an IgG Western blot meeting CDC criteria of five or more positive bands.[6] We used a stratified purposeful sampling design to identify patients with and without late Lyme disease manifestations: Lyme arthritis (ICD-9: 711.8x; ICD-10: M01.X0); facial palsy (ICD-9: 351.0, 352.9; ICD-10: G51.0; G52.9); meningoencephalitis (ICD-9: 320.7; ICD-10: G01); or myocarditis (ICD-9: 422.0; ICD-10: I41). To ensure variation in care experiences, we oversampled patients diagnosed outside of primary care. We first sent letters to notify 93 patients (47 with late manifestations and 46 without) that they were eligible for the study. Two weeks later we telephoned patients to schedule a telephone interview. Participants who completed an interview received a $50 gift card. Recruitment continued until data saturation, the point at which no new information seemed to emerge during coding.[7]

Data collection

We conducted in-depth, semi-structured, open-ended telephone interviews between August and September 2017, each lasting approximately 30 minutes. Telephone interviews allowed for capture of patient experiences across the large geographic area served by Geisinger. Geisinger's Institutional Review Board waived the requirement of written consent after determining that the study posed no more than minimal risk of harm to participants. An experienced interviewer (first author AGH) obtained verbal consent and asked participants to talk about their experience with Lyme disease, from symptom onset to treatment. The interviewer was a researcher employed by the health system that treated participants for Lyme disease. To address any potential concerns participants might have had in describing their care experiences to a health system employee, the interviewer informed participants that their responses would not impact the care received at Geisinger and would be kept confidential. The

interviewer then used an interview guide to follow-up on the account that included questions in six primary areas: Lyme disease knowledge; pre-treatment symptoms; care-seeking behavior; diagnosis process; treatment process; and post-treatment symptoms. All interviews were audio-recorded and transcribed verbatim. No additional field notes were recorded. We did not return transcripts to participants for comment or correction.

Analysis

We applied a deductive content analysis of interview transcripts, based on the GMTPD.[8] We applied an iterative coding process to identify themes corresponding to the six primary areas as well as emergent themes. After the first five interviews, one of two coders reviewed the transcripts to develop a preliminary coding framework. A second coder then applied the framework to the same five interviews. The coding team (2 members) discussed findings and reached consensus on an updated coding scheme, revising the scheme as new themes emerged. The coding team also updated the interview guide to incorporate questions around emergent themes for future interviews. In the final phase of analysis, the coders developed higher order categories representing the five delay stages of the GMTPD. Analysis was conducted using Atlas.ti.7.

Patient and Public Involvement

Patients were not involved in the development of the research question, the design, recruitment, or conduct of this study. Results of this study will be disseminated to study participants via letter and disseminated to patients via health system print newsletters and social media outlets.

RESULTS

Out of the 93 patients to whom we sent a letter, we telephoned 56 patients and reached 33. Of these, 26 (79%) agreed to be interviewed. We stopped recruitment calls after reaching saturation. While the interviewers were intended to be one-on-one, two patients had a spouse with them in the room during the interview. In one case, a spouse joined the call. However, analysis was confined to the information presented by the 26 patients.

Slightly more than half of participants were female; 30% had a history of being on Medical Assistance (a surrogate for low family socioeconomic status);[9] and participants ranged in age from 22 to 70 years (**Table 1**). Half of the participants first sought care for Lyme disease from a primary care provider and 38.5% first went to an urgent care center or emergency department.

Ten participants reported that they had a rash, three of whom described the rash as a bull's-eye. Five of the participants who reported a rash sought care because of the rash. The remaining did not seek care until other symptoms (e.g., fatigue, joint pain) appeared. Two of the five participants who saw a doctor because of the rash were initially misdiagnosed. Eleven participants reported having joint pain, though patients did not specify whether the joint pain was diagnosed as Lyme arthritis. Eight patients reported having Bell's palsy, two patients reported carditis, and one patient reported a diagnosis of Lyme meningitis.

Table 1. Characteristics and Lyme disease symptoms and diagnosis patterns of participants (n = 26)

Age, years, n (%)	
18-39	9 (34.6)
40-64	11 (42.3)
65+	6 (23.1)
Female, n (%)	14 (53.8)
Race/ethnicity, n (%)	
White, non-Hispanic	26 (100)
Ever received Medical Assistance, n (%)	8 (30.1)
Rash, n (%)	
"Bulls-eye" rash	3 (11.5)
Other rash	7 (26.9)
No rash	16 (61.5)
First symptom/condition recalled[1], n (%)	
Joint pain/swelling	8 (30.8)
Rash	4 (15.4)
Fatigue	4 (15.4)
Headache	3 (11.5)
Bell's palsy	1 (3.8)
Other[2]	7 (26.9)
No symptom recalled	1 (3.8)
Symptom/condition that triggered first contact with medical provider, n (%)	
Joint pain	9 (34.6)
Rash	5 (19.2)
Fatigue	3 (11.5)
Bell's palsy	2 (7.7)
Other[3]	5 (19.2)
No symptom recalled – rash discovered during clinic visit for other condition	2 (7.7)
Self-reported Lyme-related diagnoses, n (%)	
Joint pain (diagnosis of Lyme arthritis not specified)	10 (38.5)
Bell's Palsy	8 (30.7)
Carditis	2 (7.7)
Meningitis	1 (3.8)
First medical care provider contacted, n (%)	
Urgent care/emergency department	10 (38.5)
Primary care provider	13 (50.0)
Other	3 (11.5)
Misdiagnosed by medical provider, n (%)	9 (34.6)
Medical care provider who misdiagnosed[4], n (% of misdiagnoses)	
Urgent care/emergency department (both)	7 (77.8)
Primary care provider	4 (44.4)

1. Total greater than 26 because one participant reported pain and rash occurred at the same time.
2. Other symptoms: vomiting; shortness of breath; aches/pains, not specific to joints (3); tick bite
3. Other symptoms: Vision change (2); stiff neck; vomiting; dizziness
4. Total greater than 9 because two patients were misdiagnosed by both emergency department and primary care physician.

A number of themes emerged regarding seeking care for Lyme disease symptoms. We classified these themes into one of the five GMTPD stages (**Table 2**).

Table 2. Participant quotes regarding the General Model of Total Patient Delay stages

Stage / domain	Quotes from participants during in-depth interviews
Appraisal	
Intermittent symptoms	• I never really had more than one spot at the same time, I never had like my feet hurt, my shoulders hurt. I never had like my elbows hurt and my knee hurt. Normally it was one spot at a time. And it just rotated, like I said one spot hurt, then like it could disease be weeks later, another spot would hurt, and then it'd go back to the other spot. • It was mostly my knees and my legs, a little bit in my arms every now and then, but it wasn't consistent like it was in my legs.
Misattribution	• I got a new computer, and I thought that it was not positioned correctly and because I was just on the computer pretty much all day and maybe through I strained by neck. • I was just kind of dealing with it because I thought maybe I slept on it [elbow] wrong or something. • My joints hurt, but I have rheumatoid arthritis, so I never associated it with LYME DISEASE, because I've had rheumatoid arthritis for many years, and I thought I was just getting another flare, so all the symptoms for my joint pain, I just associated with my rheumatoid condition.
Rash pattern	• I didn't think of Lyme, because it was it wasn't a bull's eye at all. • And it started growing and growing and, interestingly enough, it didn't assume the kind of quintessential bull's eye pattern. I always jokingly refer to it as a political boundary. It looked more like a map of the world, it was very, while it was roughly circular in shape, it was very jutted… looked more like Antarctica on my arm. • Because you know we're in the kind of live in the country, you hear about it and knew a couple people that had had it, but they had all you know had gotten the typical symptoms of you know, the red bulls-eye.
Illness/behavioral delay	
Health insurance	• So, I mean I just did as good as I could [to get the tick out]… but I wasn't sure that I got it all and I didn't have insurance at the point, so I didn't bother to go to the doctor. So, I just let it go, figured I wait and see, stupid idea. • I didn't have insurance. That was one of the main things. And, like I said, I was young, and I was just starting a new job, so I didn't have a lot of money. So, I was like, I don't know how I'll pay for that.
Treatment delay	
Emergency department and urgent care settings	• I saw my primary care physician about two weeks later [after emergency department visit.] And that's when she told me that I had the Lyme disease and then she said they [emergency department] had suspected it while I was in the emergency room, and nothing was ever given to me then. The test was done in the ER. Because I remember she [primary care physician] was mad that nobody there had contacted me and she said they, you know, could've gotten me started sooner on the medication." • I went up to the ER and they told me I had bursitis. Either bursitis or tendonitis. And told me that I'm to check back if I have any more issues. Well, it was still excruciating I went back before the week was up. That's when they told me I had the opposite, either bursitis or tendonitis. One of them. One or the other was, they thought the issue was, well it never went away. My doctor was out on vacation and I had called the office and… I said when she gets back, I need to see her ASAP. So, she had called and she got a hold of me and went back down into the office and as soon as she came in, she told me right away, I bet you have Lyme disease.

Participants reported seeking care both within and external to Geisinger for their initial Lyme disease symptoms, but we did not ask in which health care system delays occurred.

GMTPD Stages

Appraisal delay

Participants consistently reported an appraisal delay, a gap between their first symptom and recognition that they were ill (**Table 2**). Some participants attributed this gap to the inconsistent nature of their symptoms. One participant explained,

> "I was just having occasional joint achiness where it kind of felt like I slept funny on my elbow. It would be sore for a day or two and then it would go away."

Patients also misattributed symptoms to minor injuries, pre-existing conditions, or the flu. One participant noted, "I also have fibromyalgia, so it's kind of hard to differentiate."

Patients ruled out Lyme disease in the absence of the bull's-eye rash perceived to be characteristic of Lyme disease, delaying medical attention even in the presence of a rash. One participant explained,

> "And then I got a like this rash on my legs, on my arms, on my back. It was really bad. And I didn't even know about Lyme disease at that time… I mean I knew that you'd get a bull's-eye rash. And it wasn't that, so I went to the doctor probably about… at least three weeks later."

Illness delay/behavioral delay

Generally, once patients decided to seek medical care (illness delay), they acted on the decision (behavioral delay). One of the 26 participants noted a gap of five or six days between deciding he needed medical care and seeking care due to health insurance:

> “Every hour or so I would take my temperature and it was just going up and up... And I didn’t have insurance. And I thought I have to make it to Monday, because Monday is when my insurance was going to kick in. I said I have got to survive until Monday. I mean I would have went that Wednesday or Thursday that I was so sick. I had called somebody I know that’s a nurse and she said, ‘I don’t want you to die on me but get in your bed and don’t frickin’ move,… until Monday if you can make it.’ So, I, I took the words she said to heart and just kind of didn’t move the entire weekend.”

While no other patients articulated this gap between deciding to seek care and acting on it, health insurance was the most commonly occurring theme regarding the delay in deciding whether to seek medical attention for their symptoms (**Table 2**).

Scheduling delay

Scheduling delay did not emerge as a problem for any of the participants. Ten of the 26 participants initially sought care for symptoms at an urgent care or emergency department setting. Some of these patients noted that they decided to seek medical attention at these establishments because of the weekend and evening hours.

Treatment delay

When present, delays between the first appointment with a health care provider about Lyme disease symptoms and treatment were generally reported to be the result of a misdiagnosis (e.g., cellulitis). Nine of the 26 participants (34.6%) reported that they were not diagnosed with Lyme disease at their first contact with a medical professional regarding Lyme disease symptoms. Seven of these nine participants (77.8%) reported a misdiagnosis that occurred at an urgent care or emergency department setting, representing 70% of patients who first sought care in these settings (**Table 2**). One participant described this experience,

> "No, they [emergency department] didn't do any blood tests... Kind of examined and kind of listened to me. It was very busy that night. I know there was 1 or 2 doctors on and they had a bunch of drunks they were taking care of and things, so I think they may have missed the boat. …the nurse tells my wife, 'You know I think you got to watch because,' I think she said, 'I think there's more here than what it appears.' But that was it, and then they discharged me."

Non-GMTPD themes

Role of family

In multiple stages of the GMTPD, the involvement of family prompted action leading to treatment of Lyme disease. Most commonly, family members prompted patients to call the doctor (reducing illness/behavioral delay). For example:

> "I could no longer read the computer screen. I couldn't read the paper. And she (my wife) said, 'That's it, we're done playing around.' And I ended up at the doctors."

Another example was:

> “She (my sister) said to me, ‘That (rash) doesn’t look right.’ And I said, ‘Eh, it’ll go away in a couple of days.’ So, she told my mom, and my mom called me and said, ‘I’m coming up to look at it. I think we should go to the doctor.’ I said, ‘Ma, it’ll be fine.’ She said, ‘No, I think we should go.’ So…, my sister calls and gets an appointment.”

Family also played a role in reducing the treatment delay phase, after the patient saw a medical professional. In one instance, a patient was hospitalized for what was originally diagnosed as pain medication dependency. It was not until a family member demanded a transfer to a different hospital that Lyme disease was diagnosed.

> “So, I was there [at the hospital] for three or four days and all of the sudden I developed Bell’s palsy. And they did a CAT scan and they determined it was not a stroke. I laid there five more days where they did nothing. My sister and mother came to visit. They would not have recognized me. My face was swollen and droopy. So my sister had me transferred to another hospital. Within hours I was diagnosed with neurological Lyme.”

Consequences of delays

The original interview guide did not include questions regarding the impact of Lyme disease on work absenteeism/presenteeism or changes in productivity at work or home. However, the detrimental impact of Lyme disease on the ability to work and fulfill caregiving roles emerged as a common theme among participants.

> "I couldn't function, and I'm a care-taker for my mother, although she's a good 92 now…She took care of me, but I could not function. I lived on the sofa or in bed. That's how tired I was. If I tried to a do a little bit of anything, I would have to get back down, because I couldn't handle it."

Another person described a change in his work productivity before getting treated for Lyme disease.

> "I'd never sit down at work ever. I have my own machine shop. And I like nobody ever sees me sit. …like it came to the point where I was sitting and then actually at lunchtime and stuff I would actually lay on the bench."

For some of these patients, the impact on work and caregiving persisted after treatment.

> "Yeah, yeah, I was off [work] for quite a while between them actually finally determining it was Lyme disease and the treatment and then the post check-up after the treatment to make sure I was fine. Yeah, I was probably off for at least two months, if not more."

A second patient explained:

> "I own my own business, I've been in business since 1990. It is definitely not the same. I have a hard time spelling words. I mean you got to go in, you got to sell yourself, you got to get all the work and, it's just tough anymore. I just don't have the, it's hard to put things together, you know what I mean, like on the fly. Like with words and everything. You seem to lose that edge and I don't know how to explain it. You know and everybody says, 'Oh you got old,' but it just like changed instantly."

DISCUSSION

We conducted the first study, to our knowledge, to explore the experiences associated with the time between onset of symptoms and treatment of Lyme disease, with a specific focus on identifying themes related to belated treatment. Our study identified barriers to timely treatment that have been observed in other disease areas, as well as barriers specific to Lyme disease. We identified potential knowledge gaps in Lyme disease among patients and medical professionals, including misperceptions about the necessity of a bull's-eye rash. Understanding the conditions that participants perceive contribute to treatment delays can inform strategies that promote prompt treatment of Lyme disease, preventing dissemination of infection and the resulting disease complications.

Application of the GMTPD to Lyme disease was very instructive and showed that Lyme disease generally conformed to the model. The appraisal stage emerged as a distinct and dominant phase, as has been observed when this model has been applied to other diseases.[3,10,11] We identified three appraisal delay themes: symptom misattribution, intermittent symptoms, and lack of bull's-eye rash. Both the intermittent nature of symptoms as well as the symptom misattribution to less serious or pre-existing conditions has been reported to account for appraisal delays in various cancers, particularly when the early symptoms were commonly occurring non-specific symptoms (e.g. fatigue).[12,13] Specific to Lyme disease, respondents misattributed the joint pain of Lyme disease to other conditions with joint pain, such as rheumatoid arthritis and fibromyalgia.

Appraisal delays also resulted from a misunderstanding of the characteristic Lyme disease rash, erythema migrans. Specifically, participants reported that they did not suspect Lyme disease if they did not have a rash with central clearing, referred to as a bull's-eye rash. Approximately 20 to 30% of people with Lyme disease do not present with erythema migrans and among those who do have the rash, only 19% have the stereotypical bull's-eye appearance.[14] The impact of the belief in the necessity of central clearing on belated treatment is compounded by the diagnostic challenges associated with Lyme disease in the absence of the rash. One study reported that 54% of patients with Lyme disease who did not have erythema migrans were initially misdiagnosed compared to 23% of patients who did have erythema migrans.[15] Our findings highlight an important knowledge gap among patients regarding the skin manifestations of Lyme disease. Patient education campaigns that address this issue could reduce the time between infection and treatment.

The illness and behavioral delay stages appeared to be most influenced by health insurance status. Our findings are consistent with delays attributed to lack of health insurance observed in other disease areas. A lack of insurance has been associated with longer pre-hospital delays in myocardial infarction[16,17] and with care-seeking behavior in cancer.[18] It is unknown whether the belated treatment due to lack of health insurance translate into an increased risk of late Lyme disease among the uninsured.

Scheduling delay was not a major contributor to belated treatment in our study, as nearly half of patients we interviewed sought care at emergency departments or urgent care centers, medical settings that typically offer same-day, evening, and weekend appointments. While the availability of urgent care clinics and emergency departments appeared to minimize scheduling delays, the patients who first sought care at these locations reported more occurrences of misdiagnoses. Thus, the time saved in the scheduling delay stage by seeking care in one of these settings could be outweighed by the treatment delays resulting from misdiagnoses in these settings. The number of urgent care settings have dramatically increased over the last decade, but little is known regarding the quality of care for Lyme disease in these settings.[19]

Family interventions were identified to decrease the time to treatment in Lyme disease, consistent with the role of family and friends in belated treatment for cancer and cardiovascular disease.[20,21] Smith and colleagues[10] reported that, for many patients with cancer, friends and family helped with the process of illness attribution by observing or discussing vague symptoms with patients, ultimately making the connection between symptoms and illness that had gone unrecognized by the patient. The extent to which family structure, marital status, and social support play a role in Lyme disease diagnosis and treatment has not been studied.

The impact of Lyme disease on work and caregiving activities emerged as a salient theme for participants, impacting patients prior to treatment and, in some cases, even after treatment. While costs occurring after a Lyme disease diagnosis have been studied,[22] these studies do not account for the time between infection and treatment of disease, likely underestimating costs. Prior studies that focused on productivity loss and activity limitations in Lyme disease have been confined to individuals reporting symptoms persisting for more than six months.[23,24] A comprehensive study of indirect and direct costs across the full spectrum of Lyme disease, before and after treatment, would give a more complete picture of the individual and population-level burden of this disease.

To our knowledge, this is the first study to evaluate the application of GMTPD to Lyme disease. Through the lens of this model we identified distinct phases between onset of first Lyme disease symptoms and Lyme disease treatment. Our study was conducted in a well-defined sample of participants with a positive IgG Western blot, a lab result present only at least six to eight weeks after Lyme disease infection. Our study had limitations. First, while our eligibility criteria was highly specific for Lyme disease, requiring a positive IgG Western blot, patients may have been excluded as a result of false-negative test results that can occur at all stages disease, but most commonly among patients tested in the first few weeks of infection, when the test is expected to be negative.[6,25,26] Second, while our patients described interactions with health systems beyond Geisinger, all participants were tested for Lyme disease at Geisinger. With more than 44 Geisinger community practice sites and 12 hospital campuses across a large geographic region, there is likely a great deal of diversity in Lyme disease diagnosis and treatment experiences within the health system. However, these findings may not be generalizable to other countries due to differences in factors such as healthcare cost and access. Finally, the objective of this study was not to quantify the extent to which each delay phase contributed to belated treatment in Lyme disease. We identified several explanations for belated treatment of Lyme disease that are intervenable and can be targeted to minimize time to treatment and reduce the burden of Lyme disease on patients and society. To prioritize resources around secondary prevention strategies in Lyme disease, a large quantitative study on patients across the full spectrum of Lyme disease is needed to both determine how much each phase contributes to belated treatment and to quantify the degree to which factors increase risk of belated treatment.

Author contribution: AH, AR, KM, JA, CH, and BS participated in the design of the study; AH conducted data collection; AH and RH conducted data analysis; all authors participated in the writing of the manuscript.

REFERENCES

1 Nelson CA, Saha S, Kugeler KJ, et al. Incidence of Clinician-Diagnosed Lyme Disease, United States, 2005-2010. *Emerg Infect Dis* 2015;21:1625-1631. doi:10.3201/eid2109.150417

2 Mead PS. Epidemiology of Lyme disease. *Infect Dis Clin North Am* 2015;29:187-210. doi:10.1016/j.idc.2015.02.010

3 Scott SE, Walter FM, Webster A, et al. The model of pathways to treatment: conceptualization and integration with existing theory. *Br J Health Psychol* 2012;18:45-65. doi:10.1111/j.2044-8287.2012.02077.x

4 Andersen BL, Cacioppo JT. Delay in seeking a cancer diagnosis: delay stages and psychophysiological comparison processes. *Br J Soc Psychol* 1995;34:33-52.

5 Centers for Disease Control and Prevention. Lyme Disease: Data and statistics. 2016. https://www.cdc.gov/lyme/stats/index.html (accessed Oct 2017).

6 Centers for Disease Control and Prevention. Lyme Disease: Understanding the Immunoblot Test. 2015. https://www.cdc.gov/lyme/diagnosistesting/labtest/twostep/westernblot/index.html (accessed Oct 2017).

7 Corbin J, Strauss A. Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory (3rd ed.). Thousand Oaks, CA: Sage 2008.

8 Elo S, Kyngäs H. The qualitative content analysis process. *J Adv Nurs* 2008;62:107-115. doi:10.1111/j.1365-2648.2007.04569.x

9 Casey JA, Pollak J, Glymour MM, et al. Measures of SES for Electronic Health Record-based Research. *Am J Prev Med* 2018;54:430-439. doi:10.1016/j.amepre.2017.10.004

10 Smith LK, Pope C, Botha JL. Patients' help-seeking experiences and delay in cancer presentation: a qualitative synthesis. *Lancet* 2005;366:825-831. doi:10.1016/S0140-6736(05)67030-4

11 Evans J, Ziebland S, McPherson A. Minimizing delays in ovarian cancer diagnosis: an expansion of Andersen's model of 'total patient delay'. *Fam Pract* 2007;24:48-55. doi:10.1093/fampra/cml063

12 Evans J, Chapple A, Salisbury H, et al. "It can't be very important because it comes and goes"--patients' accounts of intermittent symptoms preceding a pancreatic cancer diagnosis: a qualitative study. *BMJ Open* 2014;4:e004215. doi:10.1136/bmjopen-2013-004215

13 Brouha XD, Tromp DM, Hordijk GJ, et al. Oral and pharyngeal cancer: analysis of patient delay at different tumor stages. *Head Neck* 2005;27:939-945. doi:10.1002/hed.20270

14 Tibbles CD, Edlow JA. Does this patient have erythema migrans? *JAMA* 2007;297:2617-2627. doi:10.1001/jama.297.23.2617

15 Aucott J, Morrison C, Munoz B, et al. Diagnostic challenges of early Lyme disease: lessons from a community case series. *BMC Infect Dis* 2009;9:79. doi:10.1186/1471-2334-9-79

16 Nguyen HL, Saczynski JS, Gore JM, et al. Age and sex differences in duration of prehospital delay in patients with acute myocardial infarction: a systematic review. *Circ Cardiovasc Qual Outcomes* 2010;3:82-92. doi:10.1161/CIRCOUTCOMES.109.884361

17 Smolderen KG, Spertus JA, Nallamothu BK, et al. Health care insurance, financial concerns in accessing care, and delays to hospital presentation in acute myocardial infarction. *JAMA* 2010;303:1392-1400. doi:10.1001/jama.2010.409

18 Rauscher GH, Ferrans CE, Kaiser K, et al. Misconceptions about breast lumps and delayed medical presentation in urban breast cancer patients. *Cancer Epidemiol Biomarkers Prev* 2010;19:640-647. doi:10.1158/1055-9965.EPI-09-0997

19 Yee T, Lechner AE, Boukus ER. The surge in urgent care centers: emergency department alternative or costly convenience. *Res Brief* 2013;(26),1-6.

20 Perkins-Porras L, Whitehead DL, Strike PC, et al. Pre-hospital delay in patients with acute coronary syndrome: factors associated with patient decision time and home-to-hospital delay. *Eur J Cardiovasc Nurs* 2009;8:26-33. doi:10.1016/j.ejcnurse.2008.05.001

21 Barr J, McKinley S, O'Brien E, et al. Patient recognition of and response to symptoms of TIA or stroke. *Neuroepidemiology* 2006;26:168-175. doi:10.1159/000091659

22 Adrion ER, Aucott J, Lemke KW, et al. Health care costs, utilization and patterns of care following Lyme disease. *PloS One* 2015;10:e0116767. doi:10.1371/journal.pone.0116767

23 Johnson L, Aylward A, Stricker RB. Healthcare access and burden of care for patients with Lyme disease: A large United States survey. *Health Policy* 2011;102,64-71. doi:10.1016/j.healthpol.2011.05.007

24 Johnson L, Wilcox S, Mankoff J, et al. Severity of chronic Lyme disease compared to other chronic conditions: a quality of life survey. *PeerJ* 2014;2:e322. doi:10.7717/peerj.322

25 Cook MJ, Puri BK. Commercial test kits for detection of Lyme borreliosis: a meta-analysis of test accuracy. *Int J Gen Med* 2016;9:427-440. doi:10.2147/IJGM.S122313

26 Waddell LA, Greig J, Mascarenhas M. The Accuracy of Diagnostic Tests for Lyme Disease in Humans, A systematic Review and Meta-Analysis of North American Research. *PLoS One* 2016;11:e0168613. doi:10.1371/journal.pone.0168613

Standards for Reporting Qualitative Research (SRQR) Checklist

Topic	Item	Author Response
S1 Title	Concise description of the nature and topic of the study. Identifying the study as qualitative or indicating the approach or data collection methods is recommended.	Page 1, Title page: The title identifies the study as qualitative: “Obstacles to diagnosis and treatment of Lyme disease: A qualitative study”
S2 Abstract	Summary of key elements using the abstract format of the intended publication.	Page 2, Abstract: The abstract adheres to journal specifications.
S3 Problem formulation	Description and significance of the problem/phenomenon studied: review of relevant theory and empirical work; problem statement.	Page 4: Paragraph 1 describes the risks associated with late diagnosis and treatment of Lyme disease. Paragraph 2 describes the application of the General Model of Total Patient Delay to the study of delayed treatment.
S4 Purpose or research question	Purpose of the study and specific objectives or questions.	Page 5: Paragraph 1 states that the objective of the paper is “to identify themes around belated treatment, as well as to evaluate the application of the General Model of Total Patient Delay to Lyme disease…”
S5 Qualitative approach and research paradigm	Qualitative approach and guiding theory; identifying the research paradigm is also recommended.	Page 5: Paragraph 2 states that the interview findings were analyzed through the theory of General Model of Total Patient Delay. Page 6: Paragraph 1 states, “We applied a deductive content analysis of interview transcripts based on the General Model of Total Patient Delay.”
S6 Researchers’ characteristics and reflexivity	Researchers’ characteristics that may influence the research; potential or actual interaction between researchers’ characteristics and the research questions, approach, methods, results, and/or transferability.	Page 6: Paragraph 2 states: “The interviewer is a researcher employed by the health system that treated participants for Lyme disease. To address any concerns participants might have had in describing their care experiences to a health system employee, the interviewer informed participants that their responses would not impact the care received at Geisinger and would be kept confidential.”
S7 Context	Setting/site and salient contextual factors.	Page 5: The section “Study setting and sample” describes the study setting. Page 6: Paragraph 2 states: We conducted in-depth, semi-structured, open-ended telephone interviews… Telephone interviews allowed for capture of patient experiences across the large geographic area served by Geisinger.”
S8 Sampling strategy	How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary; rationale.	Pages 5-6: The “Study setting and sample” section describes the sample, how they were selected, criteria for selection, rationale for selection, and explains that recruitment continued until data saturation.
S9 Ethical issues pertaining to human subjects	Documentation of approval by an appropriate ethics review board.	Page 5: First paragraph in the “Methods” section states that the study was approved by the Geisinger Institutional Review Board.
S10 Data collection methods	Types of data collected; details of data collection procedures; rationale	Page 6: The “Data Collection” section describes the methods for data collection, including the use

		of telephone interviews; the types of questions asked; and the timeframe of the interviews. Page 7: The "Analysis" section describes the application of deductive content analysis; the coding process; and the use of the General Model of Total Patient Delay to develop higher-order codes.
S11 Data collection instruments	Description of instruments	Page 6: The "Data Collection" section describes six categories of questions included in the interview guide. Page 7: The "Analysis" section notes: "The coding team also updated the interview guide to incorporate questions around emergent themes for future interviews."
S12 Units of study	Number and relevant characteristics of participants	Pages 7-8: The first three paragraphs of the "Results" section describe the study participants. Table 1: Characteristics and Lyme disease symptoms, signs, and diagnosis patterns of participants
S13 Data processing	Methods for processing data prior to and during analysis.	Page 7: The "Data Collection" section notes that all interviews were audio-recorded and transcribed verbatim.
S14 Data analysis	Process by which inferences , themes, etc., were identified and developed.	Page 7: The "Analysis" section describes the data analysis process, including the identification of themes and the application of the General Model of Total Patient Delay.
S15 Techniques to enhance trustworthiness	Techniques to enhance trustworthiness and credibility of data analysis.	Page 7: The "Analysis" section describes the use of two coders and the requirement of consensus on the coding framework, coding, and identification of emergent themes.
S16 Synthesis and interpretation	Main findings	Pages 7-13: "Results are presented on these pages as well as in Tables 1 and 2.
S17 Links to empirical data	Evidence (e.g. quotes) to substantiate findings.	Pages 8-13: Quotes are embedded in the "Results" section and presented in Table 2.
S18 Integration with prior work, implications, transferability, and contributions to the field.	Short summary of main findings; explanation of how findings and conclusions…connect to earlier scholarship; unique contribution.	Pages 13-17: The "Discussion" section summarizes the main findings, links the findings to prior works, and describes the contribution of this manuscript to the field.
S19 Limitations	Trustworthiness and limitations of findings	Pages 16 and 17 describe the limitations of the study.
S20 Conflicts of interest	Potential sources of influence	Page 3: No competing interests were declared by authors.
S21 Funding	Sources of funding	Page 3: This work was supported by the Steve & Alexandra Cohen Foundation. The Steve and Alexandra Cohen Foundation did not participate in data collection, analysis, or the writing of this manuscript.