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Qualitative Research

When the patient is making the (wrong?) diagnosis: a biographical approach to patients consulting for presumed lyme disease.

Running head : "Lyme Disease : when the patient is making the (wrong?) diagnosis"

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Key messages:

- An original cohort of patients locked in a diagnostic impasse
- Patients with a functional somatic syndrome sometimes associated with more severe chronic conditions tend to attribute their symptoms to Lyme disease
- Personal testimonies on the Internet are often at the origin of the irruption of the LD diagnosis in patient pathways.
- Self-initiated diagnostic investigation increases the degree of belief in the Lyme diagnosis
- GPs, as managers of care pathways, should involve patients in diagnostic process to improve adherence to the diagnosis of functional somatic syndrome.

Abstract

Background: Media coverage of Lyme disease (LD) has led to an increase in consultations for presumed LD in Europe. However, LD is confirmed in only 10-20% of patients, with a significant number remaining in a diagnostic dead-end.

Objectives:
To reach a deeper understanding of how patients themselves contribute to the diagnostic process.
To describe the genesis of the LD hypothesis in care pathways.

Methods: In 2019, 30 patients from a prospective cohort consulting in the infectious diseases department at University Hospital in Marseille for presumed LD were recruited for semi-structured interviews. The inclusion criteria were : suffering from subjective symptoms for 6 months, no clinical or paraclinical argument suggesting current LD. The patients' medical trajectories were collected using a biographical approach.

Results: The diagnosis of Lyme disease was primarily triggered by identification with personal testimonies found on the internet. Most of patients were leading their own diagnostic investigation. The majority of participants were convinced they had LD despite the lack of medical evidence and the scepticism of their referring GP.

Conclusion: GPs should first systematically explore patients' etiologic representations in order to improve adherence to the diagnosis especially in the management of medically unexplained symptoms. Long COVID-19 syndrome challenge offers an opportunity to promote active patient involvement in diagnosis.

Keywords: lyme disease, clinical decision-making, medical history taking, physician-patient relation, primary health care, qualitative research.

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Introduction

Lyme disease (LD), which received little media coverage in France until the end of the 2000s, is now the subject of controversy **(1)**, with virulent public debates. Doctors and patients, represented by associations, demand recognition of a chronic form of the disease associated with non-specific symptoms including pain, asthenia, and concentration disorders **(2)**. In this context, long-term antibiotic treatments are often prescribed despite the absence of proven benefits and may cause serious adverse reactions such as catheter-related blood stream infections, pulmonary embolism, septic thrombophlebitis, and gastrointestinal bleeding, and even death **(3–6)**.

To date, there is no evidence in humans pointing towards the diagnostic criteria of a possible chronic LD **(7)**. However, media coverage of this disease has led to an increase in consultations for presumed LD in France and in Europe **(8,9)**. In France, annual incidence of Lyme Borreliosis is estimated at ≈33,000 cases with strong regional disparities, the incidence being very low around the Mediterranean area, where the vector is rare **(10)**.

Among patients consulting with a suspicion of LD the diagnosis is confirmed for only 10 to 20%, while significant numbers of patients (6-26%) with non-specific symptoms (arthralgia, asthenia, myalgia, headaches) remain undiagnosed at the end of the etiological investigation **(11,12)**.

In a context of easier access to medical information, media coverage of many health issues, and official discourse promoting patient autonomy **(13)**, physicians are now confronted with patients who produce diagnoses and seek to confirm them through health professionals **(14)**.

Using a biographical approach, we sought to describe the diagnostic pathways of patients who initially consulted for a suspicion of LD and for whom this diagnosis was rejected by an infectiologist at the time of their inclusion in the study. We sought to better understand firstly how patients themselves contribute to the diagnostic process; secondly to describe the genesis of the LD hypothesis in care pathways.

Materials and Methods

Study design and sampling

This qualitative single-centre study recruited participants from a regional clinical research program dedicated to tick-borne diseases led by University Hospital Institute (IHU) Méditerranée Infections in Marseille.

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Between 1 May and 30 June 2019, we recruited the first 30 consecutive patients from a prospective cohort consulting in infectious diseases department at the IHU for presumed LD. Patients were eligible to participate if they were 18 years or older, French-speaking, and accepted to sign an informed consent. Clinical and paraclinical inclusion criteria were as follows: presenting non-specific symptoms such as fatigue, difficulty concentrating, joint, muscle or headache pain for at least six months; having a negative Lyme serology (a negative Western Blot test); and no evidence for an organic differential diagnosis. This project was approved by an ethical committee. The reporting of this study follows the COREQ guidelines (**figure S1**).

Interview guide and biographical approach

The semi-structured interviews followed a biographical approach, using an interview guide (**table 1**) covering the history of symptoms and referrals to different medical specialties, detailed diagnostic pathway, including the history of the differential diagnoses, genesis of the LD diagnosis, the patient's prioritisation of the most likely diagnostic hypotheses, and the associated diagnostic degree of certainty (low, medium, high). The interview guide also covered patients' relationships with health professionals, the GPs role in conducting the diagnostic investigation, the impact of symptoms on daily life, and representations of the disease. The biographical approach uses a life-events calendar method (**figure S2**) consisting in a retrospective data collection tool highlighting the chronological order and proximity of events to jointly analyse several aspects of the patient's life **(15)**.

Data collection and analysis

One male investigator (RL) trained in qualitative methods conducted all interviews. The investigator had no direct clinical relationship with any participant. Interviews occurred at the IHU after a scheduled follow-up consultation. The interviews were systematically audio recorded with the patient's consent. The interview was completed by personal documents voluntarily provided by the patient: medical file, diary of the disease, medical diary. We also used the results of the clinical scores from the medical consultation by the infectiologist, established from validated clinal scales: the Montgomery and Asberg Depression Hetero-Assessment Scale (MADRS)**(16)**, the Fibromyalgia Rapid Screening Tool (FIRST)**(17)**, the Fukuda diagnostic criteria for Chronic fatigue syndrome **(18)**.

Interviews were fully transcribed, coded and analysed using the NVivo qualitative data software. Two investigators (RL and CE, the clinician who performed the medical consultation) independently coded all transcripts. All the collected data were systematically cross-checked by triangulation methods. Differences were reconciled by consensus until 100% agreement was reached.

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A clinical profile category was defined according to the patient's prioritisation of symptoms, in decreasing order of their impact on their quality of life. A category "diagnostic investigation coordinator" was coded from the combination of the following elements: the person who asked for serology test, the patient's deliberate search for a "pro-Lyme doctor" to confirm the diagnosis, spontaneous consultation of specialists (without referral by the GP), in particularly with infectious disease specialists, presence/absence of a referring GP (or other referring physician) and finally spontaneous statements during the qualitative interview such as "I conducted the investigation". The category "pro-Lyme doctor" was chosen if the patient reported during their healthcare pathway at least one consultation with a "specialist in chronic LD", whether she/he was a doctor providing non-conventional medicines (naturopath, kinesiologist, nutrition-therapist). The category of "Lyme activist" was attributed to the patient if he/she was a member of an association or an active member of a forum dedicated to LD.

Results

Participants and interview characteristics (Table 2).

We included 30 patients. Participants were mainly women (83%) with an average age of 47.3 years, with a high education level (57% with university degree). Interviews lasted 63 minutes on average (min=44, max=85), 72% of patients had a positive MADRS depression score, 69% had a positive FIRST test for fibromyalgia.,76% of patients met the diagnostic criteria for chronic fatigue syndrome.

We identified 3 main clinical profiles: the "chronic pain" profile (included neuropathic, musculo-articular, diffuse, poorly characterised or headache-type pain) was predominant (50%), followed by the "neurological" profile (27%) (included patients whose main complaint was vertigo or sensitive motor disorders or cognitive complaints) and the "chronic fatigue syndrome" profile (23%) (included patients with predominant fatigue, often associated with concentration difficulties).

The history of the disease was long with an average symptom duration of 8.5 years (median at 5 years).

Diagnostic pathway (table 3)

Recourses to specialists: numerous and unsuccessful

During their diagnostic investigation, the patients had consulted many specialists (often more than 4, including a psychiatrist), they had more often used complementary therapies (naturopathy, homeopathy, kinesiology, etc.) and most of them had consulted a pain-relief centre.

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"The infectiologist doesn't take me seriously as soon as I say the word LYME, immediately closed the file, my neurologist even told me it would have been easier if I had Multiple Sclerosis". (P18)

"The neurologist told me it is psychological, there is nothing more to look for". (P20).

Refusal of somatoform disorder diagnosis

Regarding the history of differential diagnoses, most patients mentioned the diagnosis of fibromyalgia, but rejected it because they considered it as a diagnosis by default and a way of 'psychiatriszing' their symptoms.

"I refuse to be told that all this does not exist, that it is a figment of my imagination ". (P13)

"I'm tired of being told it's all in my head or I'm having a burn out". (P2)

"It's not a comedy, it's not fake". (P9)

"Even if i appreciate the recent recognition of the diagnosis of fibromyalgia it does not explain anything" (P10).

"We send young people to psychiatry when they have Lyme disease" (P14)

Perception of the GPs place in their healthcare pathway

The role of physicians appeared paradoxical: although patients frequently solicited them, physicians were considered powerless, or unwilling, to offer a structured healthcare pathways.

"My doctor doesn't take my complaints seriously and won't help me find the diagnosis anyway". (P13)

"I want to be listened to (...) I want to be in good hands, I want to be directed to the right specialist, but my GP can't deal with me (...) he doesn't know how to handle me". (P9)

"My GP got scared when we talk about Lyme or make fun of it". (P12)

"My GP didn't even take the time to read the medical record (...)I started on a good basis, it's violent to say that it is in my head when there is a documented record! you have to respect the medical record, the work of your colleagues". (P2)

"I am fed up with the diagnosis of vagal discomfort and it bothers me to always see the GP for the same thing". (P16)

"It's hard to get your doctor for a flu, so to follow a complex case". (P22)

The patient's diagnostic activity

In the end, 23 patients reported they had coordinated alone the etiological investigation; for the others, the investigation was carried out by their referring GP.

"I had to search by myself (...) I don't accept that stress explains the whole picture (...) I find myself as I was at the beginning, without diagnosis, without treatment (...) I have to hold on". (P11)

" I have conducted my investigation in a private clinic, they are more attentive and at least they respond to our requests!" (P18)

"Since I have been investigating Lyme Disease, I feel responsible for my own health (...) it's my business after all". (P22)

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"I had to send my blood through a Lyme kit to Germany to confirm that I was infected with a chronic strain (...) some even have to send their blood to the vet!". (P23)

"I took the online Lyme diagnostic test (...) i scored very high". (P12)

"I had to choose a Lyme doctor, a GP specializing in chronic lyme to be heard"! (P29)

"The medical record I had brought with me was quite complete! it took me a lot of time to organize it, you understand". (P16)

On the road to the right diagnosis: the feeling to be at a dead-end

The long diagnostic and therapeutic wandering of these patients contributed to reinforce their feeling of being definitively misunderstood by the medical profession and that their suffering is not taken seriously.

"We bother the doctors to ask questions they can't answer" (P22).

"Lyme, this was a promising lead that we had started to explore and that we dropped, the doctor did not want to go any further and now we are in medical in des-errancy". (P19)

"Fear of being left behind diagnostically". (P1)

"The constant feeling of returning to zero point". (P11)

Genesis of the Lyme Disease diagnostic hypothesis (tables 4)

Nature of exposure to LD risk from the patient's perspective

Most patients did not report a tick bite, but often justified that they may have been bitten without noticing or remembering. For them, the main types of potential exposure to the Lyme vector were the presence of ticks in their environment, contact with traditionally tick-carrying animals, and having spent time in a region perceived to be endemic such as forests in north-eastern France or in the Michigan (USA).

"Do you remember a tick bite"? (Interviewer I)
"No, none". (P1)
"And have you ever seen a tick around"? (I)
"Yes, on my dogs and it happened to me to have to remove ticks". (P1)
"And there were ticks, do you remember?" (I)
"No, but I remember that as a child we used to spend our summers in the forests of the Ukraine, which was known to be a tick reservoir, but I never saw any". (P18)

"I remember seeing a sign warning about tick attacks while in Michigan, I immediately made the connection!". (P6)

"I remember as a child, I was invaded by fleas in a camping (...) we were disinfecting everything with my parents" (P22)

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Origin of the "chronic Lyme" hypothesis

The hypothesis of "chronic LD" in the diagnostic pathway/trajectory of patients was most often triggered by their identification with other patients' testimonies circulating on different media and social networks.

"I stumbled upon forums of patients who suffered from the same symptoms. One thing leading to another, they directed me to therapists who were able to listen to your history and take into consideration the human being that you are". (P2)

"In this TV show, I saw myself in one of the patients who described the same pain and fatigue that no one explains while the diagnosis was obvious". (P4)

"Everything leads back to Lyme when you look for information on the fibromyalgia forums, all the "fibros" encourage you to have a Lyme test". (P4)

Other circumstances triggered diagnostic investigations including presence of false positive Lyme serology during a medical check-up, family or close friends raising the question of LD and finally, this hypothesis evoked by their doctors.

Confirmation of "chronic Lyme" diagnosis

All patients had previously undergone serological testing in a laboratory. Serology was often prescribed at their request, despite the fact that their referring doctors were sceptical about the Lyme hypothesis. For half of patients, the test was negative, for the other half the result was considered a false positive by the clinician according to international and national guidelines.

For patients a negative serology was not sufficient to completely exclude the diagnosis of LD and, in the case of uncertain serologies, patients often gave more weight to the positivity of the ELISA test than to a negative Western Blot reference test.

"My doctor made it clear that he was skeptical when he agreed to prescribe me the serology (...) I was clearly advised not to get involved in Lyme serology (...) he didn't even question it when my first test came back positive! (P17)

"The first test was positive, why question it?" (P12)

Some patients had used laboratories whose techniques were not validated by international standards: private laboratories in Germany or via a self-test kit obtained on the internet, all recommended by the websites of various patient associations.

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In addition, nearly half of patients had received an antibiotic therapy for “chronic Lyme disease”, which was not justified on the basis of current recommendations given the characteristics of the cases.

Secondary benefits of LD diagnosis

Putting one word to many symptoms.

For some patients LD was an additional disease necessary to explain all the symptoms, when the singular clinical picture of the patient does not fit into the general framework of one disease. LD syndrome was clearly a way to explain all the symptoms. LD gives them the opportunity to "frame" their care pathway.

“My symptoms are not typical of multiple sclerosis, especially the pain”. (P26)

“I gladly buy the fibromyalgia diagnosis, but I know I have something else that explains all these symptoms!”. (P4)

“With Lyme I finally understand what is happening to me (...) and where I am going”(P6)

Denial of a severe diagnosed comorbidity

LD perceived as an additional disease could sometimes plays a role of a distractor: invoking Lyme rather than thinking that the symptoms were the expression of a decompensation or an aggravation of a severe chronic pathology (multiple sclerosis, heart failure, ankylosing spondylitis) for which the diagnosis had already been established and accepted by the patient.*”I know deep down that I have Multiple Sclerosis but I am afraid of its evolution. I prefer to have a phony disease like Lyme”.* (P30)

A curable disease

When patients are told all the time "it's in your head’, the infectious etiology was often more guilt-reducing and offers the prospect of a potentially curable. LD diagnoses were clearly perceived, as a hope for recovery.

“Fibromyalgia is useless it is not curable! My rheumatologist also wants a diagnosis that we can treat!”. (P17)

“After all these years it's good to make people understand that it's not our fault”. (P9).

“A tick bite can happen to anyone”(P21)

High level of belief in Lyme disease

The majority of patients stated that they believed the diagnosis of LD to be the main explanation for their symptoms

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and considered this diagnosis to be highly certain.

"I am convinced that I have an unrecognized chronic Lyme". (P28)

"I know I have lyme because the antibiotics worked". (P23)

"After searching for other diagnoses: I only see this".(P4)

"My hand to cut that it is indeed the Lyme Disease". (P21)

"For me, Lyme diagnosis is written in black and white so I don't allow anyone to discuss it". (P2)

Discussion

When patients make the diagnosis

Our study shows important role of narratives from other patients on social networks or in the media. These narratives are particularly valued by patients in situations marked by their perception of the lack of satisfactory diagnostic proposal from doctors. The general public refers to this type of information source much more often, to the detriment of more "objective" and official sources **(13,19,20)**. This is in line with the results of a qualitative survey performed in Connecticut (USA), which reported that patients with LD placed greater trust in the experiences of close relatives who had contracted Lyme disease than in information disseminated by health professionals and health authorities **(21)**. Numerous studies indicate personal testimonials play an important part on how people form opinions about health issues such as vaccination **(19)**.

Most of patients managed to convince their GP to prescribe a Lyme serology test, illustrating that the medical decision is no longer monopolised by doctors. This reflects the contemporary role of patients claiming the legitimacy of a diagnosis based on their own experience **(22)**. Studies recently described that diagnostic work was more particularly exercised by patients when physicians are unable to elucidate the causes of their disorders than when they are, with patients taking charge of the entire sequence from self-diagnosis to self-prescribing **(14,23–25)**. Moreover, patients can nowadays find online tools (diagnostic self-questionnaire) promoted by patient groups to back up their hypotheses. Finally self-initiated diagnostic investigation increased the degree of belief in the diagnosis of Lyme.

A diagnosis set in advance

One of the striking findings of our study is the high degree of belief in the diagnosis of LD, despite the absence of objective biological evidence usually accepted by the medical profession. The "Lyme activist" patient profile,

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and/or an encounter with a "pro-Lyme doctor" concerned a minority of the healthcare pathways described in this study and cannot by itself explain this high level of conviction.

The attribution of symptoms to a well-identified external cause (a bacterium) is frequent in the literature on LD and more generally on somatoform disorders. The infectious origin is often more guilt-reducing for patients and offers the prospect of a possible cure **(26–28)**.

Moreover, the higher level of certainty about the LD hypothesis in patients leading their own diagnostic pathway suggests they had a pre-established etiological scenario and were seeking to put together the different elements of the medical puzzle to support it. In cognitive psychology, this phenomenon is known as "confirmation bias": human beings tend to seek, value, and recall information that confirms or supports their previous personal beliefs **(20)**. Such bias clearly exacerbates false belief entrapment and isolation of the patient in the care pathway.

Another trap for patients was to feel deeply? the powerlessness of health professionals to provide them with satisfactory answers to their suffering. In some cases, they felt that their suffering was being denied **(20)**. Even though these patients may have mental health problems, they experienced the psychiatric framing as a form of violence.

Disappointment with science and scientific controversies

The current controversies over the chronic form of LD remind us of the strength of the population's contemporary disenchantment with science **(13,29)**. Both the general population and the medical community are disappointed in modern science, which generates a multitude of highly specialised, fragmented, temporary, and often contradictory results, especially in the biomedical field. This is especially the case in the French context of the Lyme controversy. In 2018, French scientific societies and the National Academy of Medicine refused to approve the recommendations on LD published by the Haute Autorité de Santé, a French government agency**(**. Indeed, French scientific societies (including French College of General Practitioners) did not recognise the new clinical entity new (created under pressure from patient associations) called "symptom/polymorphic syndrome persisting after a possible tick bite" arguing that the term was not based on scientific evidence and opened the door to over-diagnosis and inappropriate antibiotic prescriptions **(38)**.

Strengths and limitations

 doi:10.20944/preprints202205.0350.v3

The originality of this study lies in the population studied which consists of patients who have reached a diagnostic dead-end. There are very few studies on the care pathways of such patients.

To our knowledge, this study was also the first to apply a biographical approach to the diagnostic trajectories of patients consulting in infectious disease wards for a suspected LD. It allowed for the joint analysis of contextualised self-reported data and clinical data from medical records. The interviews, by focusing on the overlap between life, medical and clinical events, highlighted the three dimensions at work in any care pathway: biology, biography and social context **(33)**.

As for any qualitative study, it is important to be cautious about generalizing these results. In addition, convenient sampling method introduces motivation bias into the study in particular to over-select patients who are more reflective and engaged in their care pathway. However our sample was relatively diversified with a patient profile quite similar to the rest of the cohort of patients coming to consult for presumed LD. Patients with a "Lyme activist" profile were marginal in our sample. In addition our sample size (n=30) was the largest to date among the international qualitative research published on the subject **(26,27,34–36)**.

Comparison with existing literature

A previous qualitative study involving 13 patients in the Savoy region of France reported similar results regarding the role of the internet and the media in patients' care pathways and in triggering their suspicion of chronic LD **(26)**. However, the method of recruitment through a patient association led to an over-representation of 'activist' patients, who were more likely to support conspiracy theories, who were explicitly reported to be in conflict with the medical profession, and who had been "exposed to Lyme doctors". Other international qualitative studies on the subject focused only on the experience and impact of the disease in patients' daily life **(27,34,35)**.

Conclusions

GP's role proposes concrete solutions to improve the quality of life of these patients. With LD, the stakes have shifted to the diagnostic field. The clinician's ability to listen to patients' disease history rarely includes consideration of their diagnostic experience(14). Opposing the doctor as the sole custodian of the medical diagnosis, to patients reduced to the subjectivity of their symptoms, runs the risk of diagnostic dead-ends or parallel diagnostic pathways. Dissatisfaction with the medical diagnosis is the classic explanation for the use of alternative medicine

 doi:10.20944/preprints202205.0350.v3

(37,38). Finally, the empowerment of patients in the diagnostic process suggests that doctors in France in particular are insufficiently trained to deal with functional somatic syndrome **(20)**.

"Inductive foraging" **(25)** could be a relevant strategy to involve patient in the diagnostic process: at the beginning of the consultations, allow time for the patient to freely reveal the reasons for consultation and the diagnoses they think of. While the patients actively present their complaints, the general practitioners listen and take up the elements of their presentation (in the spirit of the motivational interview approach). We think this patient-centred care approach is likely to improve adherence to the functional somatic syndrome diagnosis and the therapeutic alliance. We are probably already facing a similar challenge with the recognition of patients with subjective symptoms in the context of a Long Covid for whom studies show a significant alteration in quality of life **(39,40).**

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Ethical approval: The study was conducted in accordance with the Declaration of Helsinki and approved by was approved by an ethical committee (French Committee for the Protection of Persons, authorisation No. 2019 T3-10)**.** Written Informed consent was obtained from all subjects involved in the study.

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Table 1. Interview guide for biographic interviews

Themes	Questions
Introductory remark	We are interested in knowing your care history, particularly the history of diagnoses related to the symptoms that led you to consult at the IHU but also how you experienced this journey, and the role of the doctors who accompanied you. There is no right or wrong answer. Please do not feel like you have to answer in a certain way. The questions are also NOT specific about you, meaning all questions are hypothetical.
Clinical history and impact	1) What do you do in life? (career, family, education) 2) Symptom onset, clinical history / specific dates 3) if you had to prioritize symptoms in the way they most impact your daily life What would be the first? the following in the order? What impact have these symptoms had on your professional life? your entourage? are you currently on sick leave? 4) Are there any particular life events that you would like to talk about that may have had an impact on your symptoms? 5) If you had to prioritize the probable diagnoses that best explain all of your symptoms, which would you place first? which ones would you place next? 6) For this diagnosis that you placed first: how confident/certainty do you have in your answer? low (I am not sure)/ medium (50-50%), high (I am convinced) 7) For what reasons do you think of this diagnosis mentioned first? (let speak freely ++)
Genesis of the Lyme Hypothesis	1) Have you been exposed or even bitten by a tick? If so, can you tell us about the treatment/diagnosis that took place? Erythema Migrans? 2) When did you first hear about Lyme disease? 3) In what situations do you think you have been possibly exposed to the disease? 3) Under what circumstances has the hypothesis of Lyme disease been raised to explain your health problems? Who first brought it up or thought of it? (let the person speak freely if it comes up spontaneously) 4) Do you have an attending physician, or specialist doctor who regularly follows you for these symptoms? Have you discussed it with him/her? What did your doctor think about it? Has he or she encouraged you in this diagnostic process? 5) Have you used a Lyme diagnostic questionnaire on the internet? What was the result? 6) Did you do the serology? at the request of the doctor? 7) In which laboratory did you perform it? What was the result? 8) Have you received prolonged antibiotic therapy for chronic Lyme? Who prescribed it to you? Have you felt any improvement?
Care pathway	1) Let's go back over the history of the symptoms, can you give a precise account (chronology) of the doctors you have used in this context? 2) Who referred you to the IHU? 3) Did you consult a psychiatrist, for example? pain-centre? 4) Have you been hospitalized for these health problems? 5) Can we list all the diagnoses that have been mentioned by the doctors? 6) Did you have recourse to alternative medicine? (to be explained)

 doi:10.20944/preprints202205.0350.v3

	7) Finally, have you met with professionals who are "specialists" in Lyme disease? 8) Do you regularly visit forums dedicated to Lyme disease? or are you a member of a patient association? 9) Generally speaking, have you felt that your doctors have listened enough to you about these health problems? How would you characterize the relationship with your GP?

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Table 2. Social and clinical characteristics of the 30 patients interviewed Between 1 May and 30 June 2019

Category	No.
Age, mean (SD), y	47.3
Female sex	25
Living in a couple	23
Educational level	
< Secondary school education	7
Secondary school education	6
≥ Tertiary education	17
Professional situation	
Active employment	22
Unemployed	3
Retired	4
Disability	1
Currently on sick leave	17
Geographical origin[a]	
Provence-Alpes Côte d'Azur	28
Clinical profile[a]	
Chronic pain[b]	15
Neurological symptoms[c]	8
Chronic fatigue syndrome[d]	7
Average duration of symptoms [min-max], y	8.5 [0.5-54]
Had an average duration of symptoms ≥ 5 years	15

[a] The clinical profile was defined according to patient's prioritisation of symptoms, in decreasing order of their impact on their quality of life.
[b] The "chronic pain" category included neuropathic, musculo-articular, diffuse, poorly characterised or headache-type pain.
[c] The "neurological profile" category included patients whose main complaint was vertigo or sensitive motor disorders or cognitive complaints.
[d] The "chronic fatigue syndrome" category included patients with predominant fatigue, often associated with concentration difficulties.

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Table 3. Characteristics of the diagnostic pathways of the 30 patients consulting for presumed LD

Pathway characteristics	No.
Average no. of specialties used in relation to the history of symptoms (excluding infectiology and psychiatry)	3.7
Referral to > 5 medical specialists in relation to the history of symptoms (excluding infectiology and psychiatry)	10
Referral to a psychiatrist in relation to the history of symptoms	15
Use of alternative medicine in relation to their symptoms	18
Patients treated in a pain-treatment centre	14
Fibromyalgia: diagnosis evoked by a doctor	23
Refusal of "psychiatrisation of their symptoms"	21
Main diagnostic pathway coordinator (typological approach)	
Primary care physician	4
Referring physician (other specialties)	3
Patient	23

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Table 4. Genesis of the Lyme Disease diagnostic hypothesis for the 30 patients

Clinical and medical events	Number of Patients
Reported tick bite	8
Nature of exposure from the patient's perspective (other than a tick bite)	22
Observed presence of ticks in their environment	6
History of unidentified insects bites	4
Contact with traditionally tick-carrying animals	5
Tick-bite episode in the entourage	2
Endemic region	5
Confirmed history of erythema migrans	3
Origin of the "chronic Lyme" hypothesis	
Identification with clinical narratives (TV, media, internet)	14
Physician	5
Entourage	5
Medical check-up	6
Lyme serology performed in private laboratories	30
Results of Lyme serology test	
negative	16
false-positive[a]	14
Serology performed in a non-approved laboratory	8
Internet diagnostic self-questionnaire	15
Received "anti-chronic Lyme disease" antibiotic treatment	14
Pro-Lyme Doctor intervention during their diagnostic pathway	8
Members of a pro-Lyme association ("Lyme disease activists")	3
Have requested and obtained a doctor's prescription for a Lyme disease serological test	17
Referring physician's position on the Lyme hypothesis	
Pro-active	5
Neutral	14
Sceptical	9
Absent	2
Patient's diagnostic hypotheses ranking	
Lyme disease hypothesis rank 1st	24
The degree of certainty associated with the diagnoses among patients ranking Lyme hypothesis first	
High degree of certainty	13
Moderate-low degree of certainty	11

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Supplement 1.

COREQ (COnsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	8
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	8
Occupation	3	What was their occupation at the time of the study?	8
Gender	4	Was the researcher male or female?	8
Experience and training	5	What experience or training did the researcher have?	8
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	8
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	Supplements
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	N/A
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	7-8
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	7
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	7
Sample size	12	How many participants were in the study?	7
Non-participation	13	How many people refused to participate or dropped out? Reasons?	N/A
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	8
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	8
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	9
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	7
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?	6
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	8
Field notes	20	Were field notes made during and/or after the inter view or focus group?	8
Duration	21	What was the duration of the inter views or focus group?	8
Data saturation	22	Was data saturation discussed?	N/A
Transcripts returned	23	Were transcripts returned to participants for comment and/or	N/A

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Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			
Data analysis			
Number of data coders	24	How many data coders coded the data?	8
Description of the coding tree	25	Did authors provide a description of the coding tree?	8/9
Derivation of themes	26	Were themes identified in advance or derived from the data?	8
Software	27	What software, if applicable, was used to manage the data?	8
Participant checking	28	Did participants provide feedback on the findings?	N/A
Reporting			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	N/A
Data and findings consistent	30	Was there consistency between the data presented and the findings?	9-10-11
Clarity of major themes	31	Were major themes clearly presented in the findings?	9-10-11
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	9-10-11

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.

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Supplement 2. Live-events calendar