PLEASE5+: Long-term outcomes and quality of life of patients with symptoms attributed to Lyme borreliosis

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Ancillary infectious topics
Study type	Observational invasive

Summary

ID

NL-OMON50085

Source
ToetsingOnline

Brief title
PLEASE5+

Condition

- Ancillary infectious topics

Synonym
Lyme disease, Post-treatment Lyme borreliosis Syndrome (PTLBS)

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Lyme borreliosis, Persistent symptoms, Quality of life, Treatment

Outcome measures

Primary outcome

The main study endpoint is the health-related quality of life (QoL) 5-8 years after participation in PLEASE. Health-related QoL will be assessed by the physical component summary (PCS) score of the RAND-36 Health Status Inventory, as was measured in the PLEASE study at five time points.

Secondary outcome

Secondary study endpoints are

- differences in long-term outcomes between the three PLEASE treatment groups;
- long-term impact of persistent symptoms attributed to Lyme borreliosis on (ability to) work, and social costs;
- reported use of medical or complementary interventions or support after PLEASE participation, and their association with the course of symptoms, quality of life and ability to work;
- determinants for the long-term course of symptoms and ability to work;
- the relationship between severity and duration of symptoms before treatment, and long-term outcomes; and
- the relationship between self-management strategies by patients and long-term outcomes and ability to work.

Study description

Background summary

After antibiotic treatment for Lyme borreliosis, 5-20% of patients report persistent symptoms for months to years. The effect of longer-term antibiotic treatment on these symptoms has been investigated in several studies, of which the Persistent Lyme Empiric Antibiotic Study Europe (PLEASE) study is the largest and most recent. Patients with persistent symptoms attributed to Lyme borreliosis were randomized into three arms to receive 3 months of doxycycline, clarithromycin/hydroxychloroquine, or placebo, after a standardized two weeks course of intravenous ceftriaxone. Patients were followed for up to one year. No beneficial effects were reported on neurological, neuropsychological, or quality-of-life endpoints.
Although persistent infection has not been demonstrated to be the cause of persistent symptoms in humans after antibiotic treatment, and results of randomized trials do not support prolonged antibiotic treatment for these symptoms, individual patients do report improvement of their health status after long-term antibiotic treatment or complementary therapies. After completion of the study visits, many patients in the PLEASE cohort might have continued the search for improving their persistent symptoms, both in regular and complementary health settings.
The aims of the PLEASE5+ study are to investigate the outcomes of the PLEASE participants at the longer term (between 5-8 year after PLEASE participation), as well as the impact of persistent symptoms attributed to Lyme borreliosis on work(ability). Based on the long-term outcomes in this cohort, predictors for the course of disease and ability to work will be explored. Furthermore, blood and urine samples will be collected for research on immunological and metabolic parameters and their potential influence on the course of persistent symptoms in these patients.

Study objective

The primary objective is to assess the long-term (5-8 years) quality of life in patients who previously participated in the placebo-controlled randomized controlled trial on the effect of prolonged antibiotic treatment on persistent symptoms attributed to Lyme borreliosis (PLEASE). Secondary objectives are:
- to assess differences in long-term outcome between the three treatment groups of PLEASE;
- to investigate the potential relationship between pre-treatment severity and duration of complaints, and long-term outcomes;
- to investigate the long-term impact of persistent symptoms attributed to Lyme borreliosis on societal status and ability to work;
- to collect data on the additional medical or complementary care, interventions and/or support that patients have undergone after participation in PLEASE, and to correlate these data with their course of symptoms, quality of life and ability to work;
- to assess the role self-management of patients as determinant for long-term

outcomes and ability to work;
- to assess predictors for the long-term course of complaints and workability;
- to explore a diagnostic decision model, based on the determinants for long-term outcome, including patient characteristics, self-management, outcome expectations and interventions, to guide future individual patient management; and
- to obtain blood and urine samples to investigate the role of immunological and metabolic parameters in persistent symptoms and long-term outcomes.

Study design

This is an observational cohort study, in an existing cohort of 280 participants who previously (between 5 and 8 years ago) participated in the PLEASE trial. Participants will be subjected to extensive questionnaires once and will be asked to collect blood and urine samples once. A randomly composed group of patients will be interviewed. Furthermore, focus groups will be organised for subgroups of patients with an intervention or self management strategy that is identified as determinant for beneficial long-term outcomes after analyses.

Study burden and risks

PLEASE5+ participants will be subjected to a comprehensive (online) questionnaire. Blood and urine will be collected once. A subgroup of patients, after providing additional consent, will be interviewed about their experiences related to work, medical and social care, social relationships, and self-management in relation to their persistent symptoms and long-term outcomes. If intervention methods undergone by participants are identified that are associated with beneficial effects, patients will be invited to participate in focus groups related to those specific therapies.
There are no direct benefits for individual participants. The burden and risk of venous blood collection is low. No other risks are expected.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 10
Nijmegen 6525 GA
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 10
Nijmegen 6525 GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Subjects who have been randomized into the PLEASE study and not have subsequently withdrawn informed consent for the PLEASE or PLEASE5+ study are eligible. Inclusioncriteria for PLEASE were: persistent symptoms (musculo-skeletal pain, arthritis, arthralgia, neuralgia, sensory disturbances, dysesthesia, neuro-psychological disorders, or cognitive disorders, with or without persistent fatigue) that were attributed to Lyme borreliosis, either temporally related within 4 months to a physician-confirmed episode of erythema migrans or otherwise proven symptomatic Lyme borreliosis manifestation (by positive biopsy, PCR, culture, or intrathecal antibody production); or with a positive B. burgdorferi IgG or IgM immunoblot.

Exclusion criteria

Subjects who have died, subjects who have withdrawn informed consent to PLEASE participation, have not consented to receive PLEASE5+ study information, and who do not provide written informed consent to PLEASE5+ participation are excluded.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Health services research

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-07-2020
Enrollment:	280
Type:	Actual

Ethics review

Approved WMO

Date:	13-07-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 21558
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL71890.091.20

Register	ID
Other	NL8224
OMON	NL-OMON21558