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Consumption of healthcare services and antibiotics in patients with presumed disseminated Lyme borreliosis before and after evaluation of an infectious disease specialist

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ABSTRACT

Our objective was to study the consumption of healthcare services and antibiotics in patients with suspicion of disseminated Lyme borreliosis (LB) before and after consultation of an infectious disease specialist. We evaluated retrospectively all presumed disseminated LB patients ($n = 256$) with a referral to the Department of Infectious Diseases (DID) in Helsinki University Hospital in 2013. Medical records from all healthcare providers in the area were reviewed and the number of physician contacts because of symptoms leading to LB suspicion and antimicrobial purchases were calculated 1 year before and after consultation or treatment at the DID. Patients were divided into three groups according to certainty of LB: unlikely, possible or probable/definite LB. The number of healthcare contacts 1 year before referral was higher among 121 patients with unlikely LB (6; interquartile range [IQR] 3–10), than 65 possible (4; IQR 2.5–7; $p = 0.018$) or 66 probable/definite LB patients (4; IQR 2.8–7; $p = 0.010$). The median number of contacts to healthcare during one year after consultation or treatment was 3 (IQR 0.5–7), 1 (IQR 0–3) and 0.5 (IQR 0–2.3), respectively, with a statistically significant difference between the groups ($p<0.001$). Antibiotics were purchased by 151 (60%) patients one year before referral and by 127 (50%) patients year after consultation or treatment at DID without statistically significant difference between groups with different LB certainty. These antibiotic purchases do not include the treatments prescribed by infectious disease specialists. In the case of 27 patients, an antimicrobial treatment was recommended in the consultation reply. In conclusion, patients with unlikely LB used more healthcare services than patients with possible or probable/definite LB. Antimicrobial consumption was similar between groups of different LB certainty.

Introduction

Lyme borreliosis (LB) is a tick-borne infectious disease affecting most often skin, nervous system and joints (Steere, 1989). LB is endemic in Finland with estimated incidence of 118/100 000 in 2014 (Sajanti et al., 2017). Awareness and public interest in the disease is significant and patients seek treatment from multiple healthcare providers. Overdiagnosis and overtreatment of LB are related to inappropriate use of healthcare services as well as delay of crucial treatment of underlying disease and adverse events because of unnecessary antimicrobial treatments (Goodlet and Fairman, 2018; Reid et al., 1998).

In Finland, erythema migrans (EM) is mainly treated in the primary healthcare both by the public and private sectors. In the Hospital District of Helsinki and Uusimaa with 1.6 million inhabitants, general practitioners (GPs) are guided to refer all patients with a suspicion of disseminated LB to the Department of Infectious Diseases in Helsinki University Hospital.

The aim of this retrospective study was to evaluate the utilization of services in different healthcare providers and antimicrobial treatments in patients with presumed disseminated LB. We also wanted to evaluate how consumption of healthcare services and antibiotics changed after consultation of an infectious disease specialist to improve our guidance to GPs and, also in specialist medical care.

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Methods

We included all adult (≥ 16 years) patients with a referral or consultation due to suspicion of LB to the Department of Infectious Diseases in Helsinki University Hospital from 1st January 2013 to 31st December 2013. The only exclusion criterion was insufficient information for the determination of LB certainty. Medical records of the patients were reviewed from 1st January 2012 to 31st December 2017 regardless of whether the patient was evaluated at the Department of Infectious Diseases or the referral was responded with a written consultation reply. The patients were identified by their unique identity code given to all residents in Finland and used in all healthcare services which enabled reliable follow-up of health records from various providers.

The following information was collected from medical records of Helsinki University Hospital, public healthcare centres, private healthcare clinics, The Finnish Student Health Service and the occupational health service of the patient: age, gender, co-morbidities, history of tick bites and erythema migrans, signs and symptoms of suspected LB, the duration of the symptoms, laboratory results, any antimicrobial treatments between 2012 and 2017 and visits and phone calls to any physician of different healthcare providers related to symptoms leading to LB suspicion . Treatment response to antibiotics, reported by the patient, was collected at the end of the treatment period at the Department of Infectious Diseases and categorised based on the medical records to complete (no sequelae), successful (good response, but the patient has still some symptoms), or partial response (some improvement in symptoms) or treatment failure (no improvement). Specialty healthcare means outpatient or inpatient medical care provided by secondary or tertiary care hospitals.

Table 1
Classification of the patients into groups according to certainty of Lyme borreliosis.

Criteria for probable/definite LB (criteria 1, 2, 3, 4 or 5 fulfilled)
1 Positive *B. burgdorferi* s.l. NAT from CSF, synovial fluid, or skin biopsy together with symptoms suggestive of LB[a]
1 Intrathecal production of *B. burgdorferi* s.l. -specific antibodies and CSF pleocytosis (≥ 5 leukocytes/μl) together with suggestive symptoms of LNB[a] without other obvious reasons
1 Seroconversion[b] of *B. burgdorferi* s.l. and suggestive symptoms of LB[a] without other obvious reasons
1 Markedly[c] positive *B. burgdorferi* s.l. antibody levels in serum, symptoms suggestive of LB[a] without other obvious reason and improvement after antimicrobial therapy[d]
1 Typical EM during the previous three months, symptoms suggestive of LB[a] without other obvious reason and improvement after antimicrobial therapy[d]
Criteria for possible LB (criteria 1 or 2 fulfilled)
1 Symptoms suggestive of LB[a] without other obvious reasons and *B. burgdorferi* s.l. -specific IgG antibodies in serum[e]
1 In the absence of *B. burgdorferi* s.l. -specific antibodies, the duration of symptoms less than two months, specificity of symptoms of LB[a], and response to antimicrobial treatment[d]
Criteria for unlikely LB (criteria 1, 2, or 3 fulfilled)
1 Absence of *B. burgdorferi* s.l. IgG antibodies in the serum or CSF with symptom duration for more than two months
1 Atypical symptoms and failure to respond to antimicrobial treatment
1 Other obvious reasons for symptoms

LB, Lyme borreliosis; NAT, nucleic acid amplification; CSF, cerebrospinal fluid; LNB, Lyme neuroborreliosis; EM, erythema migrans.

[a] Symptoms mentioned in review articles or guidelines were regarded as suggestive of LB (Halperin, 2003; Mygland et al., 2010; Nadelman et al., 1996; Stanek and Strle, 2003; Steere et al., 2016).

[b] Increase in IgG antibodies between concurrently analysed paired serum samples: S-VlsEAbG ≥ 30 units and S-VlsEAbG ≥ 50% units (DiaSorin) together with an increase in S-BorrAbG (Sekisui Virotech).

[c] Sum of numeric values from two EIA tests for IgG (Sekisui Virotech and Diasorin) ≥ 60.

[d] Reported by the patient.

[e] Sum of numeric values from two EIA tests for IgG (Sekisui Virotech and DiaSorin) was ≥ 25.

The patients were categorised into three groups according to certainty of LB after all information was gathered (Table 1). The classification criteria were developed for this and our previous study (Kortela et al., 2021).

Serological and statistical methods are presented in Supplementary material, page 2.

The information of all antimicrobial purchases from pharmacies are registered in Finland and identified to individual level by the unique personal identity code. The data on antimicrobial purchases of all patients were provided by The Social Insurance Institution of Finland. The research board of the Inflammation Center at the Helsinki University Hospital approved the study protocol. The Finnish Institute for Health and Welfare approved the use of patient records of the healthcare providers outside the Helsinki University Hospital. No ethical approval was obtained because of the retrospective nature of the study.

Results

The Department of Infectious Diseases of Helsinki University Hospital received referrals or consultations concerning 256 patients with LB suspicion in 2013. Among all remitted patients, 167 (65%) patients were evaluated at the Department of Infectious Diseases and 89 (35%) referrals were returned with a consultation reply. Patient chart data from publicly funded healthcare services were collected from the regional electronic data base. Additionally, the data concerning every 256 patients were collected from medical records of all those healthcare providers from whom referrals were received (Supplementary material, page 3). However, four minor private healthcare providers, with five patients in this study, were not reached.

After evaluation of medical records of all available healthcare providers, four patients lacked information of symptoms or serological tests rendering classification according to certainty of LB impossible. Thus, 252 patients were classified into groups of unlikely ($n = 121$), possible ($n = 65$) and probable/definite LB ($n = 66$) according to criteria presented in Table 1. Baseline characteristics of these patients, signs and symptoms, performed diagnostic procedures, and diagnostic conclusions with other identified diagnoses are reported previously (Kortela et al., 2021). Comparison of baseline characteristics between patients evaluated at the Department of Infectious Diseases and patients with a written consultation reply are shown in supplementary material (Supplementary Table 1). Nine asymptomatic patients were classified into unlikely LB group. Other patients had at least one sign or symptom. If the referral was responded with a written consultation reply ($n = 89$), advices concerning the diagnostics of LB ($n = 33$), differential diagnostics ($n = 29$), and indications for an antibiotic treatment ($n = 41$) were given.

Contacts to healthcare

The symptoms behind suspicion of LB and subsequent referral to the Department of Infectious Diseases in 252 patients rendered median 5 (IQR 3–8) visits or phone calls to physicians during 1 year prior to referral (Table 2, Supplementary Figure 1). In the groups of unlikely, possible and probable/definite LB, patients had in median 6 (IQR 3–10), 4 (IQR 2.5–7) and 4 (IQR 2.8–7) contacts to a physician one year before referral, respectively, with statistically significant difference between unlikely vs possible ($p = 0.018$) and probable/definite ($p = 0.010$) LB groups. Groups with possible and probable/definite LB did not differ according to number of visits. Contacts to infectious disease specialist and other healthcare providers during the treatment period at the Department of Infectious Diseases are shown in Supplementary Table 4A-B.

The median number of contacts to healthcare due to suspected LB symptoms one year after the consultation or treatment at the Department of Infectious Diseases was 1 (IQR 0–4). It was highest among unlikely LB patients, with 3 (IQR 0.5–7) contacts and significantly lower among possible (1; IQR 0–3, $p<0.001$) and probable/definite LB groups

Table 2
Contacts to healthcare in groups of different Lyme borreliosis certainty during one year before referral to and during one year after consultation or treatment at the Department of Infectious Diseases.

	Unlikely LB*n* = 121n (%)	Number of contacts, median (IQR)[a]	Possible LB*n* = 65n (%)	Number of contacts, median (IQR)[a]	Probable/definite LB*n* = 66n (%)	Number of contacts, median (IQR)[a]	p valueKruskall-Wallis[b]
Contacts to healthcare 1 year before referral							
All Contacts	121 (100%)	6 (3–10)	65 (100%)	4 (3–7)	66 (100%)	4 (3–7)	**0.003**[c]
Specialty healthcare	52 (43%)	3 (1–5)	20 (31%)	2 (1–4)	29 (44%)	2 (1–4)	0.209
Primary public healthcare	63 (52%)	3 (2–5)	34 (52%)	3 (1–4)	29 (44%)	3 (2–5)	0.366
Occupational healthcare	49 (40%)	6 (3–8)	25 (38%)	4 (2–5)	31 (47%)	4 (2–5)	0.581
Private healthcare	41 (34%)	2 (1–4)	19 (29%)	2 (1–4)	13 (20%)	2 (1–3)	0.095
Contacts to healthcare 1 year after consultation reply or treatment at DID							
All contacts	91 (75%)	4 (2–9)	37 (57%)	2 (1–5)	33 (50%)	2 (1–4)	**<0.001**[c]
Specialty healthcare	55 (45%)	3 (2–6)	18 (28%)	2 (1–4)	12 (18%)	1 (1–3)	**<0.001**[c]
Primary public healthcare	38 (31%)	3 (1–4)	12 (18%)	2 (2–3)	11 (17%)	2 (2–3)	**0.030**[c]
Occupational healthcare	29 (24%)	4 (3–7)	12 (18%)	2 (2–4)	9 (14%)	2 (1–3)	0.134
Private healthcare	22 (18%)	2 (1–4)	8 (12%)	1 (1–2)	10 (15%)	2 (1–4)	0.517

LB=Lyme borreliosis; DID=the Department of Infectious Diseases.
Data are number of patients (%) unless otherwise stated. Hospital admissions are shown in Supplementary Table 3.
[a] Columns with number of contacts are included only patients who used the healthcare services of provider in question.
[b] Comparison is made between all patients in the groups of unlikely LB patients, possible LB patients and probable/definite LB patients.
[c] Pairwise comparison between the groups of different LB certainty is shown in Supplementary Table 2.

(0.5; IQR 0–2.3, $p<0.001$) (Table 2 and Supplementary Figure 2).

Patients evaluated at the Department of Infectious Diseases ($n = 167$) had median 1 (IQR 0–4) contact to healthcare one year post treatment because of the symptoms leading to suspicion of LB initially. Patients whose referral was responded with a written consultation reply ($n = 85$) contacted healthcare more often, in median 2 times (IQR 1–5) during one year post referral ($p = 0.001$).

Antimicrobial treatments

The number of patients treated with antimicrobials within two months or one year prior to referral was 83 (33%) or 151 (60%), respectively (Table 3). After symptom onset, antibiotic treatment effective for LB manifestation in question was received by 50 (20%) patients before referral. These antimicrobials were prescribed by GPs or specialists other than infectious disease. During one year after consultation or treatment at the Department of Infectious Diseases, 127 (50%) patients received antimicrobial treatment prescribed by other physicians than infectious disease specialist. In the case of 27 patients, the consultation reply recommended antibiotics if certain diagnostic criteria fulfilled. The most often used antibiotics were doxycycline, amoxicillin, cephalexin, and azithromycin (Supplementary Figures 3–4 and Supplementary Tables 5–6).

Among patients who were evaluated at the Department of Infectious Diseases, 26/167 (16%) had already been treated with antimicrobials effective for LB (Table 3). Nevertheless, 153 (92%) patients evaluated at the Department of Infectious Diseases received a treatment course for LB prescribed by an infectious disease specialist including 13 patients who had already received effective treatment for LB before referral (Supplementary Table 7A-B). Ceftriaxone was the most common first line antibiotic used in 108 patients with a median duration of 21 days (IQR 21–21). Doxycycline was used to treat 102 patients (median duration 35

Table 3
Antimicrobial purchases during one year before the referral and one year after the consultation reply or treatment at the Department of Infectious Diseases in different groups of Lyme borreliosis certainty.

	Unlikely LB*n* = 121n (%)	**Duration in days[a], median (IQR)**	**Possible LB*n* = 65n (%)**	**Duration in days[a], median (IQR)**	**Definite/probable LB*n* = >66n (%)**	**Duration in days[a], median (IQR)**	**p valueKruskall-Wallis test[b]**
AMT before referral							
2 months	40 (33.0%)	15 (10–27)	22 (33.8%)	18 (7–29)	21 (31.8%)	20 (15–25)	0.996
1 year	71 (58.7%)	20 (10–34)	43 (66.2%)	20 (10–36)	37 (56.1%)	18 (7–27)	0.338
effective for LB	31 (25.6%)		10 (15.4%)		9 (13.6%)		0.084
AMT after consultation or treatment at DID							
2 months	28 (23%)	25 (11–41)	11 (17%)	10 (7–22)	11 (17%)	30 (13–48)	0.394
1 year	66 (55%)	25 (7–50)	36 (55%)	10 (7–20)	25 (38%)	20 (10–36)	0.077
AMT in 2012–2017	115 (95%)	72 (36–134)	65 (100%)	81 (47–125)	66 (100%)	70 (46–115)	0.492

LB=Lyme borreliosis; AMT= Antimicrobial treatment; DID=the Department of Infectious Diseases.
Data are number of treated patients (%) unless otherwise stated. Antimicrobial purchases do not include treatments prescribed during the treatment period at DID.
[a] Including only patients treated with antimicrobials.
[b] Including all patients: 121 patients with unlikely LB, 65 patients with possible LB and 66 patients with definite/probable LB.

days, IQR 28–90), of which 30 were first treated with 21 days course of ceftriaxone. Antibiotics were also switched due to adverse events and difficulties in implementing intravenous therapy. Number of patients receiving only one antimicrobial agent was 92 (52 with ceftriaxone, 39 with doxycycline, and 1 with amoxicillin). Of patients with definite/probable LB, a large proportion (92%) had a complete or successful response, whereas only 26% of unlikely LB patients experienced a complete or successful improvement (Table 4, Supplementary Table 8A-B).

Several patients at the Department of Infectious Diseases reported adverse events due to antibiotics (Supplementary Tables 9A-B). Among all patients treated with antimicrobials, 37/153 (24%) reported an adverse event, two of them both to ceftriaxone and doxycycline. An adverse event was reported by 17/51 (33%) patients with unlikely LB, 7/50 (14%) with possible LB and 14/52 (27%) with probable/definite LB, and, on the other hand by 28/108 (26%) patients with ceftriaxone and 11/102 (11%) patients with doxycycline.

In 2012–2017, the median duration of antibiotic treatment in patients with unlikely, possible and definite/probable LB were 66 (IQR 34–129), 81 (IQR 47–128) and 70 (IQR 46–117) days without statistically significant difference between the groups ($p = 0.504$). These antimicrobial treatments include both treatments at the Department of Infectious Diseases and the antimicrobials prescribed by other physicians. The median number of antimicrobial prescriptions was 5 (IQR 3–8), 6 (IQR 4–8) and 4 (IQR 3–7), respectively ($p = 0.458$). In 2012–2017, 46, 23, and 18 patients with unlikely, possible, and probable/definite LB, respectively, received more than 100 days of antimicrobial treatment. No reasons for long-term antibiotic courses such as osteomyelitis or a device-associated infection were noticed.

Eleven patients evaluated at the Department of Infectious Diseases and 7 patients with a written consultation reply sought alternative treatment options (e.g. dietary supplements or intravenous azithromycin treatment for weeks). All these patients were classified as having unlikely LB. Six of these patients reported intravenous azithromycin treatment three times a week. The information about the duration of this treatment was not available. The median duration of all antibiotic treatments in 2012–2017 was 184 (IQR 89–312) days among these 18 patients. No ceftriaxone treatments were given outside the Helsinki University Hospital.

Using negative binomial regression model holding other variables constant, the patients treated at the Department of Infectious Diseases purchased 1.4 times more antibiotics in 2012–2017 than patients, whose referral was returned with written consultation reply (adjusted incidence rate ratio (IRR) 1.408; 95% confidence interval (CI) 1.083 - 1.832). Additionally, patients who sought treatment outside of conventional healthcare purchased 1.6 times more antibiotics in 2012–2017 when compared to patients who remained only within conventional healthcare services (IRR, 1.634, 95% CI, 1.045 - 2.553). Patients with more than three to five symptoms used 1.8 (adjusted IRR, 1.797; 95% CI, 1.052–3.070) and patients with six or more symptoms used 2.5 times more antibiotics in 2012–2017 (IRR, 2.466; 95% CI, 1.392 – 4.369) compared to asymptomatic patients. Unexpectedly, gender, age, depression, fibromyalgia, duration of symptoms or certainty of LB did not affect the consumption of antibiotics in 2012–2017.

Table 4
Reported treatment response to received antimicrobial treatment in patients treated at the Department of Infectious Diseases.

	Unlikely LB*n* = 51	Possible LB*n* = 50	Definite/probable LB*n* = 52
Complete response	6 (12%)	16 (32%)	21 (40%)
Successful response	7 (14%)	14 (28%)	27 (52%)
Partial response	17 (33%)	10 (20%)	2 (4%)
Treatment failure	17 (33%)	4 (8%)	1 (2%)
No information	4 (8%)	6 (12%)	1 (2%)

LB=Lyme borreliosis.
Data are number (%) of patients.
Difference between the groups was statistically significant ($p < 0.001$). Further pairwise comparison revealed statistically significant difference between unlikely vs possible ($p = 0.002$), unlikely vs definite/probable ($p < 0.001$) and possible vs definite/probable ($p = 0.006$) LB patients.

Discussion

In this study, we investigated the consumption of healthcare services and antibiotics in patients with presumed LB. Patients with unlikely LB had more healthcare contacts before and after infectious disease specialist consultation than patients with possible or probable/definite LB. Practically all patients were treated with antimicrobials. There were no statistically significant differences between the patients in the groups of unlikely, possible and probable/definite LB in the overall antibiotic consumption. Every second patient purchased antibiotics during the year after infectious disease consultation which can be considered unexpectedly frequent. However, patients in unlikely LB group only seldom had a response to antibiotic treatment. Additionally, 24% of patients treated with antimicrobials at the Department of Infectious Diseases reported an adverse event.

Patients with a probable/definite LB had in median four contacts to healthcare before referral which suggests that these cases may still be difficult to diagnose. Lyme neuroborreliosis (LNB) with facial palsy leads quite straightforward to the diagnosis due to our practise to test *B. burgdorferi* s.l. serology for every person with facial palsy. Other disseminated LB symptoms may be more challenging to identify.

It is not surprising that patients with unlikely LB continue to consume healthcare services after infectious disease consultation. Even if many of them reported response to antibiotics, their problem was not solved and the symptoms seemed to continue. Many patients with unlikely LB had another disease, which caused the symptoms and required other treatment than antibiotics (Haddad et al., 2019). Our previous study from the same patient cohort demonstrated that 67% of patients with unlikely LB had another condition causing their symptoms (Kortela et al., 2021).

The term Post-Treatment Lyme Disease Syndrome (PTLDS) is often used when subjective LB-related symptoms continue at least six months after appropriate antimicrobial treatment to documented episode of LB (Wormser et al., 2006). Pathogenesis of PTLDS is unclear (Strle and Strle, 2020). It is estimated, that 5 to 15% of treated patients develop PTLDS (Feder et al., 2007). In our study, approximately half of the patients with possible and probable/definite LB contacted healthcare after treatment because of same symptoms. This might also be due to need for a sick leave or additional pain medication or rehabilitation. Also, the PTLDS might be a reason for additional contacts to healthcare in case of some patients. In addition, facial nerve palsy was more common in probable/definite LB group and the specialist of otorhinolaryngology often followed its improvement.

Some patients sought treatment outside of the conventional healthcare services, a phenomenon reported also previously. Dissatisfaction with the conventional healthcare system and support from alternate care givers are reported important reasons for this behavior (Boudreau et al., 2018). All our patients who sought treatment from non-conventional healthcare providers were classified into group of unlikely LB. The typical feature among these patients are frequent antimicrobial treatments without success. Some of the patients believe, that *B. burgdorferi* s.l. can persist after a standard course of 2–4 weeks treatment which leads to longer treatment courses than health authorities recommend (Macauda et al., 2011). As reported previously, long-term antibiotic courses may cause harm and adverse events (Goodlet and Fairman, 2018). Healthcare professionals should find a way to reach these patients better, consider differential diagnostics and refer them to adequate help and rehabilitation.

Antibiotics were used surprisingly widely also in the treatment of patients whose LB suspicion turned out to be unlikely after final evaluation. This might occur because of diagnostic uncertainties or expectations of the patients which may have led to more liberal antibiotic prescribing. This uncertainty may be reflected in the fairly common antibiotic prescribing also by infectious disease specialists. In total, 92% of patients evaluated at the Department of Infectious Diseases received an antibiotic course, which also included majority of those that were categorised as unlikely LB cases. In 2013, outdated prolonged doxycycline therapy after intravenous ceftriaxone treatment was still part of the practice in some situations. In addition, a remarkable proportion of patients treated in our department received ceftriaxone treatment despite the small probability of LB or the fact that doxycycline was supposed to be non-inferior to ceftriaxone in the treatment of early disseminated LB, LNB and Lyme arthritis (Ljøstad et al., 2008; Stanek et al., 2012). The phenomenon of treating LB patients against the guidelines is reported also previously (Lorentzen et al., 2017). This caution underlines the importance of continuing education and self-assessment of practices. Since 2013, the antibiotic prescribing practices have changed in favor of courses of only 14 to 28 days. Following our recent study confirmed the efficacy of doxycycline in the treatment of LNB, our practice has already been to reduce ceftriaxone treatments markedly in LB indication (Kortela et al., 2021).

The retrospective nature of our data collection might lead to inaccuracy in reporting symptoms and signs. We did not have access to all minor healthcare providers, though every major healthcare company in the District of Helsinki and Uusimaa provided the requested information. Because of this, a few patients may have had more healthcare contacts than reported. Every antibiotic prescription is registered in the The Social Insurance Institution of Finland leading to complete data about antimicrobial purchases from pharmacies. Unfortunately, the data about intravenous treatments prescribed by unconventional healthcare providers are incomplete which leads to deficient information about different unconventional treatment options as well as consumption of unconventional health services. We realize that our study setup most likely underestimates their use. Additionally, patients with possible or probable/definite LB were evaluated at the Department of Infectious Diseases more often compared to patients with unlikely LB. This may bias some of the results after the consultation.

In conclusion, healthcare seeking was common both before and after referral to infectious disease specialist in all groups but more common among unlikely LB patients than groups of possible or probable/definite LB patients. Many patients received more antibiotic courses than generally recommended for the treatment. Patients in unlikely LB group only seldom got an antibiotic treatment response.

CRediT authorship contribution statement

Elisa Kortela: Conceptualization, Methodology, Investigation, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Mari J Kanerva:** Conceptualization, Methodology, Writing – review & editing. **Satu Kurkela:** Conceptualization, Methodology, Writing – review & editing. **Jarmo Oksi:** Conceptualization, Methodology, Writing – review & editing. **Mari Koivisto:** Formal analysis, Writing – review & editing. **Asko Järvinen:** Conceptualization, Methodology, Funding acquisition, Writing – review & editing, Supervision.

Declaration of interest

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Supplementary materials

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