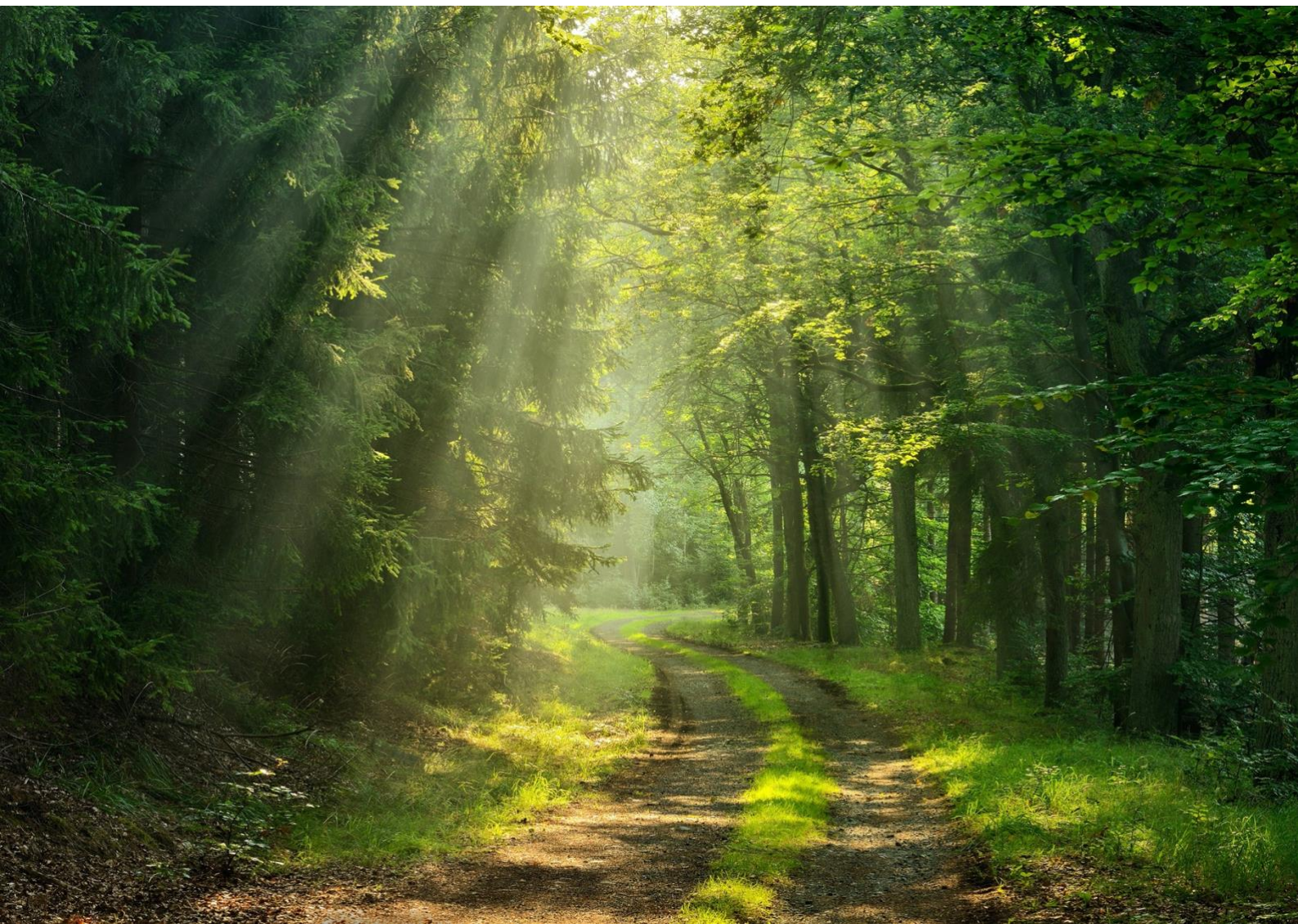


# Nordic consensus on the assessment and follow-up of persons with long-term ailments after suspected tick-borne diseases

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Report

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# Preface

Efforts are made to improve health services for patients with tick-borne diseases in the Nordic countries. Nevertheless, many people with long-term problems from suspected tick-borne diseases find that their health problems are not attended to well enough. Experience from clinics in Denmark and the Netherlands, as well as the Norwegian Lyme Disease Association and the Norwegian National Advisory Unit on Tick-borne Diseases, indicates that this applies to several hundred people every year in the Nordic countries. Many people seek out alternative health services for diagnosis and treatment.

In 2013, the Norwegian Directorate of Health was commissioned to follow up on this problem. The Directorate therefore organized a user conference in 2014. In consultation with the users and the then newly established Norwegian National Advisory Unit on Tick-borne Diseases, it was decided to prepare a Nordic consensus on the diagnosis and treatment of Lyme disease.

Following this, the Norwegian Directorate of Health invited a Nordic working group consisting of clinicians, users and researchers to shed light on the issue and propose the formulation of a consensus. However, it became clear early on that recommendations for the diagnosis and treatment of Lyme disease and tick-borne encephalitis (TBE virus) already had a good consensus in the Nordic countries. In further work processes, the mandate was sharpened to apply to common Nordic recommendations for diagnosis, treatment and follow-up of persons with long-term ailments after suspected tick-borne diseases.

It was also pointed out that it is important to prevent long-term ailments through better implementation of current recommendations. Some people experience that, despite clear symptoms of acute localised Lyme disease in the form of (typically) rash, they do not know they should see a doctor right away and that they do not always receive an adequate evaluation and antibiotic treatment from a general practitioner. Everyone who travels in areas with an abundance of ticks should also take precautions by following advice about clothing and checking for ticks after a hike or trip as well as possibly getting vaccinated against the TBE virus.

The working group presents its recommendations in this document. Several Nordic countries have also set up their own specialist outpatient clinics with a view to a uniform approach and research on vector-transmitted diseases.

Oslo, June 2020

*Bjørn Guldvog*, Health Director





Photo: Per Eikeset Knudsen

# Summary

## Main conclusions from consensus panel

- There is a need for continued focus on the prevention of tick bites and treatment at early signs of disease after a tick bite, by improving the knowledge of doctors and the population, in order to reduce the long-term consequences of tick bites.
- Antibiotic treatment should be given without further testing in case of a typical Lyme disease rash (Erythema migrans). For more general symptoms (especially neurological symptoms or joint pain), the patient should be referred directly to a hospital for extended diagnostics (spinal puncture, joint puncture). This is the latest recommendation for the treatment of Lyme disease in all the Nordic countries.
- There is a need for continued research in this area. The number of diagnostic studies on tick-borne diseases is limited, with the exception of Lyme disease and TBE.
- The consensus panel recommends preparing a standard clinical pathway that can confirm or disprove tick-borne diseases as the cause of a patient's symptoms, and possibly identifying other possible explanations. The recommended clinical pathway includes a checklist for further referral.
- To ensure equal treatment and interdisciplinary competence, the consensus panel recommends establishing a separate outpatient service within the specialist health services where an individual can be referred for assessment.
- Diagnostic recommendations, also for tick-borne pathogens other than *Borrelia* and TBE, are based on available, validated tests. A proposal has been made for differential diagnostic tests.
- Everyone with persistent problems following treatment should be offered rehabilitation. There are no specific rehabilitation measures for patients affected by tick-borne disease. The recommendations follow general principles for rehabilitation.

## **Composition of the consensus panel**

The report is based on conclusions from work carried out by 4 working groups, where their work was presented at a consensus meeting held in Oslo in the autumn of 2018.

The consensus panel consists of:

- Tone Synnestvedt, user representative, Norwegian Lyme Disease Association (NLBF)
- Gro Moen Skjøtt, user representative NLBF
- Randi Eikeland, neurologist and head of the Norwegian National Advisory Unit on Tick-borne Diseases, Sørlandet Hospital
- Anna J. Henningsson, chief physician, Microbiology and Infectious Diseases, Jönköping County / Linköping University
- Sigurður Skarphéðinsson, chief physician in infectious disease medicine, Odense University Hospital
- Marika Nordberg, infectious disease specialist, Åland's health and medical care center, Mariehamn
- Ingeborg Aaberge, immunologist and microbiologist, Norwegian Institute of Public Health
- Knut Eirik Eliassen, general practitioner, Antibiotic Center for Primary Medicine (ASP)
- Svein Høegh Henrichsen, general practitioner, senior adviser at Norwegian Directorate of Health

## **Composition of working groups and organization of work**

The work on compiling joint Nordic recommendations for diagnosis, treatment and follow-up of people with long-term ailments from suspected tick-borne diseases was organized and done by four working groups, which worked with:

1. Literature search on diagnostics and diagnosis of tick-borne infections
2. Clinical and treatment pathways
3. Laboratory process for diagnostics
4. Rehabilitation process

The participants from the individual Nordic countries are listed below. An overview of the professional background of the participants, associations and distribution into working groups is shown in the Attachment on page 41 and beyond.

### **From Norway:**

Ingeborg Aaberge, Audun Aase, Harald Reiso, Sølvi Noraas, Randi Eikeland, Tone Synnestvedt, Yvonne Kerlefsen, Knut Eirik Eliassen, Inger Johanne Wedding Hansen, Kjersti Widding, Dag Tveitnes, Pascal Brügger-Synnes, Svein Erik Valle Prinz, Tine A.M. Sollie, Gro Moen Skjøtt, Oddgeir Tjomsland, Svein Høegh Henrichsen

### **From Sweden:**

Anna J. Henningsson, Pia Forsberg, Björn Olsen, Katharina Ornstein, Barbro Hedin Skogman, Thomas Åkerlund

### **From Denmark:**

Sigurður Skarphéðinsson, Anne-Mette Lebech, Ram Dessau, Karen Angeliki Krogfelt, Thøger Gorm Jensen

### **From Finland:**

Marika Nordberg, Jukka Hytönen, Mari Kanerva, Dag Nyman, Olli Vapalahti, Jarmo Oksi

# **1. Summary of main chapters**



## **1.1 Background information**

Efforts are being made to improve health services for patients with tick-borne diseases in the Nordic countries. Nevertheless, many people with long-term problems after suspected tick-borne diseases find that their health problems are not attended to well enough. Experience from clinics in Denmark and the Netherlands, as well as the Norwegian Lyme Disease Association and the Norwegian National Advisory Unit on Tick-borne Diseases, indicates that this applies to several hundred people every year in the Nordic countries. Many people seek out alternative health services for diagnosis and treatment. In recent years, patients and patient organizations in Europe and the USA have been demanding better knowledge about tick-borne diseases.

In Norway, the demands peaked with a demonstration in front of the parliament building in 2013, organized by patients who thought they were not taken seriously. They demanded better awareness among doctors and adequate treatment; to avoid more people becoming sick. After this, the Norwegian Minister of Health at the time, Jonas Gahr Støre, convened patient associations and professionals for a meeting on Lyme disease at the Norwegian Directorate of Health. The Directorate was then commissioned to follow up these issues. After consulting various patient associations, the Directorate's first initiative was to arrange a user conference in 2014. The users of health services directed at tick-borne diseases provided some excellent input. In consultation with the users and the then newly established Norwegian National Advisory Unit on Tick-borne Diseases, it was decided to prepare a Nordic consensus on the diagnosis and treatment of Lyme disease. Early in the course of the work, from 2015 onwards, it became clear that there was already good consensus among the Nordic countries regarding existing recommendations for diagnosing and treating newly developed Lyme disease.

The mandate was sharpened in further work processes to include recommendations and a proposed *treatment pathway* to diagnose, treat and follow-up of persons with **long-term ailments** after suspected tick-borne diseases.

The work was organized into four work packages:

1. Carry out a systematic search of professional medical literature and review publications concerning diagnostics and diagnosing tick-borne diseases.
2. Develop a common Nordic consensus on the assessment and follow-up of persons with long-term ailments after suspected tick-borne diseases.
3. Develop a common Nordic clinical pathway to diagnose persons with long-term ailments after suspected tick-borne diseases.
4. Develop a common Nordic clinical and rehabilitation pathway for persons suffering from long-term symptoms and ailments after suspected tick-borne disease.

**Further presentations of the work were divided into four areas:**

- 1. Are the ailments caused by tick-borne diseases?**
- 2. Are the best available diagnostics being used?**
- 3. Recommended clinical pathway**
- 4. Rehabilitation**

## **2.1 Are the ailments caused by tick-borne diseases?**

A two-part systematic search of literature on research studies regarding the diagnosis of tick-borne diseases in humans was performed.

Part 1 of the literature search involved identifying research on methods for laboratory diagnostics of tick-borne diseases other than Lyme disease and tick-borne encephalitis (TBE):

Anaplasmosis (*Anaplasma phagocytophilum*)

Rickettsiosis (*Rickettsia helvetica*)

Neoehrlichiosis (*Candidatus Neoehrlichia mikurensis*)

Babesiosis (*Babesia* species)

Recurrent fever due to *Borrelia miyamotoi*

Tularaemia (*Francisella tularensis*)

Bartonellosis (*Bartonella* species)

In part 2 of the literature search, the purpose was to identify research on several **simultaneous** tick-borne infections, including Lyme disease, TBE and the diseases listed above.

Part 1 of the literature search included 458 references sorted by tick-borne infection type and study design. Part 2 of the literature search, on several simultaneous tick-borne infections, identified 105 references (four systematic reviews, 11 non-systematic review articles, 15 diagnostic studies, 50 case studies, 25 case studies).

Part 1 of the literature search has been published (National Institute of Public Health, 2019). Part 2 of the literature search is under consideration by a group of 10 experts from Sweden and Finland. An article will be published in 2020. The work will provide guidelines for prioritising research regarding the diagnosis of tick-borne diseases in the years ahead.

The group has already concluded that the number of diagnostic studies on tick-borne diseases, apart from Lyme disease and TBE, is limited.

## **1.3 Are the best available diagnostics being used?**

Diagnosing a tick-borne infection can be difficult. Test results must always be seen in connection with exposure, medical history and current symptoms, preferably by doctors with experience in such assessments. False positives and false test results can occur. The presence of antibodies does not necessarily represent a current, active disease. Diagnostic routines at four clinics that work with assessing tick-borne diseases in the Nordic countries and the Netherlands (Odense, Uppsala, Åland and Amsterdam) have been assessed. Diagnostic recommendations have been compiled for tick-borne pathogens based on available, validated tests that are already in clinical use. Test methods that are not validated or quality assured are not mentioned.

Symptoms and ailments after undergoing tick-borne diseases can be confusingly similar to ailments in many other conditions. Proposals have been prepared for differential diagnostic tests for other diseases

and non-tick-borne infections that can cause long-term ailments. In differential diagnostic thinking, it is important to distinguish between suspected tick-borne diseases and non-tick-borne diseases.

#### **1.4 Recommended clinical pathway**

The consensus has prepared a checklist to help physicians prepare referrals to treat long-term ailments after suspected tick-borne diseases, so these can be as good as possible. The clinical pathway aims to confirm or disprove tick-borne diseases as the cause of a patient's ailments. The clinical pathway will identify other possible explanations, initiate the right treatment and possibly recommend rehabilitation by skilled personnel at the right level of treatment.

It is important that patients are met by specialists who are dedicated to the task who work in a multidisciplinary environment. This work is best organized by establishing a specialised assessment and treatment scheme for people with long-term symptoms and ailments related to suspected tick-borne diseases. It is recommended that patients with widespread/disseminated Lyme disease are checked by the specialist health services three months after treatment (also after six months if necessary) to ensure that any remaining ailments are identified and assessed further and subject to differential diagnosis.

#### **1.5 Rehabilitation**

Rehabilitation measures are not taken into account for persons with long-term symptoms and ailments related to possible tick-borne diseases. The most common and troublesome problems following a tick-borne infection are residual paralysis, pain, fatigue, cognitive ailments and reduced ability to work. These ailments can also be seen in other diseases/conditions. A broad differential diagnostic is therefore needed to clarify the situation prior to rehabilitation.

There is much variation in incidence, symptom intensity and disability due to persistent ailments following a tick-borne infection. Research on rehabilitation measures for this group is very limited. There are no diagnosis-specific rehabilitation measures available. The recommendations follow general rehabilitation principles.

## **2. Background information**

The Norwegian Directorate of Health prepared a report in 2009 that presented the knowledge that existed at the time about diagnosing and treating Lyme disease (Norwegian Directorate of Health, 2009).

The report describes diagnostic considerations and tests that currently form the basis for diagnosis and treatment of Lyme disease. The knowledge was systematised and structured so it could be used to prepare guidelines that the Directorate would consider publishing at a later date.

The Norwegian Institute of Public Health subsequently prepared a strategy report on laboratory testing for Lyme disease (NIPH, 2011).

The Directorate expressed reservations in the 2009 report, saying no direct assessment had been made on the patient group with long-term symptoms that may be due to Lyme disease. They recommended returning to this issue by establishing a follow-up project that would mainly focus on persons suspected of having tick-borne diseases, but who felt they did not receive adequate help and assistance in finding the best treatment regimens and testing methods. The Directorate considered whether a separate project should be established to look at the main themes addressed in the 2009 report, through a new mandate and new working groups, in order to establish arenas where this patient group could be assisted in a more satisfactory manner.

A model was outlined during this work which included the establishment of a nationwide outpatient clinic. The reason was that the sickest patients needed very specific arenas in which they would receive correct diagnosis and treatment. It is important that diagnosis, assessment and treatment are properly documented through protocols, and linked to research. Treatment of advanced cancer was used as an example, where parts of the treatment are sometimes experimental, with assurances that those affected would receive an offer regardless of which doctor or hospital department they are examined at, or where in the country they live.

The Directorate has not prepared specific guidelines for Lyme disease, but recommendations do exist in national professional guidelines for how Lyme disease is to be treated and how antibiotics should be used by the primary and specialist health services in Norway. The recommendations are supported in terms of knowledge in a Swedish summary of knowledge (Behandlingstid vid borreliainfektion / Treatment Time for Lyme Disease Infections) issued by the Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU) in 2013:

*"Better research is needed on the appropriate duration of treatment. Benefits and risks must be compared via professional studies. It is currently not possible to determine whether antibiotics for more than 10–14 days improve the treatment outcome for patients with erythema migrans.*

*It is also not possible to determine whether long-term antibiotic treatment works for neuroborreliosis, Lyme disease arthritis or persistent symptoms following a Lyme disease infection.*

*With long-term treatment (>21 days) based on antibiotics (Ceftriaxone) via a central venous catheter, there is a not-insignificant risk of serious and potentially life-threatening complications."*

Studies after 2013 have not provided a basis for changing the recommended treatment time. In recent years, medical professionals have become more aware that tick-borne agents other than *Borrelia* can



cause health problems, and that other possible concurrent tick-borne diseases, and the characteristics of an individual patient's immune system, can affect whether you become ill and how sick you get from tick-borne infections.

There is a need for more research and a systematic approach with regard to diagnosis and treatment for patient groups with long-term symptoms that may be caused by tick-borne diseases. A separate outpatient clinic or treatment center is considered absolutely necessary to provide better services and facilitate clinical research.

## **2.1 Establishing the Nordic consensus working group**

There were demonstrations in front of the Norwegian parliament building in 2013 to demand better Lyme disease treatment. After this, the Norwegian Minister of Health at the time, Jonas Gahr Støre, convened patient associations and professionals for a meeting on Lyme disease at the Norwegian Directorate of Health. The Directorate was commissioned to follow up on this problem following the protests.

After consulting various patient associations, the Directorate's first initiative was to arrange a user conference in 2014. The users of health services directed at tick-borne diseases provided some excellent input. In consultation with the users and the then newly established Norwegian National Advisory Unit on Tick-borne Diseases, it was decided to prepare a Nordic consensus on the diagnosis and treatment of Lyme disease.

The National Advisory Unit and the Norwegian Directorate of Health organized the first Nordic consensus meeting in 2015. The meeting reviewed recommendations for diagnosis and treatment of Lyme disease used by the Nordic countries and discovered that their recommendations were essentially the same. There were minor differences in the duration of treatment and choice of antibiotics. The participants agreed that there was no basis for re-evaluating the recommendations since there was already a consensus regarding diagnosis and treatment of acute Lyme disease. The recommendations also complied with the European guidelines for neuroborreliosis (European Federation of Neurological Societies (EFNS) and Guidelines on the diagnosis and management of European Lyme neuroborreliosis (EFNS 2010). Further consensus work was also assessed against guidelines published by the English National Institute for Health and Care Excellence (NICE) in 2018. It also became clear that Nordic TBE recommendations were essentially the same.

The meeting in 2015 resulted in the Norwegian Directorate of Health establishing a mandate to carry out a Nordic consensus work on recommended patient procedures for diagnosis, assessment, treatment and follow-up (the clinical pathway) of persons with long-term ailments related to suspected tick-borne diseases. The Norwegian National Advisory Unit on Tick-borne Diseases, led by Randi Eikeland, was chosen to lead the work in collaboration with the Norwegian Institute of Public Health and the Norwegian Lyme Disease Association. The work was to have a Nordic foundation. The process was organized into four work packages:

1: Systematic **search of professional medical literature** and review publications concerning diagnostics and diagnosing tick-borne diseases, led by immunologist and microbiologist Ingeborg Aaberge at the Norwegian Institute of Public Health.

2: Develop a **Nordic clinical pathway** for patients who have long-term symptoms and ailments related to suspected tick-borne diseases, led by general practitioner Knut Eirik Eliassen.

3: Develop a Nordic **laboratory process for diagnostics** to diagnose patients who have long-term symptoms and ailments related to suspected tick-borne diseases, led by microbiologist and chief physician Sølvi Noraas at the Norwegian Reference Laboratory for Borrelia, and by microbiologist and infectious disease physician Anna J. Henningson at Linköping University.

4: Develop a Nordic clinical pathway for the **rehabilitation** of patients with long-term symptoms and ailments related to suspected tick-borne diseases, led by general practitioner Harald Reiso and specialist in physical medicine and rehabilitation Kjersti Widding.

The working groups presented their findings and conclusions during the Consensus Congress in Oslo on 15 and 16 October 2018. The aim was to present the work to users, and to have a constructive dialogue around the proposals offered by the consensus. The Norwegian Directorate of Health set up an editorial team to prepare a final report for the Directorate. The **editorial team** has participants from all the Nordic countries, the Norwegian Directorate of Health and the Norwegian Lyme Disease Association (NLBF). The group is led by a general practitioner and senior adviser at the Norwegian Directorate of Health; Svein Høegh Henrichsen.

An overview of the participants in the various working groups of consensus work is available in this report as an Attachment on page 41.

The Norwegian Directorate of Health has contacted the health authorities in the other Nordic countries in connection with the consensus work. The health authorities in the other Nordic countries did not want to participate directly in the work, since the process was attended to by the professionals involved. Health supervisory authorities in Sweden and Denmark have been involved as observers.

#### **The working groups focused on these questions:**

- Are the ailments caused by tick-borne diseases?
- Are the best available diagnostics being used?
- What is the recommended clinical pathway?
- What social rights and opportunities for rehabilitation does the patient group have?

Doctors are responsible for the chosen treatments. Not all patients receives medical treatment after their examinations. The Norwegian Lyme Disease Association does not want to interfere in the professional considerations that form the basis for treatment choices, but strongly emphasises that patients should be examined further if they still have residual symptoms.

**3. Are the ailments caused by tick-borne diseases?**

The Norwegian Institute of Public Health was commissioned by the Directorate of Health and the Norwegian National Advisory Unit on Tick-borne Diseases to conduct a systematic **literature search** to map existing research on the laboratory diagnostics available for tick-borne diseases. The Norwegian Institute of Public Health carried out the assignment in two parts.

Part 1 of the literature search involved identifying research on methods of laboratory diagnosis of persons with long-term ailments after Lyme disease, tick-borne encephalitis (TBE) or seven of the other tick-borne diseases: Anaplasmosis (*Anaplasma phagocytophilum*) rickettsioses (*Rickettsia helvetica*), neoehrlichiosis (*Candidatus Neoehrlichia mikurensis*), babesiosis (*Babesia* species), relapsing fever (*Borrelia miyamotoi*), tularaemia (*Francisella tularensis*) and bartonellosis (*Bartonella* species).

Part 2 of the literature search involved identifying research on several **simultaneous** tick-borne infections, including Lyme disease, TBE and the tick-borne diseases listed above.

A systematic search for relevant research published between 2007 and 2018 was conducted. The studies were assessed in relation to methodological qualities and summarised results.

In Part 1, Laboratory diagnostics, 458 references were included and sorted by type of tick-borne infection and study design (diagnostic studies, case studies and case series). This was published by the National Institute of Public Health in 2019.

Part 2 of the literature search on several simultaneous tick-borne infections identified 4 systematic reviews, 11 non-systematic review articles, 15 diagnostic studies, 50 case studies, 25 case studies. Further work, with a review of current articles in full text, was done by a group of 10 experts from Sweden and Finland. The work is being monitored by observers from several health authorities (the National Institute of Public Health in Norway, the National Board of Health and Welfare in Sweden, the Norwegian Directorate of Health and the Swedish Medicines Agency). 58 articles were included for a systematic review according to the QUADAS protocol (diagnostic studies) and the AMSTAR protocol (systematic assessments). The following articles were not included in the review: case studies, case series, articles written in languages other than English, non-systematic reviews, articles dealing with methods not intended for human diagnostics and studies where only abstracts are available. The 58 articles have been reviewed independently by at least two experts from the group. In case of disagreement, another expert has been involved with a view to a consensus assessment.

The following data was retrieved from each article: A brief description of each test that has been evaluated, which antigen or target has been used in the test, which reference test has been used, and if a reference test is available; the number of samples included in the study, as well as the study population. The risk of bias is assessed in each study. The results are expected to be published in 2020.

The group has so far concluded that the number of diagnostic studies on tick-borne diseases, apart from Lyme disease and TBE, is limited.

**4. Are the best  
available diagnostics  
being used?**



A proposal has been made for agents that should and can be tested for when tick-borne diseases are suspected. Symptoms of long-term disease can be difficult to distinguish from chronic fatigue. Therefore, tests that are recommended to be performed in connection with the assessment of chronic fatigue syndrome (CFS) in Norway have also been included. How many tests to take, and at what time, will depend on the individual patient's symptoms.

Proposals for the diagnosis of Lyme disease and TBE are based on existing recommendations. The proposal for a diagnosis of other tick-borne diseases is new.

Ticks in the Nordic countries can contain several microorganisms that can be transmitted by tick bites and cause disease in humans. The most current agents are *Borrelia burgdorferi* group, TBE virus, *Anaplasma phagocytophilum*, *Candidatus Neoehrlichia mikurensis*, *Babesia species*, *Rickettsia helvetica* and *Borrelia miyamotoi*.

The risk of getting tularemia or Bartonella infection after tick bites in the Nordic countries is assumed to be low. Therefore, routine testing for these pathogens after tick bites is not recommended.

Since ticks can contain several pathogens, ticks can be infected with several agents at the same time. The knowledge about disease patterns that can occur in infections with several pathogens at the same time is currently limited. Below is a brief description of the individual infections that should be kept in mind when examining tick bites. It is important to check for ticks on one's body after staying in areas with known tick populations. Remember to check the scalp on children. Attached ticks shall be removed as soon as possible.

The Norwegian National Advisory Unit on Tick-borne Diseases has more information on prevention here: <https://flåttsenderet.no/forebygging/>. See this video as well: <https://www.fhi.no/ml/skadedyr/flatt/hvordan-fjerner-man-flatt/>

Sigurður Skarphéðinsson, Chief physician in infectious diseases at Odense University Hospital: "*If we had been more aware of tick bite prevention and early treatment in the course of tick-borne diseases, the incidence of long-term ailments after tick-borne infections would decrease significantly.*"

#### **4.1 Borreliosis**

We use the terms *localised disease* (a rash - Erythema migrans; EM) and *disseminated* (widespread) *disease*. The latter means that Borrelia bacteria have spread from the bite site to other places in the body. In Norway, around 7000 people contract EM every year. About 450 cases of more serious, widespread illness are reported each year to the National Institute of Public Health's reporting system for infectious diseases.

The most common and often only symptom of Lyme disease is a reddish rash that grows (migrates) beyond the bite site. The rash is usually larger than 5 cm and can occur from a few days to several weeks after a tick bite. Some people also get mild generalised symptoms such as lethargy, headaches, muscle and joint pain, as well as swollen lymph nodes. Fever is not common. The rash fades and disappears gradually after treatment, but it can take a long time. If it does not go away after a long time, other skin diagnoses should be investigated.

A rarer variant of rash is *Borrelia lymphocytoma*, most often a small red or purple swelling that is most often seen on the earlobe (or as a reddish area on the top of the ear cartilage), most common in children. Lymphocytoma can also occur on the nipple and other areas of the skin.

Several EMs can occur after only one tick bite. Such multiple EMs can be considered a disseminated infection. An EM diagnosis is made on a clinical basis, i.e. based on medical history and what the rash looks like. **The EM can have very different appearances. Many doctors in the Nordic countries probably have insufficient knowledge about the diversity of appearances.** Serological tests have no place in an EM diagnosis (many people have not formed antibodies that early after infection). **All suspected EMs should be treated with antibiotics.**

In the case of widespread (disseminated) borreliosis in Europe, infection of the nervous system is most common. About half do not notice that they have had tick bites or EM. The symptoms of neuroborreliosis typically occur from a few weeks to a few months after a tick bite. Most often, the infection is located in the meninges and nerve roots, which can cause paralysis or altered sensation in muscles and skin that are supplied by the inflamed nerve roots (Bannwarth syndrome). This can cause significant pain that radiates to the neck, arms and legs, or as a belt from the back to the abdomen. The pain is typically burning, and worst at night. Ordinary painkillers often do not help much, and the pain is not relieved by a change of position. Sensory changes in the skin in the painful areas are common. Paralysis of various nerves can occur. Effects on the facial nerve that controls the muscles of the cheek and eye (facial paresis) are most common. Neuroborreliosis can cause general malaise and symptoms such as low-grade fever, headache, photophobia, stiff neck, lethargy and tiredness. (Fever is not so common.) Occasionally, the disease can have a more serious course and cause inflammation in brain tissue or in the spinal cord with neurological outcomes such as impaired balance, coordination difficulties and incontinence. A spinal puncture must be performed to diagnose neuroborreliosis. Some people may experience a loss of functionality for a long time after being treated for neuroborreliosis.

*Borrelia* bacteria sometimes spread to joints (*Borrelia* arthritis). The symptoms usually appear a few months after the tick bite. The most common symptom is inflammation of one joint (monoarthritis). A Norwegian study has shown that the vast majority of those affected get inflammation in the knee joint (approx. 80%), but some can also get inflammation in other large joints such as the ankle joint, hip joint, elbow joint or shoulder joint. The joint that is affected will often be very swollen and hot. Many patients also experience stiffness and decreased tolerance for strain in the muscles around the joint. Fever and decreased general condition are not so common. *Borrelia* arthritis is much more common in the United States than in Europe, probably because the United States has a much higher incidence of *Borrelia burgdorferi sensu stricto*, a type of borrelia bacterium that often causes symptoms in joints. *Borrelia* antibodies usually show high values.

Acrodermatitis chronica atrophicans (ACA) is a persistent change in the skin that can cause a reddish-purple/bluish discolouration. If the skin change/rash has been around for a long time, it can damage the subcutaneous tissue. This can cause skin shrinkage. The skin then becomes thinner and looks old (cigarette paper skin). ACA produces high *Borrelia* antibody levels in the blood.

**ACA is probably underdiagnosed in the Nordic countries.**

The *Borrelia* bacterium can also spread to other organs such as the heart (carditis) and eyes (panophthalmitis, uveitis). Severe symptoms from the heart with transient arrhythmia (AV block), and inflammation of the heart/pericardium (myopericarditis) may occur.

## **4.2 TBE**

Tick-borne Encephalitis (TBE) is caused by the TBE virus. The TBE virus is located in the tick's salivary glands and can be transmitted shortly after the tick has taken hold. In Norway, about 15–35 serious cases of TBE are reported each year; in Sweden about 300. The incidence of TBE in ticks varies widely within small geographical areas.

There is much variation in the clinical picture. We do not know how many people are infected but asymptomatic in Norway. The proportion of the population that has positive antibodies against TBE is very low. The incidence of TBE is increasing in the Nordic countries. In those who become seriously ill, a biphasic course is common. Symptoms usually appear 4 to 28 days after a tick bite. In phase 1, the symptoms last less than 1 week and may resemble a "summer flu" with moderate fever, headache, muscle aches, nausea and vomiting. 2/3 of those who have such symptoms recover completely, but 1/3 can get new and more severe symptoms (phase 2) after a symptom-free period of a few days. In phase 2 of the disease course, the symptoms are far more severe as the virus spreads to the brain and/or spinal cord. Typical symptoms are high fever, increasing headache, lethargy, confusion, vomiting, neck stiffness, muscle aches and paralysis. Adults (especially the elderly) often experience a more serious disease than children. The mortality rate of those who become ill is about 1% in Western Europe. In some cases, outbreaks of infection after ingestion of unpasteurised milk/cheese made from unpasteurised milk from goats, cows or sheep have been described in Central/Eastern Europe. There is a vaccine against TBE that is recommended for people who are in or travelling to endemic areas and are exposed to tick bites. In Norway, people who live in endemic areas and who have experienced many tick bites in the past are recommended to take the vaccines (see up-to-date information on the TBE virus on NIPH's website: [fhi.no](http://fhi.no)). In some areas in the Nordic region, such as Åland, the TBE vaccine is part of the childhood vaccination programme.

TBE can cause neurological outcomes and long-term problems.

## **4.3 Tick-borne infections other than Lyme disease and TBE**

Documented occurrences of other tick-borne infections other than Lyme disease and TBE in humans are rare. We will not provide figures on the incidence of this here, as few studies have been done for many of the agents in question.

## **4.4 Anaplasmosis**

Human (granulocytic) anaplasmosis (HGA) is caused by infection by *Anaplasma phagocytophilum*, a tick-borne disease that usually produces a mild self-limiting course, with nonspecific signs of infection such as fever, headache, muscle and joint pain and generalised listlessness. Few serious cases have been reported in Europe. The American *Anaplasma* strains seem to cause more serious disease. Approximately 3% of patients may develop life-threatening complications. Fatal outcome is described; mostly among the elderly and immunocompromised persons.

#### **4.5 Babesiosis**

Babesiosis is most common as a tick-borne disease, but it can also be transmitted through blood transfusions. Infections in Europe are usually caused by *Babesia divergens*, less frequently by *B. venatorum* and *B. microti*. Babesia is a parasite that destroys red blood cells. The infection produces a flu-like, transient disease with fevers above 40 °C, fatigue, headache, muscle aches and anaemia. Babesiosis can be a serious, life-threatening disease (similar to malaria). Most cases of babesiosis are seen among people who have had their spleen removed. Serious illness is further associated with old age and compromised immune systems.

#### **4.6 Rickettsioses**

Rickettsioses is a large group of diseases caused by various *Rickettsia* agents. The most current tick-borne rickettsiosis in the Nordic countries is a *Rickettsia helvetica* (RH) infection. Usually, a RH infection does not cause disease, or one sees a mild disease with nonspecific symptoms such as fever, headache and muscle aches. RH does not usually produce a rash (or eschar: a black, crust-covered wound where the tick has bitten), as can be seen in other rickettsioses.

#### **4.7 Borrelia miyamotoi infection**

Infection by *Borrelia miyamotoi* causes recurrent fever and flu-like symptoms for 2-3 periods, with fever-free days in between, in addition to concomitant headaches and muscle aches. Cases of meningitis have been reported in immunosuppressed patients.

#### **4.8 Neoehrlichiosis**

Neoehrlichiosis usually causes a self-limiting, flu-like condition. Some patients get a rash. Sustained carriers with *Candidatus Neoehrlichia mikurensis* DNA have been reported. Severe disease in immunosuppressed people may occur, with an increased risk of vascular complications.

#### **4.9 Tularemia**

Tularemia is caused by the bacterium *Francisella tularensis*. Symptoms depend on how the bacterium is transmitted; via drinking water, by inhalation, mosquito bites, or through bites/wounds. The risk of tularemia after a tick bite in the Nordic countries is low. Tularemia causes high-edged (ulceroglandular) ulcers. Symptoms may include sudden fever, chills, severe headache, lymph node swelling, muscle aches, fatigue, and non-healing sores.

#### **4.10 Bartonellosis**

There are a number of different Bartonella bacteria that can cause disease in humans. Infection caused by *Bartonella henselae* is perhaps most relevant in the Nordic countries. Cat bites or scratches are the most common cause of Cat Scratch Disease. The microbe has been detected in ticks in Europe, but whether infection is transmitted to humans by tick bites is little documented. The symptoms of cat scratch disease can vary greatly, often with low-grade fever and/or enlarged, tender lymph nodes and bacillary angiomatosis (lesions of the skin, liver, spleen, mucous membranes and other organs). Eye infections, muscle aches or encephalitis can occur, but they are rare.

Another *Bartonella* bacterium (*B. schoenbuchensis*) has been detected in deer flies and has been linked to prolonged itching after being bitten by it.

## **5. Overview of diagnostics for Lyme disease and TBE**



Lyme borreliosis	
Specimen material	Possible tests
Serum	IgG, IgM*
	Immunoblot IgG, IgM
Cerebrospinal fluid	IgG, IgM
	Immunoblot IgG
	Index IgG, IgM* (relation between antibodies in cerebrospinal fluid and in blood)
	CXCL13
	PCR (children, short medical history)
Synovial fluid	PCR
Skin and synovial biopsy	PCR

Borrelia antibodies of types IgG and IgM are usually analysed using the ELISA method (Enzyme-Linked Immunosorbent Assay)

\* IgM is not used in Åland, and is used less and less in Denmark. Immunoblot is not used in Denmark. The IgM Index is used for children (Sweden)

In case of uncertainty, tests can be repeated at 4 to 6 week intervals

CXCL 13 – cytokine, a signal protein

PCR – Polymerase Chain Reaction – a method for detecting genetic material (DNA/RNA)

Tick-borne encephalitis (TBE)	
Specimen material	Possible tests
Serum	IgG, IgM
	PCR in early phase of disease
Cerebrospinal fluid	IgG, IgM
	PCR
Urine	PCR (limited documentation)

## **6. Diagnosing other tick-borne agents**

Microorganism	Applicable diagnostics			Diagnostic test recommendations	
	Serology	PCR	Other	First choice	Confirming
<i>A. phagocytophilum</i>	Yes	Yes	Microscopy	Serology PCR (whole blood)	PCR
<i>Cand. Neoehrlichia mikurensis</i>	No	Yes		PCR (Whole blood, Skin biopsy)	Sequencing Follow-up test
<i>Babesia spp.</i>	Yes	Yes	Microscopy	Serology PCR (Whole blood)  Microscopy (Whole blood)	PCR
<i>Rickettsia helvetica</i>	Yes *	Yes		Serology PCR (Whole blood)  Skin biopsy, CSF	PCR Sequencing
<i>Borrelia miyamotoi</i>	Yes **	Yes		PCR (Whole blood, CSF)  (Plasma)  (Serology)	PCR Sequencing

\* Can cross-react with other Rickettsia species. \*\* Cannot be distinguished from other bacterial variants that cause relapsing fever

In case of uncertainty, tests can be repeated at 4 to 6 week intervals

PCR – Polymerase Chain Reaction – a method for detecting genetic material (DNA/RNA)

CSF – Cerebro Spinal Fluid

The risk of Bartonella infection after a tick bite in the Nordic countries is assumed to be low. Therefore, routine testing for Bartonella after a tick bite is not recommended. Some serological tests for diagnosing Bartonella are available.

Tularemia is mainly transmitted through contaminated drinking water, mosquito bites and contact with rodents. Diagnosis (serology and PCR) of tularemia is available at a microbiological laboratory in Trondheim.

## **7. Other analyses, non-tick-borne diseases (clinical suspicion)**



## 7.1 Other relevant analyses

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### Serology

- EBV, CMV, VZV, HSV, toxoplasmosis, Chlamydia pneumoniae\*, Mycoplasma pneumoniae\*, human parvovirus B19, hepatitis B, hepatitis C

### PCR

- human herpesvirus 6, EBV, CMV, parvovirus B19

### Medical biochemistry

- Hb, SR, leukocytes, thrombocytes, transferrin tests, Ferritin, Na, K, Ca, P, Mg, Glu, HbA1c, albumin, CRP, ASAT, ALAT, GT, bilirubin, ALP, LD, creatinine, CK, vitamin B<sub>12</sub>, folate, vitamin D, FT4, TSH and cortisol
- Albumin/creatinine ratio in urine

### Immunology

- Immunoglobulin IgG, IgM, IgA, total IgE, anti- $\alpha$ -galactose (IgE, for suspicion of allergy to red meat after tick bite), Antinuclear Antibodies (ANA), Rheumatoid factor (RF), other rheumatological tests, celiac antibodies/tests

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\* PCR alternative to serology

EBV – Epstein-Barr-virus

CMV – Cytomegalovirus

VZV – Varicella Zoster-virus

HSV – Herpes Simplex virus

PCR – Polymerase Chain Reaction – (method for detecting genetic material (DNA/RNA))

CSF – Cerebro Spinal Fluid

Hb – Haemoglobin

SR – Lowering reaction

Electrolytes: Na, K, Ca, P, Mg

Glu – glucose

HbA1c – long-term blood sugar

CRP – C-reactive protein (measure of infection)

Liver enzymes: ASAT, ALAT, GT, ALP

LD – lactate dehydrogenase

CK – creatine kinase

## **7.2 Tick-induced allergy to red meat**

In recent times, there have been several reports that show a link between tick bites and allergic reactions after eating red meat (alpha-Gal allergy). IgE antibodies to a carbohydrate (alpha-Gal) present in ticks and red meat can be detected. Symptoms can range from urticaria, itching and general malaise to anaphylactic reactions. Several cases have been reported from the Nordic countries, but the extent of the disorder has been little mapped, except in Sweden.

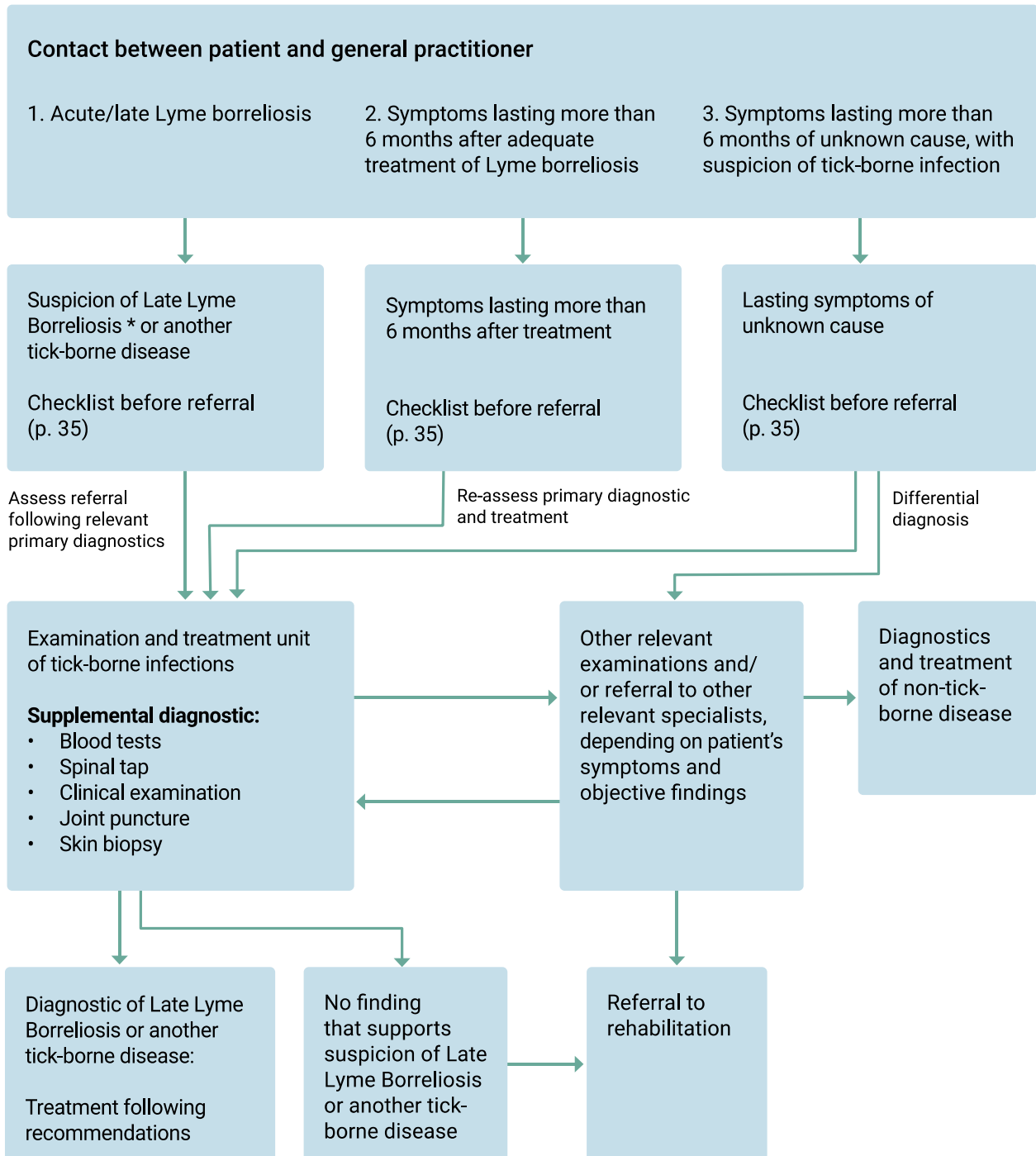
## **7.3 Freezing samples**

In case of unclear conditions and suspicion of tick-borne diseases (e.g. fever after tick bite without EM, joint ailments, or neurological outcomes), diagnostics are performed as far as possible. This includes **removing and freezing** serum and spinal fluid to compare with later samples, possibly for other/new test methods.

## **8. Recommended clinical pathway**

## 8.1 Examination. Flow chart

### Clinical pathway for patients with lasting symptoms after suspected tick-borne diseases



\*) Suspicion of Late Lyme Borreliosis shall be diagnosed locally. Make sure that all relevant diagnostics have been done, and re-assess the need for a referral: antibodies, spinal tap, MRI cerebri, ECG, joint and skin examination.

In differential diagnostic thinking, it is important to distinguish between suspected tick-borne diseases and non-tick-borne diseases.

The starting point for the work has been that the assessment process should not exclude relevant patients. The clinical pathway applies to people with symptoms of a certain severity and a duration of more than six months, where tick-borne disease is suspected. Patients with acute disease after a tick bite or known exposure to ticks, who experience fever, skin changes, flu-like symptoms, joint pain, muscle pain or neurological symptoms, should be evaluated, diagnosed and treated in the acute phase according to current recommendations, preferably by a local doctor, and **not** included in this pathway.

In some cases, Lyme disease can go undiagnosed for a long time (as with ACA). Some may have a subclinical infection and recover, but have seroconversion. At other times, people may have ailments after undergoing treatment for Lyme disease or have persistent symptoms and suspected tick-borne disease as the cause, without knowing they were bitten by a tick.

The idea is that the general practitioner refers the person to an outpatient clinic with specialist expertise in diagnosing and treating tick-borne diseases, and where relevant specialists in the field work together.

The patient's case history concerning these problems, together with test results and other relevant information, are sent with the referral to the specialist. In addition, the patient should be encouraged to write a summary of his or her medical history, explaining what the person perceives as the cause of the ailments, which is also enclosed with the referral.

An important element in the problem of long-term ailments after tick-borne diseases is that the diagnosis is sometimes unnecessarily delayed because the patient or doctor does not think about the possibility of such an infection. It is therefore important to provide information about the symptoms of tick-borne diseases. Not everyone with ailments beyond 6 months where a tick-borne infection is suspected as one of the differential diagnoses will necessarily be referred to a specialist for this clinical pathway. If a tick-borne infection is suspected as the cause of the patient's ailments, one can start the investigation at the general practitioner's office and consider tests such as antibodies, spinal puncture, MRI of the central nervous system, joint and skin examinations and ECG.

Patients with persistent symptoms of tick bites **following what is presumed to be adequate treatment** or known exposure to ticks, may be included. They may have received inadequate treatment, or inadequate information about the possibility of residual ailments of tick-borne infections. Suspicion of, or fear of, a tick bite as the cause of the ailments, is also part of the inclusion criteria for this clinical pathway/assessment process.

**It is recommended that anyone who has undergone neuroborreliosis or Borrelia arthritis is to be checked three and possibly six months after treatment, which may help reduce long-term health problems and residual symptoms.** A careful evaluation of the primary diagnosis and treatment will be important for people with persistent ailments. One must re-evaluate the situation and think differential diagnoses.

Regardless of final diagnosis and treatment, **rehabilitation** should be considered for included patients.

## **8.2 Referral**

The general practitioner is expected to summarise the patient's medical history, refer to the results of relevant tests, and provide an overview of previous treatment, including what may have been done outside the public health services. Has anything been effective or given improvement?

Other relevant diseases, an updated list of medicines, and any other conditions and events in life that may be important, are desirable.

Patients should also be asked to write down their version of medical history. Copies of relevant case summaries and lab results that are not available where the patient is referred are enclosed with the referral.

The patient should be asked to consent to have case summaries and test results from other institutions obtained if necessary. The general practitioner should inform the patient about having realistic expectations for the new assessment process. Maybe you do not quite reach the finish line. The purpose of the clinical pathway is to confirm or rule out tick-borne diseases as the cause of the patients' ailments, and to uncover other possible explanations and then provide the correct treatment and possible rehabilitation by qualified personnel at the correct treatment level.

It is reasonable to expect that samples of Borrelia antibody have been taken before the referral, perhaps also TBE antibodies. We do not recommend starting with an extended sampling for tick-borne diseases, but that the specialist at the assessment center consider this as an option. Other specialists should be included in the assessment work such as neurologists, infectious disease specialists, dermatologists, endocrinologists, rheumatologists, paediatricians, psychiatrists etc.

## **8.3 Should patients refer themselves?**

We think that all relevant patients should receive an offer, but that general practitioners should refer. The general practitioner must be involved in assessing whether other referral places can be more relevant, and ensure that adequate and up-to-date health information is available. One can imagine situations where patients feel that the collaboration with their doctor is not optimal, and that they want to be referred. In such cases, a referral to our intended assessment agency will offer multidisciplinary assistance for assessing what must often be considered long-term, complex, and sometimes locked situations which the general practitioner will also benefit from. Everyone in the target group will receive an assessment.

### **Clinical Pathway Model**

The Nordic countries face different geographical challenges and organize their health services differently. The consensus can provide adequate guidelines for recommended content. The details may vary from country to country, e.g. whether an offer is to be made somewhere in the country, or at several multidisciplinary hospitals with specialist expertise in the field.

In any case, it is important that there are dedicated doctors who can implement the recommendations and not just add work to already busy personnel at outpatient clinics.

**The clinical pathway model** recommends several steps, adapted to the individual patient:

1. Referral by a physician

2. First meeting

- Anamnesis/medical history
- Physical examination
- Relevant blood tests
- Spinal puncture? Additional examinations of joints?

3. Second meeting

- Information
- Referral to another specialist/speciality?
  - Results of examinations and laboratory tests, other referrals?
  - Treatment?

4. Follow-up

- Progression / effect of treatment / status quo?

5. Referral to rehabilitation?

## 8.4 Checklist before referral

### Checklist before referral

(For neurological symptoms: Find out if the person has neuroborreliosis, or another neurological disorder.)

Everyone:

- Known exposure to ticks

If yes, visible tick, size and similar:

- Clinical findings and symptoms?
- Strong suspicion of tick-borne disease?
- Has the patient received treatment? If Yes, what kind and how long?
- Laboratory investigations: see the tables above
  - ECG on indication
  - Is testing for other tick-borne diseases than borreliosis and TBE applicable?
- Referring physician's evaluation

The clinical pathway is shown on the flow chart on page 31 and as an Attachment on page 43.



## **9. Social Rights and Rehabilitation**

The most common and troublesome problems after tick-borne infections are pain, fatigue, cognitive ailments and reduced work ability. These ailments can also be seen in other diseases/conditions. A broad differential diagnostic is therefore needed to clarify the situation prior to rehabilitation. There may also be more specific ailments (especially in the nervous system) such as muscle weakness, reduced mobility, emotional disturbances and pain.

## **9.1 General information on rehabilitation**

The rehabilitation processes should contribute to coping with the loss of functions related to demands set by our environment and society, and hopefully provide opportunities for improving the quality of life. There are no specific principles for rehabilitation after contracting a tick-borne disease. The processes follow the general principles for rehabilitation.

Illness, diseases, injury and prolonged strain affect the body and its functions. Changes in functional abilities can affect people's roles and daily lives, which in turn can affect the psyche and social conditions. In such a framework of understanding, people are regarded as acting subjects who influence their own lives in relation to the environment and the culture of which they are a part. Rehabilitation requires focusing on the **whole** more than on the sum of the individual parts. In a rehabilitation process, insight and knowledge are therefore required from the health services – not only on biomedical conditions, but also the psychosomatic situation.

Good knowledge of people's functional ability, coping ability and the demands set by activities in different arenas are **key factors** for adapting the content of rehabilitation processes.

Rehabilitation is a **collaborative process** between those involved: users, relatives, the workplace, physicians and rehab staff. It requires an interdisciplinary collaboration, often with the participation of several professional groups, and the involvement of the individuals themselves as active, equal participants. Professionals must focus on what is healthy and what the person's resources are in creating comprehensibility, manageability and participation. Rehabilitation is an **active process** that requires effort on the part of the rehabilitating patient to relate to where he or she is at the moment with experienced symptoms, and set specific **goals** to regain control, experience mastery, live with predictability and feel security for the future.

## **9.2 Rehabilitation processes**

Rehabilitation processes must be systematic and targeted.

They can be divided into the following phases:

- Clarification (gathering information, in-depth diagnostics and treatment, assessments)
- Setting goals
- Plan the process
- Implement the plan
- Evaluate the plan
- Use the plan in follow-up

### **9.3 General guidelines for rehabilitation**

1. Holistic approaches are used in a biopsychosocial model
2. Targeted, time-limited, patient-centered, interdisciplinary rehabilitation must be prepared in collaboration with the users. Relevant measures use knowledge-based practice, where evaluating the effect of interventions is included.
3. The general practitioner has the main responsibility for referral. If necessary, assessments are obtained from other operators such as the municipal health services or the specialist health services.

Specific, local intervention is implemented (such as physical activity and exercise, coping services, specific measures for coping with stress, diet, behaviour therapy).

When local measures are not effective, in the event of complicated issues or persistent, reduced ability to work and quality of life, interdisciplinary measures are recommended locally, or in the specialist health service.

Four principles that apply to welfare benefits when rehabilitating back to work in Norway:

1. The principle of assessment of incapacity to work in the event of illness
2. The principle of participation in one's own case
3. The principle of parallelism in rehabilitation
4. The principle of the workplace as the preferred place for rehabilitation to work

In Norway, the physician must assess the patient's incapacity for work in the event of illness. One should also look at whether work promotes the effects of treatment. That means it is inappropriate to carry out medical rehabilitation without safeguarding working relationships. Our relationship to working life must be mapped out and included in the rehabilitation pathway unless there are situations where returning to work is impossible.

### **9.4 Rehabilitation in the Nordic countries**

#### ***Norway***

The regional health authorities in Norway have an overview of and provide information about the public and private rehabilitation services in their health regions (see more on page 44 in this report).

No rehabilitation institution in Norway has its own diagnosis-specific rehabilitation programme for tick-borne diseases.

Sørlandets rehabiliteringssenter (rehabilitation center for Southern Norway) has a diagnosis-independent offer for fatigue / chronic pain. The center also offers services to patients which mostly emphasise long-term fatigue, regardless of diagnosis, when combined with chronic muscle and soft tissue pain.

An overview of national rehabilitation services in Norway and services for this group that may border on various national competence services is available on page 44 in this report.

### **Denmark**

A clinical center for the diagnosis, assessment, treatment and research of vector-borne infections was established in Odense, Denmark, in 2014 (Klinisk Center for Vektorbårne Infektioner). Their offer also includes rehabilitation. A similar offer is being put together at the Rigshospitalet in Copenhagen.

### **Sweden**

Sweden has had a research-based clinic in Uppsala since 2014 that receives patients with chronic ailments from suspected tick-borne diseases (Centrum för vektorburna infektioner). Follow-up measures are based on the results of an examination and assessment here.

### **Finland**

There is a professional community working with assessment, treatment and research on tick-borne diseases in Helsingfors, Åbo and Åland in Finland. They have no special recommendations or offers regarding sick leave or rehabilitation for Lyme disease or TBE. Necessary measures are implemented based on degree and type of disability, and the need for rehabilitative measures.

### **Åland, Finland**

In Åland, the health services offer a final follow-up (telephone call) about 6 months after treatment of a widespread Lyme disease infection. The work there is described as follows by Marika Nordberg, specialist in infectious disease medicine, at the Åland Borrelia Research Group:

"The most important thing is probably to talk with the patient to identify any remaining symptoms or anything else that needs to be investigated or addressed. We often have a telephone conversation or return visit about 2-3 weeks after the start of antibiotic treatment. Additional help is offered by specialist environments, if necessary. However, everyone is told during the first examination that we will be phoning them for follow-up 6 months later. We have time during the interim to monitor and discuss the patient's various symptoms. Patients find it reassuring to know that there is a plan for them."

## **10. Attachments**

## **10.1 Overview of Working Groups**

The names of the leaders of the working groups are indicated by **italics**.

### ***Working group Norway***

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Audun Aase, PhD, immunologist, NIPH

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Harald Reiso, MD, general practitioner, adviser at the Norwegian National Advisory Unit on Tick-borne Diseases, SSHF

Sølvi Noraas, physician, microbiologist, Norwegian Reference Laboratory for Borrelia, SSHF

Svein Høegh Henrichsen, general practitioner, senior adviser, Infectious disease control, Norwegian Directorate of Health

Tone Synnøstvedt, Norwegian Lyme Disease Association

Gro Moen Skjøtt, Norwegian Lyme Disease Association

Yvonne Kerlefsen, biologist, Norwegian National Advisory Unit on Tick-borne Diseases, SSHF

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Inger Johanne Wedding Hansen, physician, rheumatologist, SSHF

Kjersti Widding, physician, specialist in physical medicine and rehabilitation, Sørlandet rehabilitation center

Dag Tveitnes, PhD, physician, paediatrician, Stavanger University Hospital

Pascal Brügger-Synnes, physician, infectious disease medicine, Ålesund Hospital, Møre & Romsdal Health Services

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Ivar Tjernberg, PhD, physician, clinical chemistry, Kalmar County Region / Linköping University

Johanna Sjöwall, PhD, physician, infectious disease medicine, Östergötland Region

Matilda Lövmär, intern physician, Motala / Linköping, Östergötland Region

Herjan Bavelaar, physician, clinical microbiology, Jönköping County Region

Thomas Åkerlund, microbiologist, investigator, Swedish Public Health Agency (observer)

Ulf Törnebladh, medical expert, Swedish National Board of Health and Welfare (observer)

Karin Söderberg Löfdal, adviser, Swedish Medical Products Agency (observer)

### ***Working group Denmark***

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Mari Kanerva, PhD, physician, infectious disease medicine, Helsinki University Hospital

Dag Nyman, professor, physician, Åland Borrelia Research Group (Mariehamn)

Olli Vapalahti, PhD, MD, professor of zoonotic virology, University of Helsinki

Jarmo Oksi, PhD, physician, professor of infectious disease medicine, University Hospital and University of Åbo

### ***Steering group***

**Svein Høegh Henriksen**, Anna J. Henningsson, Randi Eikeland, Harald Reiso, Gro Moen Skjøtt, Tone Synnestvedt, Ingeborg Aaberge, Marika Nordberg, Sigurður Skarphéðinsson, Yvonne Kerlefsen.

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### ***Working group 2 (Patient clinical pathway)***

**Knut Eirik Eliassen**, Pascal Brügger-Synnes, Dag Tveitnes, Randi Eikeland, Svein Høegh Henriksen, Inger Johanne Wedding Hanssen.

### ***Working group 4 (Rehabilitation)***

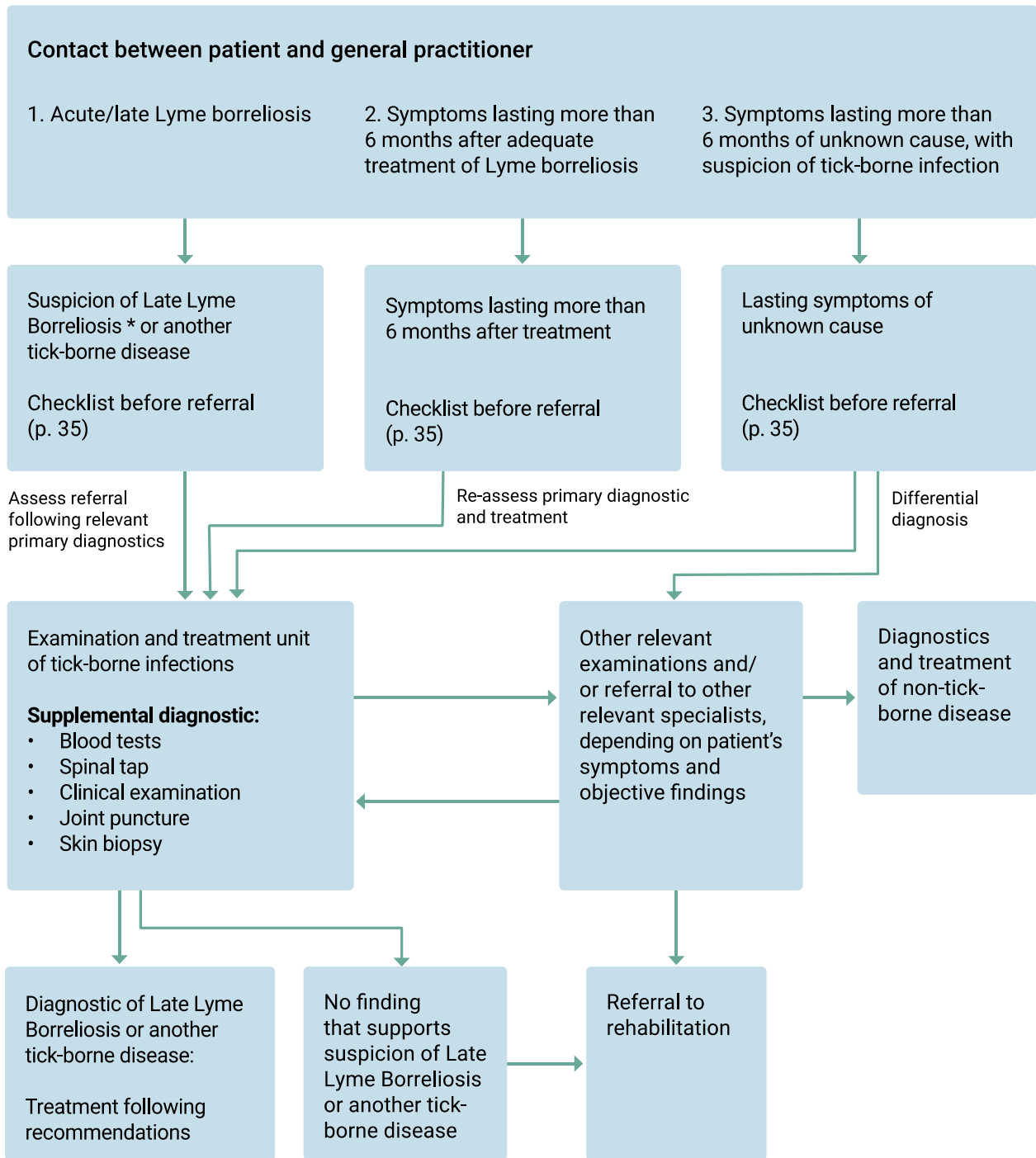
**Harald Reiso**, Kjersti Widding, Svein Erik Valle Prinz, Oddgeir Tjomsland.

### ***Editorial team***

**Svein Høegh Henriksen**, Tone Synnestvedt, Gro Moen Skjøtt, Randi Eikeland, Ingeborg Aaberge, Audun Aase, Knut Eirik Eliassen, Anna J. Henningsson, Sigurður Skarphéðinsson, Marika Nordberg, Kjersti Widding, Harald Reiso (Editor).

## 10.2 Model for recommended clinical pathway

### Clinical pathway for patients with lasting symptoms after suspected tick-borne diseases



\*) Suspicion of Late Lyme Borreliosis shall be diagnosed locally. Make sure that all relevant diagnostics have been done, and re-assess the need for a referral: antibodies, spinal tap, MRI cerebri, ECG, joint and skin examination.

Nordisk konsensus



### **10.3 More information about rehabilitation services in Norway**

An overview of national rehabilitation services in Norway can be found [here](#), and at the Regional Coordinating Unit ([RKE](#)) at the South-Eastern Norway Health Authority. The national [Rehabilitation Hotline](#) (800 300 61) that advises the public and health actors.

It is logical to look at what is offered for this group and compare it to the guidelines from the national competence services for:

1. employment rehabilitation ([more info here](#))
2. complex symptom disorders ([more info here](#))
3. CSF/ME ([more info here](#))
4. neuropathic pain ([more info here](#))
5. complex, severe psychosomatic conditions in children and adolescents ([more info here](#))
6. learning and mastery in health ([more info here](#))
7. children and adolescents with functional disabilities ([more info here](#))
8. sleep disorders ([more info here](#))

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**Design**

Itera as

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