Lyme Disease Training and Knowledge Translation Resources Available to Canadian Healthcare Professionals: A Gray Literature Review

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Abstract

Introduction: Lyme Disease (LD) is the most common tick-borne disease in North America. With the number of cases increasing yearly, Canadian healthcare professionals (HCP) rely on up-to-date and evidence-informed guidelines, instruction, and resources to effectively prevent, diagnose, and treat Lyme disease (LD). This review is the first of its kind to examine gray literature and analyze the diversity of recommendations provided to Canadian HCP about the prevention, diagnosis, and treatment of Lyme disease. Methods: A gray literature review consisting of 4 search strategies was conducted to retrieve materials targeted to Canadian HCP. Searches within targeted websites, targeted Google searches, and gray literature databases, and consultation with content experts were done to look for continuing medical education (CME) events, clinical flow charts, webinars, videos, and reference documents that discussed the prevention, diagnosis, and treatment of Lyme disease. Results: A total of 115 resources were included in this study. Recommendations surrounding prevention strategies were less varied between materials, whereas diagnosis and treatment recommendations were more varied. Our findings suggest that Canadian HCP are met with varying and sometimes contradictory recommendations for diagnosing and treating LD. Conclusions: Due to the increasing incidence of LD in Canada, there is a greater need for resource consistency. Providing this consistency may help mitigate LD burden, standardize approaches to prevention, diagnosis and treatment, and improve patient outcomes.

Keywords

diagnosis, gray literature, Lyme disease, medical education, treatment

Introduction

Lyme disease (LD) is an infectious tick-borne disease caused by bacteria strains of *Borrelia burgdorferi* sensu lato complex. In North America, LD is commonly transmitted through infected ticks belonging to the *Ixodes scapularis* or *Ixodes pacificus* species.1,2 The number of LD cases in Canada has increased 10-fold between 2009 and 2018.3 The impact of LD has not been felt equally across Canada, with some provinces seeing much higher infection numbers than other provinces and/or territories.3 However, all healthcare professionals need to have access to evidence-based protocols regardless of the LD infection rates in their area, due to travel-based infections.

Symptoms of LD are typically characterized with disease progression across 3 stages; early localized, early disseminated, and late disseminated.4 The initial stage of the disease, early localized LD, is generally associated with symptoms such as headaches, fatigue, fevers, and muscle pain often with an erythema migrans rash.5 Early disseminated LD symptoms can include multiple cutaneous rashes, joint pain, fatigue, cardiac (eg, palpitations, atrioventricular block) and neurological symptoms (eg, facial palsy, headache).5,6 Late disseminated LD symptoms are often characterized as including worsening joint pain and/or arthritis, and cardiac and neurological symptoms (eg, encephalitis, chronic meningitis).5,6 In some patients, those

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ongoing research investigating the basis for HCP LD pre-
HCP messaging consistency and inconsistency to inform
and treatment. The goal of our work is to establish areas of
pathic practitioners) regarding LD prevention, diagnosis,
and treatment. Recent 2 Canadian studies found vary-
ing information and recommendations presented on provin-
cial public health websites14 as well as patient groups, and
provincial and federal government websites.15 The present
study extends the work of these studies.

Materials and Methods

Our preliminary gray literature review was completed in
May 2020, and secondary revisions were conducted when
disabling symptoms have been shown to persist after antibi-
otic treatment and this stage has been termed post-treatment
LD syndrome (PTLDS).79 There is another group of indi-
viduals who have been diagnosed or self-diagnosed with
chronic Lyme disease (CLD). While there is no singularly
agreed upon definition of chronic Lyme disease, these are
individuals with real and debilitating symptoms that fit
PTLD, but have not been previously diagnosed with LD.10,11

Current preventative practices for LD include personal
protective behaviors as well as landscape preventative mea-
urses. Depending on the symptoms, LD is generally diag-
nosed using a combination of a clinical assessment, history
of potential exposure to ticks, and/or serology testing.12,13
Reducing the risk of LD disease progression requires
prompt and accurate diagnosis and effective LD treatment.
With the increasing burden of LD in certain regions of
Canada, there is a need for consistent and evidence-based
guidance for Canada healthcare professionals (HCP).

Public health units, professional organizations, and pro-
vincial and federal governments use their websites to share
information and recommendations for the prevention, diag-
nosis, and treatment of various health conditions and public
health concerns. Recently, 2 Canadian studies found vary-
ing information and recommendations presented on provin-
cial public health websites14 as well as patient groups, and
provincial and federal government websites.15 The present
study extends the work of these studies.

Table 1. Inclusion/Exclusion Criteria.

| Inclusion criteria                                                                 | Exclusion criteria                                                                 |
|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| Workshop, webinar/video, podcast, reference document, clinical flow chart, CPD/CME event, guidelines, or training seminar (with/without accreditation) relating to Lyme disease. | Materials not available to Canadian HCPs. Conference presentations, research seminars, poster presentations, newsletters, abstracts. |
| Intended for healthcare professionals (HCPs) within the context of practice (preventing, diagnosing, and treating LD). | Intended solely for personal use and information (community facing messaging). |
| Must be accessible to Canadians HCPs (eg, can be international source, if Canadian HCPs have access). | Training specific to students (medical, nursing, pharmacy) or residents. |
| Within the last ten years (≥2010). English and/or French. | Primary research findings (eg, epidemiology of LD, microbiology/biochemistry of LD, surveillance of LD). |

The process for systematically collecting gray literature
was divided into 4 steps based on a framework developed
by Godin et al17 and included: (1) targeted website searches,
(2) Google searches, (3) targeted database searches, and (4)
consultations with content experts (eg, LD patient advoca-
tes, clinical, patient and community, academic, and/or
political members of the Canadian Lyme Disease Research
Network). We used a broad set of search terms (Table 2)
that were adapted for each website/database. The first 100
returned search results from each step were reviewed for
relevancy. If a resource was incomplete (eg, a resource
listed a date and time of a webinar, but not a recording of
the webinar) a note was made to follow up and attempt to
retrieve the missing materials. If materials could not be
acquired, the document was excluded from the study. All formal searches were conducted between May 14th, 2020 and May 19th, 2020.

We also contacted content experts to identify knowledge translation and or educational materials. Clinical, patient and community, academic, and/or political members of the Canadian Lyme Disease Research Network were contacted with a survey asking them the following information: their profession, their experience with Lyme disease in their profession, their geographic location (within Canada), and any links to training materials they have used if applicable. The survey was created using Qualtrics and distributed via email. Each resource provided by content experts was reviewed for eligibility.

After duplicates were removed from within and across search strategies, each document/resource was reviewed by 2 blinded and independent reviewers (S.S., V.A.) for eligibility. Similar to a full systematic review each document was reviewed in full to assess eligibility. Discussion between the reviewers occurred when there was a disagreement or an “unclear” opinion regarding any of the documents. When required, a third reviewer was brought into discussions (A.C.B.).

**Data Extraction**

A deductive coding approach was used to analyze the documents and was completed using NVivo. Top and mid-level codes were pre-defined to address known themes: early localized LD, early disseminated LD, late LD, PTLD, CLD (top levels) and etiology, prevention, diagnosis, and treatment (mid-level codes). Subsequent level themes were developed with an iterative approach as coding progressed. Transcripts of webinars and other videos were obtained from YouTube’s transcription option. If this was not possible, they were transcribed by our research team (V.A., S.S.). French language documents and webinars were translated into English.

Resources were characterized using Case Classifications in NVivo and included: country of publication, date of publication, province (where relevant), type of document (knowledge translation, continuing professional development, etc.), and estimates of LD activity based on case counts in the region where a document originated. The estimates of LD infections were used to label regions of Canada into 4 groups: no cases, low endemic area (regions with small number of cases), moderate endemic area, and high endemic area (see Table 3). The number of LD cases was chosen over incidence rate (LD cases per unit of population) for 3 reasons: (1) provinces with large populations also have large urban areas that are less likely to be exposed to ticks, (2) some provinces with smaller populations can also have relatively higher densities of populations living within tick areas, and (3) the incidence of LD cases can be diluted in large populations living in urban areas. Documents retrieved from the Canadian federal government or other Canadian national organizations were labeled under “national” and those retrieved from international sources were labeled under “international”, regardless of the level of LD within those countries. This approach to international documents was chosen as it is unclear how the information would influence the clinical decision making of doctors in different regions of Canada.

**Results**

The initial search yielded 914 resources across all 4 search strategies (Figure 1). Duplicate resources were removed from within each search method, yielding a remaining 286 resources. Duplicates were then removed from between search strategies, yielding a remaining 242 materials. These 242 documents were then reviewed for eligibility and 127 materials were excluded at this stage. Reasons for exclusion included having inaccessible or incomplete materials,
Figure 1. PRISMA diagram. The diagram outlines the flow of search findings from each of the 4 search strategies, removal of duplicates within and across search strategies, and retention of documents after screening.

$s$, refers to the number of databases, websites, etc. that were searched. $n$, refers to the number of documents returned.
materials were primarily for patients and/or families, or were published before 2010. In total, 115 resources were included in this review. A total of 128 documents were coded within the NVivo file because some resources had to be broken up and coded using multiple files (e.g., a single website might have 2 webinars).

A total of 128 documents were identified and classified. Of the 128 documents, 86 documents were from different Canadian provinces, 10 from the Canadian national level, and 32 documents came from international sources. The largest number of provincial documents came from the province of Ontario \( (n=25) \), followed by Quebec \( (n=22) \). No documents were retrieved from the provinces of Saskatchewan, Prince Edward Island, Yukon, or Nunavut. Of the provincial documents, most \( (n=82) \) came from high endemic regions, 3 from low endemic regions, and 1 from region with no reported cases. Additionally, the majority of documents \( (n=72) \) were published within between 2019 and 2020 (see Figure 2).

**Prevention**

We examined the documents to see what strategies are recommended to prevent LD. Thirty-eight documents discussed some aspect of prevention. Discussed prevention strategies included personal protective measures \( (82\%) \), proper removal of a tick \( (56\%) \), landscape management \( (15\%) \), checking pets \( (9\%) \), and management of deer population \( (6\%) \) (see Table 4). Personal protective measures included: avoiding tick infested areas, wearing long pants and sleeves, using bug repellent with DEET, wearing light colors, and removing ticks immediately. Documents recommending prevention strategies came from regions within Canada with no officially reported cases of LD, low and high numbers of cases, as well as from national and international sources. The largest number of documents \( (50\%) \) came from high-endemic areas and the fewest came from regions with no cases \( (3\%) \). Most resources \( (61\%) \) were published in the 2019 and 2020.

Twenty-six documents included details on the attachment time needed for a tick to transmit LD causing bacteria to its human (Table 5). Twelve \( (46\%) \) of those documents reported that it took a minimum of 24 h after a tick bites its host for LD causing bacteria to be transmitted. Six \( (23\%) \) of the documents reported less that 24 h and another 6 \( (23\%) \) reported that it took a minimum of 36 to 48 h. Most of the documents came from high endemic regions of Canada. The publication dates ranged from 2013 to 2020.

Thirty-one documents reported clinical criteria for offering a patient antibiotic prophylaxis treatment for a tick bite (Table 6). Fifteen documents \( (48\%) \) reported that patients must meet 4 criteria: the tick was a black legged tick, the tick was removed \(<72\) h ago, the patient must have been bitten in a high endemic area, and the tick was attached for \(>36\) h. Eight documents \( (26\%) \) reported the same 3 initial criteria, but that the tick was attached for \(>24\) h.

**Diagnosis**

Twenty-nine documents provided a reference for the incubation period after a tick bite. All 29 documents referenced overlapping windows of time of between 1 and 32 days (data not shown).

**Symptoms of early localized LD.** Sixty documents discussed the symptoms of early localized (EL) Lyme disease (see Table 7). Six categories of symptoms were reported for early localized LD: cutaneous, joint pain/arthritis, myalgia,
Table 4. Recommended Prevention Strategies (n = 38 documents).

| Mechanism                                | Prevention document count | Endemic level | Region      | Publication date |
|------------------------------------------|---------------------------|---------------|-------------|------------------|
| Personal protective measures*            | 32                        | No cases = 1  | Natl = 5    | 2013 = 1         |
|                                          |                           | Low = 1       | Intl = 10   | 2014 = 5         |
|                                          |                           | High = 15     |             | 2016 = 3         |
|                                          |                           |               |             | 2017 = 3         |
| Checking pets to protect humans          | 3                         | No cases = 1  | No data     | 2017 = 1         |
| Landscape management                     | 4                         | High = 2      | Natl = 1    | 2013 = 1         |
|                                          |                           |               | Intl = 1    | 2018 = 1         |
| Management of deer population            | 2                         | High = 1      | Intl = 1    | 2020 = 2         |
| Proper removal of a tick                 | 23                        | Low = 1       | Natl = 4    | 2013 = 1         |
|                                          |                           | High = 8      | Intl = 10   | 2017 = 1         |
|                                          |                           |               |             | 2018 = 5         |

*Avoid tick infested areas (e.g., wooded areas), wear long pants/sleeves, wear light colors (to help spot ticks), use bug repellent with DEET, remove ticks immediately.

Table 5. Attachment Time Needed for Bacteria to Move From Tick to Host (n = 26 documents).

| Time frame          | Document count | Endemic level | Region | Date      |
|---------------------|----------------|---------------|--------|-----------|
| Less than 24 h      | 6              | High = 5      | Intl   | 2013 = 2  |
|                     |                |               |        | 2019 = 2  |
| A minimum of 24 h   | 12             | High = 8      | Natl   | 2016 = 1  |
|                     |                |               | Intl   | 2017 = 1  |
|                     |                |               |        | 2020 = 4  |
| A minimum of 24-48 h| 3              | High = 2      | Intl   | 2016 = 1  |
|                     |                |               |        | 2020 = 1  |
| A minimum of 36-48 h| 6              | High = 5      | Natl   | 2013 = 2  |
|                     |                |               |        | 2018 = 1  |
| A minimum of 36-72 h| 1              | Low = 1       | No data| 2018 = 1  |
| A minimum of 48 h   | 2              | High = 2      | No data| 2013 = 1  |
|                     |                |               |        | 2014 = 1  |

Table 6. Clinical Criteria for Offering Prophylaxis Antibiotic Treatment (n = 31 documents).

| Criteria                         | Document count | Endemic level | Region | Date      |
|----------------------------------|----------------|---------------|--------|-----------|
| Must meet four criteria: tick was a black legged tick, was removed less than 72 h ago, patient must have been bitten in high endemic area, AND tick was attached for 24-36 h. | 2              | High = 2      | No data| 2017 = 1  |
|                                  |                |               |        | 2019 = 1  |
| Must meet four criteria: black legged tick, tick was removed less than 72 h ago, patient must have been bitten in high endemic area, AND tick attached for MORE than 24 h. | 8              | High = 7      | Natl   | 2014 = 2  |
|                                  |                |               |        | 2019 = 4  |
|                                  |                |               |        | 2020 = 2  |
| Must meet four criteria: black legged tick, tick was removed less than 72 h ago, patient must have been bitten in high endemic area, AND tick attached for more than 36 h. | 15             | Low = 1       | Natl   | 2013 = 1  |
|                                  |                | High = 7      | Intl   | 2014 = 1  |
|                                  |                |               |        | 2018 = 2  |
|                                  |                |               |        | 2019 = 2  |
|                                  |                |               |        | 2020 = 5  |
|                                  |                |               |        | 2017 = 2  |
| Anyone with black legged tick bite | 1              | No data       | Intl   | 2020 = 1  |
| Based on prevalence of LD in area | 2              | High = 2      | No data| 2016 = 1  |
|                                  |                |               |        | 2019 = 1  |
| Routine Prophylaxis not recommended. | 9              | High = 5      | Natl   | 2013 = 1  |
|                                  |                |               | Intl   | 2014 = 1  |
|                                  |                |               |        | 2016 = 1  |
|                                  |                |               |        | 2019 = 1  |
|                                  |                |               |        | 2020 = 4  |
Table 7. Symptoms Associated With Early Localized and Early Disseminated Stages of LD.

| Stage                              | Symptoms | Cardiac | Cognitive | Cutaneous | Joint pain/ | Myalgias | Neurological | Ocular | Systemic |
|------------------------------------|----------|---------|-----------|-----------|-------------|----------|--------------|--------|----------|
| Early localized (n = 60 documents about EL symptoms) |          |         |           |           |             |          |              |        |          |
| Document count                     | No data  | No data | 56 (93%)  | 27 (45%)  | 22 (37%)    | 4 (7%)   | 1 (2%)       | 39 (65%)|          |
| Regional endemic level             | No data  | No data | Low = 3   | Low = 2   | Low = 2    | N/A      | N/A          | N/A    | No cases = 1 |
| National or international sources  | No data  | No data | Natl = 8  | Natl = 4  | Natl = 3   | Intl = 4  | Intl = 1     | Intl = 6| No cases = 1 |
| Date                               | No data  | No data | 2013 = 2  | 2014 = 1  | 2014 = 1   | 2018 = 1  | 2020 = 1     | 2014 = 3|          |
|                                    |          |         | 2014 = 4  | 2015 = 1  | 2015 = 1   | 2019 = 2  |              | 2015 = 2|          |
|                                    |          |         | 2015 = 2  | 2016 = 2  | 2016 = 2   | 2020 = 1  |              | 2016 = 2|          |
|                                    |          |         | 2016 = 4  | 2017 = 2  | 2017 = 2   | 2020 = 1  |              | 2017 = 3|          |
|                                    |          |         | 2017 = 5  | 2018 = 2  | 2018 = 2   | 2020 = 1  |              | 2018 = 4|          |
|                                    |          |         | 2018 = 4  | 2019 = 9  | 2019 = 6   |          |              | 2019 = 12|          |
|                                    |          |         | 2019 = 20 | 2020 = 10 | 2020 = 8   |          |              | 2020 = 13|          |
|                                    |          |         | 2020 = 15 |          |           |          |              |        |          |
| Early disseminated (n = 46 documents about ED symptoms) |          |         |            |           |             | 40 (87%) | 10 (22%)     | 20 (43%)|          |
| Document count                     | 39 (85%) | 3 (7%)  | 35 (76%)  | 28 (61%)  | 8 (17%)    |          |              |        |          |
| Regional endemic level             | No cases = 1 | Low = 1 | Low = 1   | Low = 1   | High = 6   | No cases = 1 | Low = 1 | Low = 1 | No cases = 1 |
| National or international sources  | Natl = 6 | Intl = 4 | Natl = 5  | Intl = 4  | Intl = 2   | Natl = 6  | Intl = 4 | Intl = 3 | Natl = 1   |
| Date                               | 2013 = 1 | 2013 = 1 | 2013 = 2  | 2013 = 1  | 2013 = 1   | 2013 = 1  | 2018 = 1 | Intl = 4 | No cases = 1 |
|                                    | 2014 = 5 | 2014 = 4 | 2014 = 4  | 2018 = 1  | 2014 = 4   | 2019 = 2  | 2017 = 1 | 2018 = 7 | No cases = 1 |
|                                    | 2015 = 1 | 2015 = 1 | 2019 = 3  | 2015 = 1  | 2015 = 1   | 2015 = 1  | 2019 = 9 | 2019 = 12| No cases = 1 |
|                                    | 2016 = 4 | 2016 = 4 | 2020 = 3  | 2020 = 3  | 2016 = 3   | 2016 = 3  | 2019 = 9 | 2019 = 12| No cases = 1 |
|                                    | 2017 = 2 | 2017 = 2 | 2017 = 2  | 2020 = 3  | 2017 = 2   | 2017 = 2  | 2019 = 9 | 2020 = 8 | No cases = 1 |
|                                    | 2018 = 3 | 2018 = 3 | 2018 = 3  | 2018 = 3  | 2018 = 4   | 2018 = 4  | 2018 = 8 | 2020 = 8 | No cases = 1 |
|                                    | 2019 = 14| 2019 = 6 | 2019 = 6  | 2019 = 14 | 2019 = 14 | 2019 = 14 | 2020 = 8 | 2020 = 8 | No cases = 1 |
|                                    | 2020 = 9 | 2020 = 8 | 2020 = 8  | 2020 = 10 | 2020 = 10 | 2020 = 10 | 2020 = 8 | 2020 = 8 | No cases = 1 |
neurological, ocular, and systemic symptoms. These categories of symptoms were based on the individual symptoms listed within and across documents (see Supplemental Appendix 1 for a complete list of reported EL symptoms).

Symptoms of early disseminated LD. Forty-six documents discussed the symptoms of early disseminated (ED) Lyme disease (see Table 7). Eight categories of symptoms were reported for early disseminated LD: cardiac, cognitive, cutaneous, joint pain/arthrits, musculoskeletal (MSK), neurological, ocular, and systemic symptoms. These categories of symptoms were based on the individual symptoms listed within and across documents (see Supplemental Appendix 2 for a complete list of reported ED symptoms).

Neurological (87%), cardiac (85%), and cutaneous symptoms (76%) were most commonly reported, followed by joint pain/arthrits (61%) and systemic symptoms (43%). Most documents were published in high endemic areas. These documents were published between 2013 and 2020, with most documents being published in recent years.

Symptoms of late disseminated LD. Forty-four documents discussed the symptoms of late disseminated (LD) Lyme Disease (see Table 8). Eight categories of symptoms were reported for late LD: cardiac, cognitive, cutaneous, joint pain/arthrits, myalgias, neurological, ocular, and systemic symptoms. These categories of symptoms were based on the individual symptoms listed within and across documents (see Supplemental Appendix 3 for a complete list of reported LD symptoms).

Joint pain/arthrits (98%) and neurological symptoms (82%) were most commonly reported, and most documents were published in high endemic areas. These documents were published between 2013 and 2020, which most document being published in the later years.

Symptoms of post treatment Lyme disease. Nineteen documents discussed the symptoms of Post Treatment Lyme Disease (PTLD) (see Table 8). Seven categories of symptoms were reported for PTLD: cardiac, cognitive, joint pain/arthrits, musculoskeletal (MSK), neurological, ocular, and systemic symptoms. These categories of symptoms were based on the individual symptoms listed within and across documents (see Supplemental Appendix 4 for a complete list of reported PTLD symptoms).

Systemic symptoms (89%) and cognitive (79%) symptoms were most commonly reported however, 1 resource published in 2019 in a high endemic region also listed gastrointestinal and reproductive symptoms as symptoms of PTLD. Most documents were published in high endemic areas, between 2013 and 2020.

Diagnostic criteria of early localized. Thirty-eight documents discussed the diagnostic criteria for early localized Lyme disease (see Table 9). The reported criteria included: ‘diagnosis is clinical’, ‘diagnosis is clinical supported by potential exposure’, ‘diagnosis is based on clinical presentation and supported by serology’, and ‘serology is not recommended’. The criteria ‘serology is not recommended’ was most commonly mentioned (66%), and most documents were published in high endemic areas. The documents were published between 2013 and 2020, with most published in recent years.

Diagnostic criteria of late disseminated Lyme disease. Twenty-two documents discussed the diagnostic criteria for late disseminated Lyme Disease (see Table 9). The reported criteria included: some conditions should prompt questions about potential tick exposure (18%) and diagnosis is based on clinical presentation and positive serology (86%). The documents were published between 2013 and 2020, with most of them being published in recent years.

Diagnostic criteria of early disseminated. Twenty documents discussed the diagnostic criteria for early disseminated Lyme Disease (see Table 9). The reported criteria included: some conditions should prompt questions about potential tick exposure (9%) and diagnosis is based on clinical presentation and positive serology (91%). Diagnosis is based on clinical presentation and positive serology, and serology is effective were mentioned the most, and most documents were published in high endemic areas. The documents were published between 2013 and 2020.

Average onset of late disseminated LD. Twenty documents provided estimates of the average onset of late disseminated LD after initial tick bite (see Table 10). These estimates ranged from “less than 3 months,” through to “months to years” post tick bite. The most common estimate was “months to years” (40%), followed by “weeks to months” (30%). The majority of these documents were published between 2018 and 2020.

Average onset of PTLD. Eight documents provided an estimated prevalence of PTLD (see Table 11). The estimated prevalence ranges included: 10% to 20%, 10% to 15%, and 10% of individuals who have received treatment for LD. Only documents published in high endemic areas and at the national level included estimates of PTLD prevalence. The documents were published between 2014 and 2020.

Eight documents provided the reported prevalence of PTLD (See Table 12). The reported prevalence included: months to years after initial treatment and 6 months after...
### Table 8. Symptoms Associated With Late Disseminated and PTLD.

| Stage                                    | Document count | Cardiac | Cognitive | Cutaneous | Joint pain/arthritis | Myalgias | Neurological | Ocular | Systemic |
|------------------------------------------|----------------|---------|-----------|-----------|----------------------|----------|--------------|--------|----------|
| Late disseminated Lyme disease (n = 44 documents about LD symptoms) | Document count | 23 (52%) | 26 (59%) | 4 (9%)    | 43 (98%)             | 2 (5%)   | 36 (82%)     | 2 (5%) | 6 (14%)  |
| Regional endemic level                   |                | No cases = 1 | Low = 2 | High = 10 | No cases = 1 | High = 18 | No cases = 1 | High = 2 | Low = 1 |
|                                          |                | Low = 1   |           |           | Low = 2             | High = 28 | No cases = 1 | High = 22 | Low = 1 |
| Nati or international sources            | Nati = 4       | Nati = 3  | Natl = 6  | Intl = 3  | Natl = 6  | Intl = 1  | Natl = 5  | N/A    | Intl = 2 |
| Date                                     | 2014 = 2       | 2013 = 1  | 2018 = 1  | 2013 = 1  | 2016 = 1  | 2013 = 1  | 2019 = 1  | 2018 = 2 |
|                                          | 2015 = 1       | 2014 = 3  | 2020 = 3  | 2019 = 1  | 2019 = 1  | 2019 = 1  | 2020 = 1  | 2019 = 3 |
|                                          | 2016 = 2       | 2015 = 1  | 2015 = 1  | 2016 = 2  | 2016 = 2  | 2016 = 2  | 2016 = 2  | 2016 = 2 |
|                                          | 2017 = 2       | 2016 = 1  | 2016 = 3  | 2017 = 3  | 2017 = 3  | 2017 = 3  | 2017 = 3  | 2017 = 3 |
|                                          | 2018 = 2       | 2017 = 2  | 2017 = 3  | 2018 = 3  | 2018 = 3  | 2018 = 3  | 2018 = 3  | 2018 = 3 |
|                                          | 2019 = 4       | 2018 = 3  | 2019 = 3  | 2019 = 6  | 2019 = 11 | 2019 = 11 | 2019 = 11 | 2019 = 11 |
|                                          | 2020 = 10      | 2019 = 8  | 2020 = 12 | 2017 = 1  | 2017 = 2  | 2017 = 1  | 2017 = 2  | 2017 = 2 |
|                                          | 2020 = 7       | 2020 = 12 |           |           |           |           |           |        |
| Post treatment Lyme disease* (n = 19 documents about PTLD symptoms) | Document count | 1 (5%)    | 15 (79%)  | No data   | No data   | No data   | No data   | No data | 17 (89%) |
| Regional endemic level                   | High = 1       | No cases = 1 | No cases = 1 | No cases = 1 | No cases = 1 | No cases = 1 | No cases = 1 | No cases = 1 |
|                                          | Low = 1        | Low = 1   | Low = 1   | Low = 1   | Low = 1   | Low = 1   | Low = 1   | Low = 1   |
|                                          | High = 11      | High = 6  | High = 5  | High = 5  | High = 5  | High = 5  | High = 5  | High = 5  |
| Nati or international sources            | N/A            | Nati = 1  | No Data   | Intl = 4  | Nati = 1  | Intl = 6  | N/A      | Nati = 1  |
| Date                                     | 2019 = 1       | 2014 = 2  | 2019 = 2  | 2019 = 2  | 2016 = 1  | 2015 = 1  | 2019 = 1  | 2013 = 1  |
|                                          | 2014 = 2       | 2019 = 4  | 2017 = 4  | 2017 = 4  | 2017 = 1  | 2017 = 2  | 2014 = 2  | 2019 = 4  |
|                                          | 2016 = 2       | 2020 = 3  | 2018 = 1  | 2018 = 1  | 2018 = 1  | 2018 = 2  | 2016 = 2  | 2019 = 4  |
|                                          | 2017 = 1       | 2019 = 1  | 2019 = 3  | 2019 = 1  | 2019 = 1  | 2019 = 1  | 2017 = 3  | 2019 = 4  |
|                                          | 2020 = 3       | 2020 = 1  | 2020 = 1  | 2020 = 4  | 2020 = 1  | 2020 = 4  | 2020 = 3  | 2020 = 3  |

*One document from a high endemic region and published in 2019 also listed reproductive and gastrointestinal symptoms as symptoms of PTLD.
| Stage | Metric | Diagnosis is clinical | Diagnosis is clinical supported by potential exposure | Some conditions should prompt questions about potential tick exposure | Diagnosis is based on clinical presentation and supported by serology | Serology is NOT recommended |
|-------|--------|-----------------------|-----------------------------------------------------|------------------------------------------------------------|---------------------------------------------------------------|-----------------------------|
| Early localized Lyme disease (n = 38 documents) | Document count | 11 (29%) | 10 (26%) | No data | 11 (29%) | 25 (66%) |
| | Endemic level | High = 5 | Low = 1 | No data | Low = 1 | Low = 1 |
| | Natl or Intl | Natl = 2 | Intl = 2 | No data | Intl = 1 | Intl = 6 |
| | Date | 2014 = 1, 2016 = 2, 2017 = 1 | 2016 = 2, 2019 = 2 | No data | 2013 = 3, 2016 = 1, 2017 = 1 | 2013 = 1, 2017 = 2 |
| Early disseminated Lyme disease (n = 22 documents) | Document count | No data | No data | 4 (18%) | 19 (86%) | No data |
| | Endemic level | No data | No data | High = 2 | Low = 1 | No data |
| | Natl or Intl | No data | No data | Intl = 2 | Intl = 1 | No data |
| | Date | No data | No data | 2017 = 1 | 2013 = 1 | No data |
| Late disseminated Lyme disease (n = 22 documents) | Document count | No data | No data | 2 (9%) | 20 (91%) | No data |
| | Endemic level | No data | No data | No data | Low = 1 | No data |
| | Natl or Intl | No data | No data | Intl = 2 | Intl = 13 | No data |
| | Date | No data | No data | 2019 = 2 | 2013 = 1 | No data |
treatment. Most documents published in high endemic areas and at the national level included the average onset time of symptoms of PTLD. The documents were published between 2014 and 2020.

Whereas there were thirteen documents that described the symptoms associated with PTLD (Table 8), only a few discussed how PTLD is diagnosed. One document from a high endemic area described how a PTLD diagnosis requires a previous confirmed diagnosis of Lyme disease that was treated properly.21 Other documents from high endemic and a national source described the need for prolonged and debilitating symptoms.10

**Treatment**

**Prophylactic treatment.** Twenty nine documents included specific details on what antibiotics should be used as prophylactic treatment (Table 13). Most documents (79%) recommended a single, 200mg dose of doxycycline while only 2 documents (7%) recommended a 20-day course of doxycycline. None of the documents published in Canada recommended a 20-day course. Canadian documents recommending a single dose of doxycycline came from low and high endemic areas as well as at the national level. Canadian documents were published between 2013 and 2020, with most published between 2018 and 2020.

**Treatment during pregnancy.** Fourteen documents discussed antibiotic options during pregnancy (Table 14). Most documents (86%) reported that Doxycycline was contraindicated during pregnancy, while 3 documents from high endemic areas reported that a single dose of Doxycycline was safe during pregnancy. Five documents recommended other antibiotic options for treating LD.

**Treatment recommendations based on symptoms.** Adult antibiotic treatment recommendations were also examined (Table 15). Antibiotic treatment recommendations were generally made based on the symptoms of the presenting patient. Across early localized, early disseminated, and late disseminated LD, we found that symptoms for treatment were categorized into “Arthritis or Joint Pain,” “Cardiac,” “Cutaneous,” and “Neurological.” Oral antibiotic options generally included: Doxycycline, Amoxicillin, and Cefuroxime and intravenous (IV) antibiotic options included: Ceftriaxone, Cefotaxime, and Penicillin. A list

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**Table 10. Average Onset of Late Disseminated LD (n=20).**

| Average Onset | Document count (%) | Endemic level | Region | Date |
|---------------|--------------------|---------------|--------|------|
| More than 4 to 6 weeks, but less than 3 months | 1 (5) | No data | Natl = 1 | 2015 = 1 |
| >3 months | 4 (20) | High = 2 | Natl = 1 | 2019 = 1 | 2019 = 3 |
| Weeks to months | 6 (30) | Low = 1 | No data | 2018 = 1 | 2019 = 5 |
| 6 months | 2 (10) | Low = 1 | No data | 2018 = 1 | 2019 = 1 |
| Months to years | 8 (40) | High = 1 | Intl = 1 | 2013 = 1 | 2019 = 3 |

**Table 11. Reported Prevalence of PTLD (n=8).**

| Estimated prevalence | Document count (%) | Endemic level | Region | Date |
|----------------------|--------------------|---------------|--------|------|
| 10%-20% | 5 (63) | High = 4 | Natl = 1 | 2014 = 2 | 2019 = 1 |
| 10%-15% | 2 (25) | High = 1 | Natl = 1 | 2015 = 1 | 2019 = 1 |
| 10% | 1 (13) | High = 1 | No data | 2019 = 1 |

**Table 12. Average Onset Time of Symptoms of PTLD (n=8).**

| Onset of symptoms | Document count (%) | Endemic level | Region | Date |
|-------------------|--------------------|---------------|--------|------|
| Months to years after initial treatment | 5 (6) | Low = 1 | Natl = 2 | 2015 = 1 | 2018 = 1 |
| 6 months after initial treatment | 3 (38) | High = 3 | No data | 2014 = 1 | 2019 = 2 |
or grouping of antibiotic recommendations means that documents included 2 or more of those options in their recommendations.

**Treatment recommendations for children.** Twenty-two documents provided antibiotic treatment recommendations for children diagnosed with LD (Table 16). Thirteen of those documents (59%) recommended against the use of Doxycycline in young children (<8 years of age), whereas 8 (36%) indicated that Doxycycline is safe in children of all ages. Additionally, 3 documents (14%) indicated that Doxycycline was safe for short durations in young children. All documents indicating that Doxycycline is safe in young children (or at least in short durations) were published since 2019, whereas documents indicating that it is not safe were published between 2013 and 2020.

**Discussion**

We found recommendations for the prevention, diagnosis, and treatment of all stages of LD that varied by specificity and consistency. When analyzing the recommendations for the prevention of LD, the recommendations were generally consistent across documents and provinces. Out of the 38 documents that mentioned a preventive measure, 84% discussed personal protective measures including avoiding tick infested areas, wearing long and light-colored clothes, and using insect repellent with DEET. However, we found that the recommendations for diagnosis and treatment were often inconsistent and at times lacked specificity. For example, recommendations regarding the diagnosis of LD varied across resources and there was conflicting advice regarding the usefulness of serology. Additionally, treatment recommendations across documents were at times conflicting. For example, while the majority of Canadian documents indicated that Doxycycline is contraindicated during pregnancy, 3 resources from high endemic areas indicated that a single dose of Doxycycline was safe during pregnancy.

There are conflicting perspectives and mounting tensions and conflict amongst physicians and patients. Such experiences have prompted some patients to pursue alternative medicine in Canada or receive treatment outside of the country.22 Patients have expressed a desire for change within the healthcare system (eg, more open communication and better physician-patient relations),23 and physicians must stay abreast of the latest clinical recommendations.

Patient frustration is not unique to Canada. Drew and Hewitt24 reported negative experiences associated with LD care in the US, including frustrations with having to visit multiple physicians, prolonged diagnosis process, financial stress, and the need for self-advocacy if experiencing unresolved symptoms after treatment. Similar experiences were documented over a decade later, where patients continued to report experiences of strained physician-patient relationships and dissatisfaction with their care.23

Inconsistent information could impede healthcare professionals’ ability to effectively diagnosis and treat LD. A

### Table 13. Prophylaxis Antibiotic Treatments (n=29).

| Treatment recommendations | Document count (%) | Endemic level | Region | Date |
|---------------------------|--------------------|---------------|--------|------|
| 20 days of doxycycline    | 2 (7)              | No data       | Intl = 2 | 2020 = 2 |
| Single dose of doxycycline (200mg for adults) | 23 (79)           | Low = 1       | Natl = 2 | 2013 = 1 | 2018 = 2 |
|                           |                    | High = 15     | Intl = 5 | 2014 = 2 | 2019 = 9 | 2016 = 2 | 2017 = 2 | 2020 = 5 |
| 2 weeks of doxycycline    | 1 (3)              | No data       | Intl = 1 | 2020 = 1 |
| Routine prophylaxis is not recommended. | 9 (31)           | High = 5      | Natl = 2 | 2013 = 1 | 2018 = 1 | 2014 = 1 | 2019 = 1 | 2016 = 1 | 2020 = 4 |

### Table 14. Treatment Options During Pregnancy (n=14).

| Recommendation | Document count (%) | Endemic Level | Region | Date |
|----------------|--------------------|---------------|--------|------|
| Doxycycline is contraindicated during pregnancy | 12 (86) | Low = 1       | Natl = 3 | 2013 = 1 | 2019 = 5 |
| Single doxycycline (200mg—prophylaxis) for pregnant women | 3 (21) | High = 5      | Intl = 2 | 2018 = 1 | 2020 = 5 |
| Amoxicillin or cefuroxime instead of doxycycline | 3 (21) | High = 2      | Natl = 1 | 2013 = 1 | 2020 = 1 |
| Tetracycline HCl (acromycin, and others) instead of doxycycline | 2 (14) | High = 1      | Intl = 1 | 2019 = 1 | 2020 = 1 |
| Symptoms                                      | Antibiotic choices                                                                 | Document count | Endemic level | Region | Date       |
|-----------------------------------------------|-------------------------------------------------------------------------------------|----------------|--------------|--------|------------|
| Arthritis \((n=?)\)                           | Uncomplicated arthritis: Treat with oral doxycycline or amoxicillin or cefuroxime.  | 7              | High = 4     | Intl = 3 | 2013 = 1   |
|                                               |                                                                                     |                |              |        | 2017 = 1   |
|                                               |                                                                                     |                |              |        | 2019 = 2   |
|                                               | Arthritis and neurological symptoms: Treat with IV ceftriaxone, cefotaxime, or penicillin | 1              | High = 1     | No data  | 2017 = 1   |
|                                               | Recurrent or persistent arthritis: Treat with another course of oral antibiotics.    | 2              | No data      | Intl = 2 | 2020 = 2   |
|                                               | Treat with IV if showed no improvements with oral antibiotics.                      | 2              | High = 1     | Intl = 1 | 2016 = 1   |
|                                               | Treat with another course oral, or IV.                                              | 4              | High = 4     | No data  | 2013 = 1   |
|                                               |                                                                                     |                |              |        | 2017 = 1   |
|                                               | More serious arthritis: Treat with IV ceftriaxone or penicillin.                    | 1              | No data      | Intl = 1 | 2020 = 1   |
| Cardiac                                       | Cardiac disease in early Lyme: Treat with oral antibiotics*                         | 2              | High = 1     | Intl = 1 | 2013 = 1   |
|                                               | First degree AV Block: Treat with oral antibiotics*                                 | 4              | High = 3     | Intl = 1 | 2017 = 1   |
|                                               |                                                                                     |                |              |        | 2020 = 1   |
|                                               | More serious cardiac symptoms*: Treat with IV antibiotics**                         | 4              | High = 1     | Intl = 3 | 2017 = 1   |
|                                               | Treat myocarditis or pericarditis: Treat with IV antibiotics**                      | 1              | High = 1     | No data  | 2019 = 1   |
|                                               | Erythema Migrans Rash: Treat with doxycycline                                       | 1              | No data      | Intl = 1 | 2017 = 1   |
|                                               | Treat with oral antibiotics*                                                        | 6              | High = 4     | Intl = 2 | 2013 = 1   |
|                                               |                                                                                     |                |              |        | 2017 = 1   |
|                                               | Neurological symptoms: Treat with oral antibiotics*                                 | 3              | High = 3     | No data  | 2013 = 1   |
|                                               | More serious neurological symptoms: Treat with IV antibiotics**                     | 9              | High = 7     | Intl = 2 | 2013 = 1   |
|                                               |                                                                                     |                |              |        | 2019 = 4   |
|                                               |                                                                                     |                |              |        | 2017 = 1   |
|                                               | Neurological symptoms generally: Treat with IV antibiotics**                        | 3              | High = 2     | Intl = 1 | 2016 = 1   |
|                                               | Peripheral nervous symptoms (including facial palsy): Treat with oral antibiotics*   | 7              | High = 5     | Intl = 2 | 2019 = 4   |

*Oral antibiotic options typically included doxycycline, amoxicillin, or cefuroxime.
**IV antibiotic options typically included ceftriaxone, cefotaxime, or penicillin.
^First degree AV block with PR interval >300 ms, or second or third degree AV blocks.
Table 16. Treatment Recommendations for Children With EL (n=22).

| Antibiotic options | Document count (%) | Endemic level | Region | Date |
|--------------------|--------------------|---------------|--------|------|
| Doxycycline contraindicative in young children (<8 years of age) | 13 (59) | Low = 1 | Natl = 2 | 2013 = 2 |
|                    |                    | High = 7      | Intl = 3 | 2014 = 1 |
|                    |                    |               |        | 2015 = 1 |
|                    |                    |               |        | 2016 = 1 |
|                    |                    |               |        | 2017 = 1 |
| Doxycycline is safe to use in young children. | 8 (36) | High = 3 | Natl = 2 | 2019 = 2 |
|                     |                    |               | Intl = 3 | 2020 = 6 |
| Doxycycline is safe in young children for short periods | 3 (14) | High = 2 | Natl = 1 | 2019 = 2 |

Conclusions

This analysis of 115 materials discussing the prevention, diagnosis, and treatment of Lyme disease for healthcare professionals revealed that recommendations vary in specificity and consistency. Recommendations surrounding prevention strategies were less varied between materials, whereas diagnosis and treatment recommendations were more varied across the different stages of Lyme disease. Knowledge translation tools must acknowledge the diversity of literature available to HCPs, patients, and fundamental scientists, as a lack of consistency may lead to contentious approaches to diagnosis and treatment.

The Canadian Lyme Disease Research Network has been funded to co-develop a publicly accessible and comprehensive database of stage-dependent LD research, as well as research that may narrow the variations in diagnosis and treatment recommendations. This gray literature review will help inform the development of the database. This database will be collaboratively developed by, and translated to, patient partners, fundamental scientists, and clinicians. This initiative may render the complexity of diagnosis and treatment more transparent and accessible to all invested parties.

Additional research is also needed to understand how this variability in information affects healthcare professionals and their knowledge, beliefs, and practices regarding Lyme disease. Also, we need to understand what interventions are most effective for disseminating information needed to improve the prevention, diagnosis, and treatment of Lyme disease in Canada. Doing so can help healthcare professionals make timely, informed clinical decisions which have a profound effect on patient outcomes, and mitigate the burden that Lyme disease imposes on the Canadian healthcare system.

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