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

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

Annemarie G. Hirsch¹, PhD, MPH; Rachel J. Herman²; Alison Rebman³, MPH;
Katherine Moon⁴, PhD; John Aucott³, 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 conducted among patients from a single integrated health system that includes 44 community practice sites and 12 hospital campuses across a large geographic region.

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Competing interests: None declared

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

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3 Lyme disease is a tick-borne infectious disease that is on the rise in the
4
5 Northeast, Mid-Atlantic, and Upper Midwest regions of the United States (Nelson et al.,
6
7 2015). Delays in diagnosis or treatment (hereafter referred to as belated treatment) of
8
9 Lyme disease can lead to preventable complications, representing later stages of the
10
11 disease when the infection disseminates, including neurologic manifestations, cardiac
12
13 abnormalities, and arthritis (Mead, 2015). While little is known about the prevalence of
14
15 belated treatment in Lyme disease, the observation that 32% of Lyme disease cases
16
17 are diagnosed with arthritis, 12% with neurologic conditions, and 1-2% with carditis
18
19 (Mead, 2015) suggests that belated treatment may occur in as many as 40% of cases.
20
21 To date, the study of time to treatment has largely focused on cancer and
22
23 cardiovascular events (Scott, Walter, Webster, Sutton, & Emery, 2012). No study has
24
25 examined which factors account for belated treatment of Lyme disease, despite the
26
27 benefits of prompt treatment of this disease.
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33 The General Model of Total Patient Delay (GMTPD) (Andersen, Cacioppo, &
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35 Roberts, 1995) is a widely used, five-stage model that describes the decisional
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37 processes and potential delays prior to treatment (Scott et al., 2012). Appraisal delay is
38
39 the time between when a person first notices an unexplained symptom until the person
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41 concludes he/she is ill. Appraisal has generally been found to be the key determinant in
42
43 delay in seeking help (Scott et al., 2012). Illness delay is the time between inferring
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45 illness and deciding to seek help; behavioral delay represents the time between
46
47 deciding an illness requires medical care and acting; scheduling delay is the time
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49 between deciding to seek help and attending an appointment; and treatment delay is
50
51 the time between the first appointment with a health care provider and onset of
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3 treatment (Andersen et al., 1995). While this model has been widely applied to cancer
4 and myocardial infarction, it has not been applied to Lyme disease. Thus, the primary
5 drivers of belated treatment in Lyme disease remain unknown.
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10 To identify themes around belated treatment, as well as to evaluate the
11 application of the GMTPD to Lyme disease, we interviewed 26 patients with a diagnosis
12 of Lyme disease to gain insight into their experiences between onset of Lyme disease
13 symptoms and treatment. Such understanding is critical to informing strategies that
14 would reduce time to diagnosis and treatment and prevent late stage Lyme disease.
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24 **METHODS**

25
26 We conducted a qualitative study using in-depth telephone interviews of
27 Geisinger patients with a Lyme disease diagnosis to understand what happens between
28 the onset of Lyme disease symptoms and treatment. We analyzed interview findings
29 through the GMTPD framework. This study was approved by the Geisinger Institutional
30 Review Board.
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38 **Study setting and sample**

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40 We identified study participants using the electronic health record (EHR) from
41 Geisinger, an integrated health system servicing more than 45 counties in Pennsylvania
42 and New Jersey, both high-incidence states for Lyme disease (Centers for Disease
43 Control and Prevention [CDC], 2017). Patients were eligible if they were at least 18
44 years of age; had an International Classification of Disease code (ICD-9: 088.81 or ICD-
45 10: A69.20) for Lyme disease associated with at least one clinical encounter between
46 2014 and 2017; and an IgG Western blot meeting CDC criteria of five or more positive
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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;

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

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

43 Out of the 93 patients to whom we sent a letter, we telephoned 56 patients and
44 reached 33. Of these, 26 (79%) agreed to be interviewed. We stopped recruitment calls
45 after reaching saturation. While the interviewers were intended to be one-on-one, two
46 patients had a spouse with them in the room during the interview. In one case, a spouse
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3 joined the call. However, analysis was confined to the information presented by the 26
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5 patients.
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8 Slightly more than half of participants were female; 30% had a history of being
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10 on Medical Assistance (a surrogate for low family socioeconomic status); and
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12 participants ranged in age from 22 to 70 years (**Table 1**). Half of the participants first
13
14 sought care for Lyme disease from a primary care provider and 38.5% first went to an
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16 urgent care center or emergency department.
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20 Ten participants reported that they had a rash, three of whom described the rash
21
22 as a bull's-eye. Four of the participants who reported a rash sought care because of the
23
24 rash. The remaining did not seek care until other symptoms (e.g., fatigue, joint pain)
25
26 appeared. Two of the four participants who saw a doctor because of the rash were
27
28 initially misdiagnosed. Eleven participants reported having joint pain, though patients
29
30 did not specify whether the joint pain was diagnosed as Lyme arthritis. Eight patients
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32 reported having Bell's palsy, two patients reported carditis, and one patient reported a
33
34 diagnosis of Lyme meningitis.
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38 A number of themes emerged regarding seeking care for Lyme disease
39
40 symptoms. We classified these themes into one of the five GMTDP stages (**Table 2**).
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42 Participants reported seeking care both within and external to Geisinger for their initial
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44 Lyme disease symptoms, but we did not ask in which health care system delays
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46 occurred.
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49 **GMTDP Stages**

50 *Appraisal delay*

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3 Participants consistently reported an appraisal delay, a gap between their first
4 symptom and recognition that they were ill (**Table 2**). Some participants attributed this
5 gap to the inconsistent nature of their symptoms. One participant explained,
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10 “I was just having occasional joint achiness where it kind of felt like I slept
11 funny on my elbow. It would be sore for a day or two and then it would go away.”
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14 Patients also misattributed symptoms to minor injuries, pre-existing conditions, or
15 the flu. One participant noted, “I also have fibromyalgia, so it’s kind of hard to
16 differentiate.”
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20 Patients ruled out Lyme disease in the absence of the bull’s-eye rash perceived
21 to be characteristic of Lyme disease, delaying medical attention even in the presence of
22 a rash. One participant explained,
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27 “And then I got a like this rash on my legs, on my arms, on my back. It was
28 really bad. And I didn’t even know about Lyme disease at that time... I mean I
29 knew that you’d get a bull’s-eye rash. And it wasn’t that, so I went to the doctor
30 probably about... at least three weeks later.”
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37 *Illness delay/behavioral delay*

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39 Generally, once patients decided to seek medical care (illness delay), they acted on
40 the decision (behavioral delay). One of the 26 participants noted a gap of five or six
41 days between deciding he needed medical care and seeking care due to health
42 insurance:
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49 “Every hour or so I would take my temperature and it was just going up
50 and up... And I didn’t have insurance. And I thought I have to make it to Monday,
51 because Monday is when my insurance was going to kick in. I said I have got to
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3 survive until Monday. I mean I would have went that Wednesday or Thursday
4 that I was so sick. I had called somebody I know that's a nurse and she said, 'I
5 don't want you to die on me but get in your bed and don't frickin' move,... until
6 Monday if you can make it.' So, I, I took the words she said to heart and just
7 kind of didn't move the entire weekend."
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14 While no other patients articulated this gap between deciding to seek care and
15 acting on it, health insurance was the most commonly occurring theme regarding the
16 delay in deciding whether to seek medical attention for their symptoms (**Table 2**).
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21 *Scheduling delay*

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

33 When present, delays between the first appointment with a health care provider
34 about Lyme disease symptoms and treatment were generally reported to be the result
35 of a misdiagnosis (e.g., cellulitis). Nine of the 26 participants (34.6%) reported that they
36 were not diagnosed with Lyme disease at their first contact with a medical professional
37 regarding Lyme disease symptoms. Seven of these nine participants (77.8%) reported a
38 misdiagnosis that occurred at an urgent care or emergency department setting,
39 representing 70% of patients who first sought care in these settings (**Table 2**). One
40 participant described this experience,
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3 “No, they [emergency department] didn’t do any blood tests... Kind of
4 examined and kind of listened to me. It was very busy that night. I know there
5 was 1 or 2 doctors on and they had a bunch of drunks they were taking care of
6 and things, so I think they may have missed the boat. ...the nurse tells my wife,
7
8 ‘You know I think you got to watch because,’ I think she said, ‘I think there’s more
9
10 here than what it appears.’ But that was it, and then they discharged me.”
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17 **Non-GMTPD themes**

18 *Role of family*

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20 In multiple stages of the GMTPD, the involvement of family prompted action
21 leading to treatment of Lyme disease. Most commonly, family members prompted
22 patients to call the doctor (reducing illness/behavioral delay). For example:
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28 “I could no longer read the computer screen. I couldn’t read the paper.
29
30 And she (my wife) said, ‘That’s it, we’re done playing around.’ And I ended up at
31
32 the doctors.”
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35 Another example was:

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37 “She (my sister) said to me, ‘That (rash) doesn’t look right.’ And I said, ‘Eh,
38
39 it’ll go away in a couple of days.’ So, she told my mom, and my mom called me
40
41 and said, ‘I’m coming up to look at it. I think we should go to the doctor.’ I said,
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43 ‘Ma, it’ll be fine.’ She said, ‘No, I think we should go.’ So..., my sister calls and
44
45 gets an appointment.”
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49 Family also played a role in reducing the treatment delay phase, after the patient
50 saw a medical professional. In one instance, a patient was hospitalized for what was
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3 originally diagnosed as pain medication dependency. It was not until a family member
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5 demanded a transfer to a different hospital that Lyme disease was diagnosed.
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8 “So, I was there [at the hospital] for three or four days and all of the
9
10 sudden I developed Bell’s palsy. And they did a CAT scan and they determined it
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12 was not a stroke. I laid there five more days where they did nothing. My sister
13
14 and mother came to visit. They would not have recognized me. My face was
15
16 swollen and droopy. So my sister had me transferred to another hospital. Within
17
18 hours I was diagnosed with neurological Lyme.”
19
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21 *Consequences of delays*

22
23 The original interview guide did not include questions regarding the impact of
24
25 Lyme disease on work absenteeism/presentism or changes in productivity at work or
26
27 home. However, the detrimental impact of Lyme disease on the ability to work and fulfill
28
29 caregiving roles emerged as a common theme among participants.
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33 “I couldn’t function, and I’m a care-taker for my mother, although she’s a
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35 good 92 now...She took care of me, but I could not function. I lived on the sofa or
36
37 in bed. That’s how tired I was. If I tried to do a little bit of anything, I would have
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39 to get back down, because I couldn’t handle it.”
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42 Another person described a change in his work productivity before getting treated for
43
44 Lyme disease.
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47 “I’d never sit down at work ever. I have my own machine shop. And I like
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49 nobody ever sees me sit. ...like it came to the point where I was sitting and then
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51 actually at lunchtime and stuff I would actually lay on the bench.”
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3 For some of these patients, the impact on work and caregiving persisted after
4
5 treatment.
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7 “Yeah, yeah, I was off [work] for quite a while between them actually finally
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9 determining it was Lyme disease and the treatment and then the post check-up
10
11 after the treatment to make sure I was fine. Yeah, I was probably off for at least
12
13 two months, if not more.”
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17 A second patient explained:
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19 “I own my own business, I’ve been in business since 1990. It is definitely
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21 not the same. I have a hard time spelling words. I mean you got to go in, you got
22
23 to sell yourself, you got to get all the work and, it’s just tough anymore. I just don’t
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25 have the, it’s hard to put things together, you know what I mean, like on the fly.
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27 Like with words and everything. You seem to lose that edge and I don’t know
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29 how to explain it. You know and everybody says, ‘Oh you got old,’ but it just like
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31 changed instantly.”
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38 **DISCUSSION**

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40 We conducted the first study, to our knowledge, to explore the experiences
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42 associated with the time between onset of symptoms and treatment of Lyme disease,
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44 with a specific focus on identifying themes related to belated treatment. Our study
45
46 identified barriers to timely treatment that have been observed in other disease areas,
47
48 as well as barriers specific to Lyme disease. We identified potential knowledge gaps in
49
50 Lyme disease among patients and medical professionals, including misperceptions
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52 about the necessity of a bull’s-eye rash. Understanding the conditions that participants
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3 perceive contribute to treatment delays can inform strategies that promote prompt
4 treatment of Lyme disease, preventing dissemination of infection and the resulting
5 disease complications.
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10 Application of the GMTDPD to Lyme disease was very instructive and showed that
11 Lyme disease generally conformed to the model. The appraisal stage emerged as a
12 distinct and dominant phase, as has been observed when this model has been applied
13 to other diseases (Scott et al., 2012; Smith, Pope, & Botha, 2005; Evans, Ziebland, &
14 McPherson, 2006). We identified three appraisal delay themes: symptom
15 misattribution, intermittent symptoms, and lack of bull's-eye rash. Both the intermittent
16 nature of symptoms as well as the symptom misattribution to less serious or pre-existing
17 conditions has been reported to account for appraisal delays in various cancers,
18 particularly when the early symptoms were commonly occurring non-specific symptoms
19 (e.g. fatigue) (Evans, Chapple, Salisbury, Corrie, & Ziebland, 2014; Brouha, Tromp,
20 Hordijk, Winnubst, & de Leeuw, 2005). Specific to Lyme disease, respondents
21 misattributed the joint pain of Lyme disease to other conditions with joint pain, such as
22 rheumatoid arthritis and fibromyalgia.
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40 Appraisal delays also resulted from a misunderstanding of the characteristic
41 Lyme disease rash, erythema migrans. Specifically, participants reported that they did
42 not suspect Lyme disease if they did not have a rash with central clearing, referred to as
43 a bull's-eye rash. Approximately 20 to 30% of people with Lyme disease do not present
44 with erythema migrans and among those who do have the rash, only 19% have the
45 stereotypical bull's-eye appearance (Tibbles & Edlow, 2007). The impact of the belief in
46 the necessity of central clearing on belated treatment is compounded by the diagnostic
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3 challenges associated with Lyme disease in the absence of the rash. One study
4 reported that 54% of patients with Lyme disease who did not have erythema migrans
5 were initially misdiagnosed compared to 23% of patients who did have erythema
6 migrans (Aucott et al., 2009). Our findings highlight an important knowledge gap among
7 patients regarding the skin manifestations of Lyme disease. Patient education
8 campaigns that address this issue could reduce the time between infection and
9 treatment.
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19 The illness and behavioral delay stages appeared to be most influenced by
20 health insurance status. Our findings are consistent with delays attributed to lack of
21 health insurance observed in other disease areas. A lack of insurance has been
22 associated with longer pre-hospital delays in myocardial infarction (Nguyen, Saczynski,
23 Gore, & Goldberg, 2010; Smolderen et al., 2010) and with care-seeking behavior in
24 cancer (Rauscher et al., 2010). It is unknown whether the belated treatment due to lack
25 of health insurance translate into an increased risk of late Lyme disease among the
26 uninsured.
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37 Scheduling delay was not a major contributor to belated treatment in our study,
38 as nearly half of patients we interviewed sought care at emergency departments or
39 urgent care centers, medical settings that typically offer same-day, evening, and
40 weekend appointments. While the availability of urgent care clinics and emergency
41 departments appeared to minimize scheduling delays, the patients who first sought care
42 at these locations reported more occurrences of misdiagnoses. Thus, the time saved in
43 the scheduling delay stage by seeking care in one of these settings could be
44 outweighed by the treatment delays resulting from misdiagnoses in these settings. The
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3 number of urgent care settings have dramatically increased over the last decade, but
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5 little is known regarding the quality of care for Lyme disease in these settings (Yee,
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7 Lechner, & Boukus, 2013).
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10 Family interventions were identified to decrease the time to treatment in Lyme
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12 disease, consistent with the role of family and friends in belated treatment for cancer
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14 and cardiovascular disease (Perkins-Porrás, Whitehead, Strike, & Steptoe, 2009; Barr,
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16 McKinley, O'Brien, & Herkes, 2006). Smith and colleagues (2005) reported that, for
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18 many patients with cancer, friends and family helped with the process of illness
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20 attribution (Smith et al., 2005) by observing or discussing vague symptoms with
21
22 patients, ultimately making the connection between symptoms and illness that had gone
23
24 unrecognized by the patient. The extent to which family structure, marital status, and
25
26 social support play a role in Lyme disease diagnosis and treatment has not been
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28 studied.
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33 The impact of Lyme disease on work and caregiving activities emerged as a
34
35 salient theme for participants, impacting patients prior to treatment and, in some cases,
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37 even after treatment. While costs occurring after a Lyme disease diagnosis have been
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39 studied (Adrion, Aucott, Lemke, & Weiner, 2015), these studies do not account for the
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41 time between infection and treatment of disease, likely underestimating costs.
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43 Specifically, little is known about the indirect costs resulting from lost productivity
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45 (Zhang et al., 2006). A comprehensive study of indirect and direct costs of Lyme
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47 disease before and after treatment would give a more complete picture of the individual
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49 and population-level burden of this disease.
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3 To our knowledge, this is the first study to evaluate the application of GMTPD to
4 Lyme disease. Through the lens of this model we identified distinct phases between
5 onset of first Lyme disease symptoms and Lyme disease treatment. Our study was
6 conducted in a well-defined sample of participants with a positive IgG Western blot, a
7 lab result present only at least six to eight weeks after Lyme disease infection. Our
8 study had limitations. First, while our patients described interactions with health systems
9 beyond Geisinger, all participants were tested for Lyme disease at Geisinger. However,
10 with more than 44 Geisinger community practice sites and 12 hospital campuses across
11 a large geographic region, there is likely a great deal of diversity in Lyme disease
12 diagnosis and treatment experiences within the health system. Second, the objective of
13 this study was not to quantify the extent to which each delay phase contributed to
14 belated treatment in Lyme disease. We identified several explanations for belated
15 treatment of Lyme disease that are intervenable and can be targeted to minimize time to
16 treatment and reduce the burden of Lyme disease on patients and society. To prioritize
17 resources around secondary prevention strategies in Lyme disease, a quantitative study
18 is needed to both determine how much each phase contributes to belated treatment and
19 to quantify the degree to which factors increase risk of belated treatment.
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44 **Author contribution:** AH, AR, KM, JA, CH, and BS participated in the design of the
45 study; AH conducted data collection; AH and RH conducted data analysis; all authors
46 participated in the writing of the manuscript.
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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 recalled¹, 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 misdiagnosed², 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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 jugged 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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.

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

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Manuscripts

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

Annemarie G. Hirsch¹, PhD, MPH; Rachel J. Herman²; Alison Rebman³, MPH;
Katherine Moon⁴, PhD; John Aucott³, 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.

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

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3 Lyme disease is a tick-borne infectious disease that is on the rise in the
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5 Northeast, Mid-Atlantic, and Upper Midwest regions of the United States (Nelson et al.,
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7 2015). Delays in diagnosis or treatment (hereafter referred to as belated treatment) of
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9 Lyme disease can lead to preventable complications, representing later stages of the
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11 disease when the infection disseminates, including neurologic manifestations, cardiac
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13 abnormalities, and arthritis (Mead, 2015). While little is known about the prevalence of
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15 belated treatment in Lyme disease, the observation that 32% of Lyme disease cases
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17 are diagnosed with arthritis, 12% with neurologic conditions, and 1-2% with carditis
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19 (Mead, 2015) suggests that belated treatment may occur in as many as 40% of cases.
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21 To date, the study of time to treatment has largely focused on cancer and
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23 cardiovascular events (Scott, Walter, Webster, Sutton, & Emery, 2012). No study has
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25 examined which factors account for belated treatment of Lyme disease, despite the
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27 benefits of prompt treatment of this disease.
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33 The General Model of Total Patient Delay (GMTPD) (Andersen, Cacioppo, &
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35 Roberts, 1995) is a widely used, five-stage model that describes the decisional
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37 processes and potential delays prior to treatment (Scott et al., 2012). Appraisal delay is
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39 the time between when a person first notices an unexplained symptom until the person
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41 concludes he/she is ill. Appraisal has generally been found to be the key determinant in
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43 delay in seeking help (Scott et al., 2012). Illness delay is the time between inferring
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45 illness and deciding to seek help; behavioral delay represents the time between
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47 deciding an illness requires medical care and acting; scheduling delay is the time
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49 between deciding to seek help and attending an appointment; and treatment delay is
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51 the time between the first appointment with a health care provider and onset of
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3 treatment (Andersen et al., 1995). While this model has been widely applied to cancer
4 and myocardial infarction, it has not been applied to Lyme disease. Thus, the primary
5 drivers of belated treatment in Lyme disease remain unknown.
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10 To identify themes around belated treatment, as well as to evaluate the
11 application of the GMTDP to Lyme disease, we interviewed 26 patients with a diagnosis
12 of Lyme disease to gain insight into their experiences between onset of Lyme disease
13 symptoms and treatment. Such understanding is critical to informing strategies that
14 would reduce time to diagnosis and treatment and prevent late stage Lyme disease.
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24 **METHODS**

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26 We conducted a qualitative study using in-depth telephone interviews of
27 Geisinger patients with a Lyme disease diagnosis to understand what happens between
28 the onset of Lyme disease symptoms and treatment. We analyzed interview findings
29 through the GMTDP framework. This study was approved by the Geisinger Institutional
30 Review Board.
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37 **Study setting and sample**

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39 We identified study participants using the electronic health record (EHR) from
40 Geisinger, an integrated health system servicing more than 45 counties in Pennsylvania
41 and New Jersey, both high-incidence states for Lyme disease (Centers for Disease
42 Control and Prevention [CDC], 2017). Patients were eligible if they were at least 18
43 years of age; had an International Classification of Disease code (ICD-9: 088.81 or ICD-
44 10: A69.20) for Lyme disease associated with at least one clinical encounter between
45 2014 and 2017; and an IgG Western blot meeting CDC criteria of five or more positive
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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

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

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

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46 Patients were not involved in the development of the research question, the
47 design, recruitment, or conduct of this study. Results of this study will be disseminated
48 to study participants via letter and disseminated to patients via health system print
49 newsletters and social media outlets.
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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 GMTDP stages (**Table 2**).

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2
3 Participants reported seeking care both within and external to Geisinger for their initial
4 Lyme disease symptoms, but we did not ask in which health care system delays
5
6 occurred.
7
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9 10 **GMTPD Stages**

11 *Appraisal delay*

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14 Participants consistently reported an appraisal delay, a gap between their first
15 symptom and recognition that they were ill (**Table 2**). Some participants attributed this
16 gap to the inconsistent nature of their symptoms. One participant explained,
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21 “I was just having occasional joint achiness where it kind of felt like I slept
22
23 funny on my elbow. It would be sore for a day or two and then it would go away.”
24

25
26 Patients also misattributed symptoms to minor injuries, pre-existing conditions, or
27 the flu. One participant noted, “I also have fibromyalgia, so it’s kind of hard to
28
29 differentiate.”
30
31

32
33 Patients ruled out Lyme disease in the absence of the bull’s-eye rash perceived
34 to be characteristic of Lyme disease, delaying medical attention even in the presence of
35
36 a rash. One participant explained,
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39
40 “And then I got a like this rash on my legs, on my arms, on my back. It was
41
42 really bad. And I didn’t even know about Lyme disease at that time... I mean I
43
44 knew that you’d get a bull’s-eye rash. And it wasn’t that, so I went to the doctor
45
46 probably about... at least three weeks later.”
47
48

49 *Illness delay/behavioral delay*

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51 Generally, once patients decided to seek medical care (illness delay), they acted on
52
53 the decision (behavioral delay). One of the 26 participants noted a gap of five or six
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1
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3 days between deciding he needed medical care and seeking care due to health
4
5 insurance:

6
7
8 “Every hour or so I would take my temperature and it was just going up
9
10 and up... And I didn’t have insurance. And I thought I have to make it to Monday,
11
12 because Monday is when my insurance was going to kick in. I said I have got to
13
14 survive until Monday. I mean I would have went that Wednesday or Thursday
15
16 that I was so sick. I had called somebody I know that’s a nurse and she said, ‘I
17
18 don’t want you to die on me but get in your bed and don’t frickin’ move,... until
19
20 Monday if you can make it.’ So, I, I took the words she said to heart and just
21
22 kind of didn’t move the entire weekend.”
23
24

25
26 While no other patients articulated this gap between deciding to seek care and
27
28 acting on it, health insurance was the most commonly occurring theme regarding the
29
30 delay in deciding whether to seek medical attention for their symptoms (**Table 2**).
31
32

33 *Scheduling delay*

34
35 Scheduling delay did not emerge as a problem for any of the participants. Ten of
36
37 the 26 participants initially sought care for symptoms at an urgent care or emergency
38
39 department setting. Some of these patients noted that they decided to seek medical
40
41 attention at these establishments because of the weekend and evening hours.
42
43

44 *Treatment delay*

45
46
47 When present, delays between the first appointment with a health care provider
48
49 about Lyme disease symptoms and treatment were generally reported to be the result
50
51 of a misdiagnosis (e.g., cellulitis). Nine of the 26 participants (34.6%) reported that they
52
53 were not diagnosed with Lyme disease at their first contact with a medical professional
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2
3 regarding Lyme disease symptoms. Seven of these nine participants (77.8%) reported a
4
5 misdiagnosis that occurred at an urgent care or emergency department setting,
6
7 representing 70% of patients who first sought care in these settings (**Table 2**). One
8
9 participant described this experience,

10
11
12 “No, they [emergency department] didn’t do any blood tests... Kind of
13
14 examined and kind of listened to me. It was very busy that night. I know there
15
16 was 1 or 2 doctors on and they had a bunch of drunks they were taking care of
17
18 and things, so I think they may have missed the boat. ...the nurse tells my wife,
19
20 ‘You know I think you got to watch because,’ I think she said, ‘I think there’s more
21
22 here than what it appears.’ But that was it, and then they discharged me.”
23
24
25

26 **Non-GMTPD themes**

27 *Role of family*

28
29
30 In multiple stages of the GMTPD, the involvement of family prompted action
31
32 leading to treatment of Lyme disease. Most commonly, family members prompted
33
34 patients to call the doctor (reducing illness/behavioral delay). For example:
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36

37
38 “I could no longer read the computer screen. I couldn’t read the paper.
39
40 And she (my wife) said, ‘That’s it, we’re done playing around.’ And I ended up at
41
42 the doctors.”
43

44
45 Another example was:

46
47 “She (my sister) said to me, ‘That (rash) doesn’t look right.’ And I said, ‘Eh,
48
49 it’ll go away in a couple of days.’ So, she told my mom, and my mom called me
50
51 and said, ‘I’m coming up to look at it. I think we should go to the doctor.’ I said,
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1
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3 'Ma, it'll be fine.' She said, 'No, I think we should go.' So..., my sister calls and
4 gets an appointment."
5
6

7
8 Family also played a role in reducing the treatment delay phase, after the patient
9 saw a medical professional. In one instance, a patient was hospitalized for what was
10 originally diagnosed as pain medication dependency. It was not until a family member
11 demanded a transfer to a different hospital that Lyme disease was diagnosed.
12
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14

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16
17 "So, I was there [at the hospital] for three or four days and all of the
18 sudden I developed Bell's palsy. And they did a CAT scan and they determined it
19 was not a stroke. I laid there five more days where they did nothing. My sister
20 and mother came to visit. They would not have recognized me. My face was
21 swollen and droopy. So my sister had me transferred to another hospital. Within
22 hours I was diagnosed with neurological Lyme."
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30 31 *Consequences of delays*

32
33 The original interview guide did not include questions regarding the impact of
34 Lyme disease on work absenteeism/presenteeism or changes in productivity at work or
35 home. However, the detrimental impact of Lyme disease on the ability to work and fulfill
36 caregiving roles emerged as a common theme among participants.
37
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40

41
42 "I couldn't function, and I'm a care-taker for my mother, although she's a
43 good 92 now...She took care of me, but I could not function. I lived on the sofa or
44 in bed. That's how tired I was. If I tried to do a little bit of anything, I would have
45 to get back down, because I couldn't handle it."
46
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51 Another person described a change in his work productivity before getting treated for
52 Lyme disease.
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1
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3 “I’d never sit down at work ever. I have my own machine shop. And I like
4 nobody ever sees me sit. ...like it came to the point where I was sitting and then
5 actually at lunchtime and stuff I would actually lay on the bench.”
6
7
8
9

10 For some of these patients, the impact on work and caregiving persisted after
11 treatment.
12
13

14 “Yeah, yeah, I was off [work] for quite a while between them actually finally
15 determining it was Lyme disease and the treatment and then the post check-up
16 after the treatment to make sure I was fine. Yeah, I was probably off for at least
17 two months, if not more.”
18
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24 A second patient explained:
25

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

45 We conducted the first study, to our knowledge, to explore the experiences
46 associated with the time between onset of symptoms and treatment of Lyme disease,
47 with a specific focus on identifying themes related to belated treatment. Our study
48 identified barriers to timely treatment that have been observed in other disease areas,
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3 as well as barriers specific to Lyme disease. We identified potential knowledge gaps in
4 Lyme disease among patients and medical professionals, including misperceptions
5 about the necessity of a bull's-eye rash. Understanding the conditions that participants
6 perceive contribute to treatment delays can inform strategies that promote prompt
7 treatment of Lyme disease, preventing dissemination of infection and the resulting
8 disease complications.
9

10
11 Application of the GMTPD to Lyme disease was very instructive and showed that
12 Lyme disease generally conformed to the model. The appraisal stage emerged as a
13 distinct and dominant phase, as has been observed when this model has been applied
14 to other diseases (Scott et al., 2012; Smith, Pope, & Botha, 2005; Evans, Ziebland, &
15 McPherson, 2006). We identified three appraisal delay themes: symptom
16 misattribution, intermittent symptoms, and lack of bull's-eye rash. Both the intermittent
17 nature of symptoms as well as the symptom misattribution to less serious or pre-existing
18 conditions has been reported to account for appraisal delays in various cancers,
19 particularly when the early symptoms were commonly occurring non-specific symptoms
20 (e.g. fatigue) (Evans, Chapple, Salisbury, Corrie, & Ziebland, 2014; Brouha, Tromp,
21 Hordijk, Winnubst, & de Leeuw, 2005). Specific to Lyme disease, respondents
22 misattributed the joint pain of Lyme disease to other conditions with joint pain, such as
23 rheumatoid arthritis and fibromyalgia.
24

25
26 Appraisal delays also resulted from a misunderstanding of the characteristic
27 Lyme disease rash, erythema migrans. Specifically, participants reported that they did
28 not suspect Lyme disease if they did not have a rash with central clearing, referred to as
29 a bull's-eye rash. Approximately 20 to 30% of people with Lyme disease do not present
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3 with erythema migrans and among those who do have the rash, only 19% have the
4
5 stereotypical bull's-eye appearance (Tibbles & Edlow, 2007). The impact of the belief in
6
7 the necessity of central clearing on belated treatment is compounded by the diagnostic
8
9 challenges associated with Lyme disease in the absence of the rash. One study
10
11 reported that 54% of patients with Lyme disease who did not have erythema migrans
12
13 were initially misdiagnosed compared to 23% of patients who did have erythema
14
15 migrans (Aucott et al., 2009). Our findings highlight an important knowledge gap among
16
17 patients regarding the skin manifestations of Lyme disease. Patient education
18
19 campaigns that address this issue could reduce the time between infection and
20
21 treatment.
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26 The illness and behavioral delay stages appeared to be most influenced by
27
28 health insurance status. Our findings are consistent with delays attributed to lack of
29
30 health insurance observed in other disease areas. A lack of insurance has been
31
32 associated with longer pre-hospital delays in myocardial infarction (Nguyen, Saczynski,
33
34 Gore, & Goldberg, 2010; Smolderen et al., 2010) and with care-seeking behavior in
35
36 cancer (Rauscher et al., 2010). It is unknown whether the belated treatment due to lack
37
38 of health insurance translate into an increased risk of late Lyme disease among the
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40 uninsured.
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45 Scheduling delay was not a major contributor to belated treatment in our study,
46
47 as nearly half of patients we interviewed sought care at emergency departments or
48
49 urgent care centers, medical settings that typically offer same-day, evening, and
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51 weekend appointments. While the availability of urgent care clinics and emergency
52
53 departments appeared to minimize scheduling delays, the patients who first sought care
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3 at these locations reported more occurrences of misdiagnoses. Thus, the time saved in
4 the scheduling delay stage by seeking care in one of these settings could be
5
6 outweighed by the treatment delays resulting from misdiagnoses in these settings. The
7
8 number of urgent care settings have dramatically increased over the last decade, but
9
10 little is known regarding the quality of care for Lyme disease in these settings (Yee,
11
12
13 Lechner, & Boukus, 2013).
14
15

16
17 Family interventions were identified to decrease the time to treatment in Lyme
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19 disease, consistent with the role of family and friends in belated treatment for cancer
20
21 and cardiovascular disease (Perkins-Porras, Whitehead, Strike, & Steptoe, 2009; Barr,
22
23 McKinley, O'Brien, & Herkes, 2006). Smith and colleagues (2005) reported that, for
24
25 many patients with cancer, friends and family helped with the process of illness
26
27 attribution (Smith et al., 2005) by observing or discussing vague symptoms with
28
29 patients, ultimately making the connection between symptoms and illness that had gone
30
31 unrecognized by the patient. The extent to which family structure, marital status, and
32
33 social support play a role in Lyme disease diagnosis and treatment has not been
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38
39 studied.

40 The impact of Lyme disease on work and caregiving activities emerged as a
41
42 salient theme for participants, impacting patients prior to treatment and, in some cases,
43
44 even after treatment. While costs occurring after a Lyme disease diagnosis have been
45
46 studied (Adrion, Aucott, Lemke, & Weiner, 2015), these studies do not account for the
47
48 time between infection and treatment of disease, likely underestimating costs. Prior
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50 studies that focused on productivity loss and activity limitations in Lyme disease have
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53
54 been confined to individuals reporting symptoms persisting for more than six months
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(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 GMTDP 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

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3 prevention strategies in Lyme disease, a large quantitative study on patients across the
4
5 full spectrum of Lyme disease is needed to both determine how much each phase
6
7 contributes to belated treatment and to quantify the degree to which factors increase
8
9 risk of belated treatment.
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14 **Author contribution:** AH, AR, KM, JA, CH, and BS participated in the design of the
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16 study; AH conducted data collection; AH and RH conducted data analysis; all authors
17
18 participated in the writing of the manuscript.
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For peer review only

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 recalled¹, 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 misdiagnosed³, n (% of misdiagnoses)	
Urgent care/emergency department (both)	7 (77.8)
Primary care provider	4 (44.4)
<ol style="list-style-type: none"> 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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 juttied 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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.

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Manuscripts

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

Annemarie G. Hirsch¹, PhD, MPH; Rachel J. Herman²; Alison Rebman³, MPH;
Katherine Moon⁴, PhD; John Aucott³, 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

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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.

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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

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2
3 infarction, it has not been applied to Lyme disease. Thus, the primary drivers of belated
4
5 treatment in Lyme disease remain unknown.
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8 To identify themes around belated treatment, as well as to evaluate the application of
9
10 the GMTPD to Lyme disease, we interviewed 26 patients with a diagnosis of Lyme
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12 disease to gain insight into their experiences between onset of Lyme disease symptoms
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14 and treatment. Such understanding is critical to informing strategies that would reduce
15
16 time to diagnosis and treatment and prevent late stage Lyme disease.
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21 **METHODS**

22
23 We conducted a qualitative study using in-depth telephone interviews of
24
25 Geisinger patients with a Lyme disease diagnosis to understand what happens between
26
27 the onset of Lyme disease symptoms and treatment. We analyzed interview findings
28
29 through the GMTPD framework. This study was approved by the Geisinger Institutional
30
31 Review Board.
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38 **Study setting and sample**

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40 We identified study participants using the electronic health record (EHR) from
41
42 Geisinger, an integrated health system servicing more than 45 counties in Pennsylvania
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44 and New Jersey, USA, both high-incidence states for Lyme disease.[5] Patients were
45
46 eligible if they were at least 18 years of age; had an International Classification of
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48 Disease code (ICD-9: 088.81 or ICD-10: A69.20) for Lyme disease associated with at
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50 least one clinical encounter between 2014 and 2017; and an IgG Western blot meeting
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52 CDC criteria of five or more positive bands.[6] We used a stratified purposeful sampling
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3 design to identify patients with and without late Lyme disease manifestations: Lyme
4 arthritis (ICD-9: 711.8x; ICD-10: M01.X0); facial palsy (ICD-9: 351.0, 352.9; ICD-10:
5
6 G51.0; G52.9); meningoencephalitis (ICD-9: 320.7; ICD-10: G01); or myocarditis (ICD-
7
8 9: 422.0; ICD-10: I41). To ensure variation in care experiences, we oversampled
9
10 patients diagnosed outside of primary care. We first sent letters to notify 93 patients (47
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12 with late manifestations and 46 without) that they were eligible for the study. Two weeks
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14 later we telephoned patients to schedule a telephone interview. Participants who
15
16 completed an interview received a \$50 gift card. Recruitment continued until data
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18 saturation, the point at which no new information seemed to emerge during coding.[7]
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26 **Data collection**

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28 We conducted in-depth, semi-structured, open-ended telephone interviews
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30 between August and September 2017, each lasting approximately 30 minutes.
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32 Telephone interviews allowed for capture of patient experiences across the large
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34 geographic area served by Geisinger. Geisinger's Institutional Review Board waived the
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36 requirement of written consent after determining that the study posed no more than
37
38 minimal risk of harm to participants. An experienced interviewer (first author AGH)
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40 obtained verbal consent and asked participants to talk about their experience with Lyme
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42 disease, from symptom onset to treatment. The interviewer was a researcher employed
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44 by the health system that treated participants for Lyme disease. To address any
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46 potential concerns participants might have had in describing their care experiences to a
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48 health system employee, the interviewer informed participants that their responses
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50 would not impact the care received at Geisinger and would be kept confidential. The
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3 interviewer then used an interview guide to follow-up on the account that included
4 questions in six primary areas: Lyme disease knowledge; pre-treatment symptoms;
5 care-seeking behavior; diagnosis process; treatment process; and post-treatment
6 symptoms. All interviews were audio-recorded and transcribed verbatim. No additional
7 field notes were recorded. We did not return transcripts to participants for comment or
8 correction.
9

19 **Analysis**

20 We applied a deductive content analysis of interview transcripts, based on the
21 GMTTPD.[8] We applied an iterative coding process to identify themes corresponding to
22 the six primary areas as well as emergent themes. After the first five interviews, one of
23 two coders reviewed the transcripts to develop a preliminary coding framework. A
24 second coder then applied the framework to the same five interviews. The coding team
25 (2 members) discussed findings and reached consensus on an updated coding scheme,
26 revising the scheme as new themes emerged. The coding team also updated the
27 interview guide to incorporate questions around emergent themes for future interviews.
28 In the final phase of analysis, the coders developed higher order categories
29 representing the five delay stages of the GMTTPD. Analysis was conducted using
30 Atlas.ti.7.
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49 **Patient and Public Involvement**

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

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12 Out of the 93 patients to whom we sent a letter, we telephoned 56 patients and
13 reached 33. Of these, 26 (79%) agreed to be interviewed. We stopped recruitment calls
14 after reaching saturation. While the interviewers were intended to be one-on-one, two
15 patients had a spouse with them in the room during the interview. In one case, a spouse
16 joined the call. However, analysis was confined to the information presented by the 26
17 patients.
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26 Slightly more than half of participants were female; 30% had a history of being
27 on Medical Assistance (a surrogate for low family socioeconomic status);^[9] and
28 participants ranged in age from 22 to 70 years (**Table 1**). Half of the participants first
29 sought care for Lyme disease from a primary care provider and 38.5% first went to an
30 urgent care center or emergency department.
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38 Ten participants reported that they had a rash, three of whom described the rash
39 as a bull's-eye. Five of the participants who reported a rash sought care because of the
40 rash. The remaining did not seek care until other symptoms (e.g., fatigue, joint pain)
41 appeared. Two of the five participants who saw a doctor because of the rash were
42 initially misdiagnosed. Eleven participants reported having joint pain, though patients
43 did not specify whether the joint pain was diagnosed as Lyme arthritis. Eight patients
44 reported having Bell's palsy, two patients reported carditis, and one patient reported a
45 diagnosis of Lyme meningitis.
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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 recalled¹, 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 misdiagnosed⁴, 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 GMTDP 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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:

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3 “Every hour or so I would take my temperature and it was just going up
4 and up... And I didn’t have insurance. And I thought I have to make it to Monday,
5 because Monday is when my insurance was going to kick in. I said I have got to
6 survive until Monday. I mean I would have went that Wednesday or Thursday
7 that I was so sick. I had called somebody I know that’s a nurse and she said, ‘I
8 don’t want you to die on me but get in your bed and don’t frickin’ move,... until
9 Monday if you can make it.’ So, I, I took the words she said to heart and just
10 kind of didn’t move the entire weekend.”
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21 While no other patients articulated this gap between deciding to seek care and
22 acting on it, health insurance was the most commonly occurring theme regarding the
23 delay in deciding whether to seek medical attention for their symptoms (**Table 2**).
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30 Scheduling delay

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

45 When present, delays between the first appointment with a health care provider
46 about Lyme disease symptoms and treatment were generally reported to be the result
47 of a misdiagnosis (e.g., cellulitis). Nine of the 26 participants (34.6%) reported that they
48 were not diagnosed with Lyme disease at their first contact with a medical professional
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3 regarding Lyme disease symptoms. Seven of these nine participants (77.8%) reported a
4 misdiagnosis that occurred at an urgent care or emergency department setting,
5
6 representing 70% of patients who first sought care in these settings (**Table 2**). One
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8 participant described this experience,
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11 “No, they [emergency department] didn’t do any blood tests... Kind of
12 examined and kind of listened to me. It was very busy that night. I know there
13 was 1 or 2 doctors on and they had a bunch of drunks they were taking care of
14 and things, so I think they may have missed the boat. ...the nurse tells my wife,
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16 ‘You know I think you got to watch because,’ I think she said, ‘I think there’s more
17 here than what it appears.’ But that was it, and then they discharged me.”
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28 **Non-GMTPD themes**

29 **Role of family**

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31 In multiple stages of the GMTPD, the involvement of family prompted action
32 leading to treatment of Lyme disease. Most commonly, family members prompted
33 patients to call the doctor (reducing illness/behavioral delay). For example:
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38 “I could no longer read the computer screen. I couldn’t read the paper.
39
40 And she (my wife) said, ‘That’s it, we’re done playing around.’ And I ended up at
41
42 the doctors.”
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47 Another example was:

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49 “She (my sister) said to me, ‘That (rash) doesn’t look right.’ And I said, ‘Eh,
50
51 it’ll go away in a couple of days.’ So, she told my mom, and my mom called me
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53 and said, ‘I’m coming up to look at it. I think we should go to the doctor.’ I said,
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3 'Ma, it'll be fine.' She said, 'No, I think we should go.' So..., my sister calls and
4 gets an appointment."
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8 Family also played a role in reducing the treatment delay phase, after the patient
9 saw a medical professional. In one instance, a patient was hospitalized for what was
10 originally diagnosed as pain medication dependency. It was not until a family member
11 demanded a transfer to a different hospital that Lyme disease was diagnosed.
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17 "So, I was there [at the hospital] for three or four days and all of the
18 sudden I developed Bell's palsy. And they did a CAT scan and they determined it
19 was not a stroke. I laid there five more days where they did nothing. My sister
20 and mother came to visit. They would not have recognized me. My face was
21 swollen and droopy. So my sister had me transferred to another hospital. Within
22 hours I was diagnosed with neurological Lyme."
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32 33 Consequences of delays

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35 The original interview guide did not include questions regarding the impact of
36 Lyme disease on work absenteeism/presenteeism or changes in productivity at work or
37 home. However, the detrimental impact of Lyme disease on the ability to work and fulfill
38 caregiving roles emerged as a common theme among participants.
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45 "I couldn't function, and I'm a care-taker for my mother, although she's a
46 good 92 now...She took care of me, but I could not function. I lived on the sofa or
47 in bed. That's how tired I was. If I tried to do a little bit of anything, I would have
48 to get back down, because I couldn't handle it."
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3 Another person described a change in his work productivity before getting treated for
4
5 Lyme disease.
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8 “I’d never sit down at work ever. I have my own machine shop. And I like
9
10 nobody ever sees me sit. ...like it came to the point where I was sitting and then
11
12 actually at lunchtime and stuff I would actually lay on the bench.”
13

14 For some of these patients, the impact on work and caregiving persisted after
15
16 treatment.
17

18
19 “Yeah, yeah, I was off [work] for quite a while between them actually finally
20
21 determining it was Lyme disease and the treatment and then the post check-up
22
23 after the treatment to make sure I was fine. Yeah, I was probably off for at least
24
25 two months, if not more.”
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28 A second patient explained:
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31 “I own my own business, I’ve been in business since 1990. It is definitely
32
33 not the same. I have a hard time spelling words. I mean you got to go in, you got
34
35 to sell yourself, you got to get all the work and, it’s just tough anymore. I just don’t
36
37 have the, it’s hard to put things together, you know what I mean, like on the fly.
38
39 Like with words and everything. You seem to lose that edge and I don’t know
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41 how to explain it. You know and everybody says, ‘Oh you got old,’ but it just like
42
43 changed instantly.”
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49 **DISCUSSION**

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51 We conducted the first study, to our knowledge, to explore the experiences
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53 associated with the time between onset of symptoms and treatment of Lyme disease,
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3 with a specific focus on identifying themes related to belated treatment. Our study
4 identified barriers to timely treatment that have been observed in other disease areas,
5
6 as well as barriers specific to Lyme disease. We identified potential knowledge gaps in
7
8 Lyme disease among patients and medical professionals, including misperceptions
9
10 about the necessity of a bull's-eye rash. Understanding the conditions that participants
11
12 perceive contribute to treatment delays can inform strategies that promote prompt
13
14 treatment of Lyme disease, preventing dissemination of infection and the resulting
15
16 disease complications.
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21 Application of the GMTDPD to Lyme disease was very instructive and showed that
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23 Lyme disease generally conformed to the model. The appraisal stage emerged as a
24
25 distinct and dominant phase, as has been observed when this model has been applied
26
27 to other diseases.[3,10,11] We identified three appraisal delay themes: symptom
28
29 misattribution, intermittent symptoms, and lack of bull's-eye rash. Both the intermittent
30
31 nature of symptoms as well as the symptom misattribution to less serious or pre-existing
32
33 conditions has been reported to account for appraisal delays in various cancers,
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35 particularly when the early symptoms were commonly occurring non-specific symptoms
36
37 (e.g. fatigue).[12,13] Specific to Lyme disease, respondents misattributed the joint pain
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39 of Lyme disease to other conditions with joint pain, such as rheumatoid arthritis and
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41 fibromyalgia.
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47 Appraisal delays also resulted from a misunderstanding of the characteristic
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49 Lyme disease rash, erythema migrans. Specifically, participants reported that they did
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51 not suspect Lyme disease if they did not have a rash with central clearing, referred to as
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53 a bull's-eye rash. Approximately 20 to 30% of people with Lyme disease do not present
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3 with erythema migrans and among those who do have the rash, only 19% have the
4 stereotypical bull's-eye appearance.[14] The impact of the belief in the necessity of
5 central clearing on belated treatment is compounded by the diagnostic challenges
6 associated with Lyme disease in the absence of the rash. One study reported that 54%
7 of patients with Lyme disease who did not have erythema migrans were initially
8 misdiagnosed compared to 23% of patients who did have erythema migrans.[15] Our
9 findings highlight an important knowledge gap among patients regarding the skin
10 manifestations of Lyme disease. Patient education campaigns that address this issue
11 could reduce the time between infection and treatment.
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24 The illness and behavioral delay stages appeared to be most influenced by
25 health insurance status. Our findings are consistent with delays attributed to lack of
26 health insurance observed in other disease areas. A lack of insurance has been
27 associated with longer pre-hospital delays in myocardial infarction[16,17] and with care-
28 seeking behavior in cancer.[18] It is unknown whether the belated treatment due to lack
29 of health insurance translate into an increased risk of late Lyme disease among the
30 uninsured.
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40 Scheduling delay was not a major contributor to belated treatment in our study,
41 as nearly half of patients we interviewed sought care at emergency departments or
42 urgent care centers, medical settings that typically offer same-day, evening, and
43 weekend appointments. While the availability of urgent care clinics and emergency
44 departments appeared to minimize scheduling delays, the patients who first sought care
45 at these locations reported more occurrences of misdiagnoses. Thus, the time saved in
46 the scheduling delay stage by seeking care in one of these settings could be
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3 outweighed by the treatment delays resulting from misdiagnoses in these settings. The
4
5 number of urgent care settings have dramatically increased over the last decade, but
6
7 little is known regarding the quality of care for Lyme disease in these settings.[19]
8
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10 Family interventions were identified to decrease the time to treatment in Lyme
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12 disease, consistent with the role of family and friends in belated treatment for cancer
13
14 and cardiovascular disease.[20,21] Smith and colleagues[10] reported that, for many
15
16 patients with cancer, friends and family helped with the process of illness attribution by
17
18 observing or discussing vague symptoms with patients, ultimately making the
19
20 connection between symptoms and illness that had gone unrecognized by the patient.
21
22 The extent to which family structure, marital status, and social support play a role in
23
24 Lyme disease diagnosis and treatment has not been studied.
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28 The impact of Lyme disease on work and caregiving activities emerged as a
29
30 salient theme for participants, impacting patients prior to treatment and, in some cases,
31
32 even after treatment. While costs occurring after a Lyme disease diagnosis have been
33
34 studied,[22] these studies do not account for the time between infection and treatment
35
36 of disease, likely underestimating costs. Prior studies that focused on productivity loss
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38 and activity limitations in Lyme disease have been confined to individuals reporting
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40 symptoms persisting for more than six months.[23,24] A comprehensive study of
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42 indirect and direct costs across the full spectrum of Lyme disease, before and after
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44 treatment, would give a more complete picture of the individual and population-level
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46 burden of this disease.
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51 To our knowledge, this is the first study to evaluate the application of GMTDP to
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53 Lyme disease. Through the lens of this model we identified distinct phases between
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3 onset of first Lyme disease symptoms and Lyme disease treatment. Our study was
4 conducted in a well-defined sample of participants with a positive IgG Western blot, a
5 lab result present only at least six to eight weeks after Lyme disease infection. Our
6 study had limitations. First, while our eligibility criteria was highly specific for Lyme
7 disease, requiring a positive IgG Western blot, patients may have been excluded as a
8 result of false-negative test results that can occur at all stages disease, but most
9 commonly among patients tested in the first few weeks of infection, when the test is
10 expected to be negative.[6,25,26] Second, while our patients described interactions with
11 health systems beyond Geisinger, all participants were tested for Lyme disease at
12 Geisinger. With more than 44 Geisinger community practice sites and 12 hospital
13 campuses across a large geographic region, there is likely a great deal of diversity in
14 Lyme disease diagnosis and treatment experiences within the health system. However,
15 these findings may not be generalizable to other countries due to differences in factors
16 such as healthcare cost and access. Finally, the objective of this study was not to
17 quantify the extent to which each delay phase contributed to belated treatment in Lyme
18 disease. We identified several explanations for belated treatment of Lyme disease that
19 are intervenable and can be targeted to minimize time to treatment and reduce the
20 burden of Lyme disease on patients and society. To prioritize resources around
21 secondary prevention strategies in Lyme disease, a large quantitative study on patients
22 across the full spectrum of Lyme disease is needed to both determine how much each
23 phase contributes to belated treatment and to quantify the degree to which factors
24 increase risk of belated treatment.
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3 **Author contribution:** AH, AR, KM, JA, CH, and BS participated in the design of the
4 study; AH conducted data collection; AH and RH conducted data analysis; all authors
5 participated in the writing of the manuscript.
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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.

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

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Manuscripts

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

Annemarie G. Hirsch¹, PhD, MPH; Rachel J. Herman²; Alison Rebman³, MPH;
Katherine Moon⁴, PhD; John Aucott³, 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

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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.

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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

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3 infarction, it has not been applied to Lyme disease. Thus, the primary drivers of belated
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5 treatment in Lyme disease remain unknown.
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8 To identify themes around belated treatment, as well as to evaluate the application of
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10 the GMTTPD to Lyme disease, we interviewed 26 patients with a diagnosis of Lyme
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12 disease to gain insight into their experiences between onset of Lyme disease symptoms
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14 and treatment. Such understanding is critical to informing strategies that would reduce
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16 time to diagnosis and treatment and prevent late stage Lyme disease.
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21 **METHODS**

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23 We conducted a qualitative study using in-depth telephone interviews of
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25 Geisinger patients with a Lyme disease diagnosis to understand what happens between
26
27 the onset of Lyme disease symptoms and treatment. We analyzed interview findings
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29 through the GMTTPD framework. This study was approved by the Geisinger Institutional
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31 Review Board.
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38 **Study setting and sample**

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40 We identified study participants using the electronic health record (EHR) from
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42 Geisinger, an integrated health system servicing more than 45 counties in Pennsylvania
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44 and New Jersey, USA, both high-incidence states for Lyme disease.[5] Patients were
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46 eligible if they were at least 18 years of age; had an International Classification of
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48 Disease code (ICD-9: 088.81 or ICD-10: A69.20) for Lyme disease associated with at
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50 least one clinical encounter between 2014 and 2017; and an IgG Western blot meeting
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52 CDC criteria of five or more positive bands.[6] We used a stratified purposeful sampling
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3 design to identify patients with and without late Lyme disease manifestations: Lyme
4 arthritis (ICD-9: 711.8x; ICD-10: M01.X0); facial palsy (ICD-9: 351.0, 352.9; ICD-10:
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6 G51.0; G52.9); meningoencephalitis (ICD-9: 320.7; ICD-10: G01); or myocarditis (ICD-
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8 9: 422.0; ICD-10: I41). To ensure variation in care experiences, we oversampled
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10 patients diagnosed outside of primary care. We first sent letters to notify 93 patients (47
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12 with late manifestations and 46 without) that they were eligible for the study. Two weeks
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14 later we telephoned patients to schedule a telephone interview. Participants who
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16 completed an interview received a \$50 gift card. Recruitment continued until data
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18 saturation, the point at which no new information seemed to emerge during coding.[7]
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26 **Data collection**

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28 We conducted in-depth, semi-structured, open-ended telephone interviews
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30 between August and September 2017, each lasting approximately 30 minutes.
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32 Telephone interviews allowed for capture of patient experiences across the large
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34 geographic area served by Geisinger. Geisinger's Institutional Review Board waived the
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36 requirement of written consent after determining that the study posed no more than
37
38 minimal risk of harm to participants. An experienced interviewer (first author AGH)
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40 obtained verbal consent and asked participants to talk about their experience with Lyme
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42 disease, from symptom onset to treatment. The interviewer was a researcher employed
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44 by the health system that treated participants for Lyme disease. To address any
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46 potential concerns participants might have had in describing their care experiences to a
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48 health system employee, the interviewer informed participants that their responses
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50 would not impact the care received at Geisinger and would be kept confidential. The
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3 interviewer then used an interview guide to follow-up on the account that included
4 questions in six primary areas: Lyme disease knowledge; pre-treatment symptoms;
5 care-seeking behavior; diagnosis process; treatment process; and post-treatment
6 symptoms. All interviews were audio-recorded and transcribed verbatim. No additional
7 field notes were recorded. We did not return transcripts to participants for comment or
8 correction.
9

19 **Analysis**

20 We applied a deductive content analysis of interview transcripts, based on the
21 GMTTPD.[8] We applied an iterative coding process to identify themes corresponding to
22 the six primary areas as well as emergent themes. After the first five interviews, one of
23 two coders reviewed the transcripts to develop a preliminary coding framework. A
24 second coder then applied the framework to the same five interviews. The coding team
25 (2 members) discussed findings and reached consensus on an updated coding scheme,
26 revising the scheme as new themes emerged. The coding team also updated the
27 interview guide to incorporate questions around emergent themes for future interviews.
28 In the final phase of analysis, the coders developed higher order categories
29 representing the five delay stages of the GMTTPD. Analysis was conducted using
30 Atlas.ti.7.
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49 **Patient and Public Involvement**

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

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12 Out of the 93 patients to whom we sent a letter, we telephoned 56 patients and
13 reached 33. Of these, 26 (79%) agreed to be interviewed. We stopped recruitment calls
14 after reaching saturation. While the interviewers were intended to be one-on-one, two
15 patients had a spouse with them in the room during the interview. In one case, a spouse
16 joined the call. However, analysis was confined to the information presented by the 26
17 patients.
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26 Slightly more than half of participants were female; 30% had a history of being
27 on Medical Assistance (a surrogate for low family socioeconomic status);^[9] and
28 participants ranged in age from 22 to 70 years (**Table 1**). Half of the participants first
29 sought care for Lyme disease from a primary care provider and 38.5% first went to an
30 urgent care center or emergency department.
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38 Ten participants reported that they had a rash, three of whom described the rash
39 as a bull's-eye. Five of the participants who reported a rash sought care because of the
40 rash. The remaining did not seek care until other symptoms (e.g., fatigue, joint pain)
41 appeared. Two of the five participants who saw a doctor because of the rash were
42 initially misdiagnosed. Eleven participants reported having joint pain, though patients
43 did not specify whether the joint pain was diagnosed as Lyme arthritis. Eight patients
44 reported having Bell's palsy, two patients reported carditis, and one patient reported a
45 diagnosis of Lyme meningitis.
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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 recalled¹, 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 misdiagnosed⁴, 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 GMTDP 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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 jugged... 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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.

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

11 Appraisal delay

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14 Participants consistently reported an appraisal delay, a gap between their first
15 symptom and recognition that they were ill (**Table 2**). Some participants attributed this
16 gap to the inconsistent nature of their symptoms. One participant explained,
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21 “I was just having occasional joint achiness where it kind of felt like I slept
22 funny on my elbow. It would be sore for a day or two and then it would go away.”
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26 Patients also misattributed symptoms to minor injuries, pre-existing conditions, or
27 the flu. One participant noted, “I also have fibromyalgia, so it’s kind of hard to
28 differentiate.”
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33 Patients ruled out Lyme disease in the absence of the bull’s-eye rash perceived
34 to be characteristic of Lyme disease, delaying medical attention even in the presence of
35 a rash. One participant explained,
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40 “And then I got a like this rash on my legs, on my arms, on my back. It was
41 really bad. And I didn’t even know about Lyme disease at that time... I mean I
42 knew that you’d get a bull’s-eye rash. And it wasn’t that, so I went to the doctor
43 probably about... at least three weeks later.”
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51 Illness delay/behavioral delay

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3 Generally, once patients decided to seek medical care (illness delay), they acted on
4 the decision (behavioral delay). One of the 26 participants noted a gap of five or six
5 days between deciding he needed medical care and seeking care due to health
6 insurance:
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12 “Every hour or so I would take my temperature and it was just going up
13 and up... And I didn’t have insurance. And I thought I have to make it to Monday,
14 because Monday is when my insurance was going to kick in. I said I have got to
15 survive until Monday. I mean I would have went that Wednesday or Thursday
16 that I was so sick. I had called somebody I know that’s a nurse and she said, ‘I
17 don’t want you to die on me but get in your bed and don’t frickin’ move,... until
18 Monday if you can make it.’ So, I, I took the words she said to heart and just
19 kind of didn’t move the entire weekend.”
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31 While no other patients articulated this gap between deciding to seek care and
32 acting on it, health insurance was the most commonly occurring theme regarding the
33 delay in deciding whether to seek medical attention for their symptoms (**Table 2**).
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40 Scheduling delay

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

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3 When present, delays between the first appointment with a health care provider
4 about Lyme disease symptoms and treatment were generally reported to be the result
5 of a misdiagnosis (e.g., cellulitis). Nine of the 26 participants (34.6%) reported that they
6 were not diagnosed with Lyme disease at their first contact with a medical professional
7 regarding Lyme disease symptoms. Seven of these nine participants (77.8%) reported a
8 misdiagnosis that occurred at an urgent care or emergency department setting,
9 representing 70% of patients who first sought care in these settings (**Table 2**). One
10 participant described this experience,
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21 “No, they [emergency department] didn’t do any blood tests... Kind of
22 examined and kind of listened to me. It was very busy that night. I know there
23 was 1 or 2 doctors on and they had a bunch of drunks they were taking care of
24 and things, so I think they may have missed the boat. ...the nurse tells my wife,
25 ‘You know I think you got to watch because,’ I think she said, ‘I think there’s more
26 here than what it appears.’ But that was it, and then they discharged me.”
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38 **Non-GMTPD themes**

39 **Role of family**

40 In multiple stages of the GMTPD, the involvement of family prompted action
41 leading to treatment of Lyme disease. Most commonly, family members prompted
42 patients to call the doctor (reducing illness/behavioral delay). For example:
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49 “I could no longer read the computer screen. I couldn’t read the paper.
50 And she (my wife) said, ‘That’s it, we’re done playing around.’ And I ended up at
51 the doctors.”
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3 Another example was:
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5 “She (my sister) said to me, ‘That (rash) doesn’t look right.’ And I said, ‘Eh,
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7 it’ll go away in a couple of days.’ So, she told my mom, and my mom called me
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9 and said, ‘I’m coming up to look at it. I think we should go to the doctor.’ I said,
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11 ‘Ma, it’ll be fine.’ She said, ‘No, I think we should go.’ So..., my sister calls and
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13 gets an appointment.”
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17 Family also played a role in reducing the treatment delay phase, after the patient
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19 saw a medical professional. In one instance, a patient was hospitalized for what was
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21 originally diagnosed as pain medication dependency. It was not until a family member
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23 demanded a transfer to a different hospital that Lyme disease was diagnosed.
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26 “So, I was there [at the hospital] for three or four days and all of the
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28 sudden I developed Bell’s palsy. And they did a CAT scan and they determined it
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30 was not a stroke. I laid there five more days where they did nothing. My sister
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32 and mother came to visit. They would not have recognized me. My face was
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34 swollen and droopy. So my sister had me transferred to another hospital. Within
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36 hours I was diagnosed with neurological Lyme.”
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42 Consequences of delays

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44 The original interview guide did not include questions regarding the impact of
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46 Lyme disease on work absenteeism/presenteeism or changes in productivity at work or
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48 home. However, the detrimental impact of Lyme disease on the ability to work and fulfill
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50 caregiving roles emerged as a common theme among participants.
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3 “I couldn’t function, and I’m a care-taker for my mother, although she’s a
4 good 92 now...She took care of me, but I could not function. I lived on the sofa or
5 in bed. That’s how tired I was. If I tried to a do a little bit of anything, I would have
6 to get back down, because I couldn’t handle it.”
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12 Another person described a change in his work productivity before getting treated for
13 Lyme disease.
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17 “I’d never sit down at work ever. I have my own machine shop. And I like
18 nobody ever sees me sit. ...like it came to the point where I was sitting and then
19 actually at lunchtime and stuff I would actually lay on the bench.”
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24 For some of these patients, the impact on work and caregiving persisted after
25 treatment.
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28 “Yeah, yeah, I was off [work] for quite a while between them actually finally
29 determining it was Lyme disease and the treatment and then the post check-up
30 after the treatment to make sure I was fine. Yeah, I was probably off for at least
31 two months, if not more.”
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38 A second patient explained:
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40 “I own my own business, I’ve been in business since 1990. It is definitely
41 not the same. I have a hard time spelling words. I mean you got to go in, you got
42 to sell yourself, you got to get all the work and, it’s just tough anymore. I just don’t
43 have the, it’s hard to put things together, you know what I mean, like on the fly.
44 Like with words and everything. You seem to lose that edge and I don’t know
45 how to explain it. You know and everybody says, ‘Oh you got old,’ but it just like
46 changed instantly.”
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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 GMTDPD 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.

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3 Appraisal delays also resulted from a misunderstanding of the characteristic
4 Lyme disease rash, erythema migrans. Specifically, participants reported that they did
5 not suspect Lyme disease if they did not have a rash with central clearing, referred to as
6 a bull's-eye rash. Approximately 20 to 30% of people with Lyme disease do not present
7 with erythema migrans and among those who do have the rash, only 19% have the
8 stereotypical bull's-eye appearance.[14] The impact of the belief in the necessity of
9 central clearing on belated treatment is compounded by the diagnostic challenges
10 associated with Lyme disease in the absence of the rash. One study reported that 54%
11 of patients with Lyme disease who did not have erythema migrans were initially
12 misdiagnosed compared to 23% of patients who did have erythema migrans.[15] Our
13 findings highlight an important knowledge gap among patients regarding the skin
14 manifestations of Lyme disease. Patient education campaigns that address this issue
15 could reduce the time between infection and treatment.
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33 The illness and behavioral delay stages appeared to be most influenced by
34 health insurance status. Our findings are consistent with delays attributed to lack of
35 health insurance observed in other disease areas. A lack of insurance has been
36 associated with longer pre-hospital delays in myocardial infarction[16,17] and with care-
37 seeking behavior in cancer.[18] It is unknown whether the belated treatment due to lack
38 of health insurance translate into an increased risk of late Lyme disease among the
39 uninsured.
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49 Scheduling delay was not a major contributor to belated treatment in our study,
50 as nearly half of patients we interviewed sought care at emergency departments or
51 urgent care centers, medical settings that typically offer same-day, evening, and
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3 weekend appointments. While the availability of urgent care clinics and emergency
4 departments appeared to minimize scheduling delays, the patients who first sought care
5 at these locations reported more occurrences of misdiagnoses. Thus, the time saved in
6 the scheduling delay stage by seeking care in one of these settings could be
7 outweighed by the treatment delays resulting from misdiagnoses in these settings. The
8 number of urgent care settings have dramatically increased over the last decade, but
9 little is known regarding the quality of care for Lyme disease in these settings.[19]

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

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38 The impact of Lyme disease on work and caregiving activities emerged as a
39 salient theme for participants, impacting patients prior to treatment and, in some cases,
40 even after treatment. While costs occurring after a Lyme disease diagnosis have been
41 studied,[22] these studies do not account for the time between infection and treatment
42 of disease, likely underestimating costs. Prior studies that focused on productivity loss
43 and activity limitations in Lyme disease have been confined to individuals reporting
44 symptoms persisting for more than six months.[23,24] A comprehensive study of
45 indirect and direct costs across the full spectrum of Lyme disease, before and after
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3 treatment, would give a more complete picture of the individual and population-level
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5 burden of this disease.
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8 To our knowledge, this is the first study to evaluate the application of GMTPD to
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10 Lyme disease. Through the lens of this model we identified distinct phases between
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12 onset of first Lyme disease symptoms and Lyme disease treatment. Our study was
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14 conducted in a well-defined sample of participants with a positive IgG Western blot, a
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16 lab result present only at least six to eight weeks after Lyme disease infection. Our
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18 study had limitations. First, while our eligibility criteria was highly specific for Lyme
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20 disease, requiring a positive IgG Western blot, patients may have been excluded as a
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22 result of false-negative test results that can occur at all stages disease, but most
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24 commonly among patients tested in the first few weeks of infection, when the test is
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26 expected to be negative.[6,25,26] Second, while our patients described interactions with
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28 health systems beyond Geisinger, all participants were tested for Lyme disease at
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30 Geisinger. With more than 44 Geisinger community practice sites and 12 hospital
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32 campuses across a large geographic region, there is likely a great deal of diversity in
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34 Lyme disease diagnosis and treatment experiences within the health system. However,
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36 these findings may not be generalizable to other countries due to differences in factors
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38 such as healthcare cost and access. Finally, the objective of this study was not to
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40 quantify the extent to which each delay phase contributed to belated treatment in Lyme
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42 disease. We identified several explanations for belated treatment of Lyme disease that
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44 are intervenable and can be targeted to minimize time to treatment and reduce the
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46 burden of Lyme disease on patients and society. To prioritize resources around
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48 secondary prevention strategies in Lyme disease, a large quantitative study on patients
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3 across the full spectrum of Lyme disease is needed to both determine how much each
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5 phase contributes to belated treatment and to quantify the degree to which factors
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7 increase risk of belated treatment.
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12 **Author contribution:** AH, AR, KM, JA, CH, and BS participated in the design of the
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14 study; AH conducted data collection; AH and RH conducted data analysis; all authors
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16 participated in the writing of the manuscript.
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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.