The Netherlands ME/CFS Cohort and Biobank (NMCB)

Published: 08-04-2024
Last updated: 27-12-2024

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON56812

Source
ToetsingOnline

Brief title
NMCB

Condition

- Other condition
- Autoimmune disorders

Synonym
chronic fatigue syndrome, Myalgic Encephalomyelitis

Health condition

neurological disorders; disorders with unknown etiology

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Biobank, Biomedical research, ME/CFS, Patient registry

Outcome measures

Primary outcome

All 2100 participants (including ME/CFS patients, healthy and clinical controls) will be assessed at one time point for phenotypic characterization. We will collect self-report (demographic (including ethnicity), behavioral, symptoms), clinical, and neurocognitive data, coupled with the collection of biomaterials for a national biobank. Cohort-wide analyses such as whole genome sequencing, RNA sequencing, and measurements of cells, proteins or compounds are both part of the primary study objective to characterize ME/CFS patients, as well as part of the secondary objective to have this data available in a large and extensive biobank, along with additional biomaterials for specific research questions.

Secondary outcome

The collection of biomaterials for a national biobank for storing plasma, serum, PBMCs, DNA, RNA, nasal swabs, and saliva, urine and fecal samples. Cohort-wide measured data of part of the materials (i.e. RNA sequencing of all PAXgene whole blood samples under the scope of this study protocol) will be part of the biobank.

MRI-results (for part of the subjects)

Study description

Background summary

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a prolonged debilitating disease, with unknown aetiology and unexplained pathophysiology, resulting in a substantial reduction in previous activity levels and quality of life. Diagnosis remains a challenge in the absence of biomarkers (e.g. laboratory or imaging tests) and relies on the presence of characteristic symptoms and the exclusion of disorders that may explain the symptoms, as well as the patient*s clinical history. Patients often report an array of symptoms, including extreme exhaustion with exercise intolerance and post-exertional malaise, impaired sleep, cognitive dysfunction, musculoskeletal and/or neuropathic pain, and orthostatic intolerance, and the inability to stand for any length of time due to symptoms related to autonomic nervous system dysfunction. However, the presence and severity of symptoms vary between patients and can fluctuate over time. For healthcare professionals who encounter ME/CFS*s characteristically heterogeneous symptom profiles and illness course, management of these patients also remains a challenge.

The prevalence of myalgic encephalomyelitis or chronic fatigue syndrome (ME/CFS) in the Netherlands is unknown but, based on international surveys, estimated to be between 40,000 and 150,000 patients. Notwithstanding, the Netherlands has invested little in biomedical research into ME/CFS; research is scattered, with limited (inter)national collaboration, lacks an infrastructure for patient data and sample collections, and provides poor funding prospects to early career researchers creating a self-perpetuating situation. Meanwhile, such research is urgently needed: patients experience debilitating physical symptoms with little hope of spontaneous recovery. In the absence of a biomarker the diagnosis relies on clinical judgment while treatment is symptomatic. Further, ME/CFS is often stigmatized and linked with high unemployment rates, causing substantial personal and societal costs.

It is important to acknowledge that ME/CFS research initiatives should be informed by the experiences and desires of the patient community. ME/CFS patients, along with their families and advocates, have consistently expressed a strong desire for increased research efforts to understand the root causes, improve diagnostic accuracy, and develop effective treatments. The patient community has been vocal about the urgent need to validate the reality and severity of this condition, combat stigma, and mitigate the substantial impact it has on their daily lives.

To address this situation, ZonMw developed a *ME/CFS Research Agenda* (RA) to initiate *substantive and long-term biomedical research into ME/CFS*. The Netherlands ME/CFS Cohort and Biobank (NMCB) consortium was co-created with

Dutch patient organizations to implement the clear directives provided by this RA. The NMCB mission is to establish a collaborative national research infrastructure that collects and secures high-quality patient data, to test hypotheses that will lead to a sound mechanistic understanding of ME/CFS, and to see their translation into rational diagnosis and treatment. The NMCB will actively disseminate its scientific output to improve the lives of patients and their position in society. It builds on the principles of multidisciplinarity, patient and stakeholder involvement, and (inter)national cooperation. Hence, open science and FAIR data use are the core principles of the ME/CFS patient registry and biobank.

ME/CFS patients have been and will continue to be involved throughout this research process. Through the integration of patient perspectives, the NMCB endeavours to bridge the gap between research and patient experiences, ultimately leading to better understanding, improved healthcare practices, and enhanced quality of life for people living with ME/CFS. By conducting this research, not only will our scientific knowledge of ME/CFS be expanded but also the ME/CFS community will be empowered and foster a sense of hope, solidarity, and validation.

Study objective

The primary objective is to characterise and understand the heterogeneity in patients with ME/CFS (i.e. comorbidities, variability in symptoms and disease progression, severity, and cognitive and autonomic impairment). Therefore, the secondary objective is to develop a biobank with extensive and uniformly collected clinical data and biological samples for the identification and validation of biomarker panels and data-driven approaches. This biobank will facilitate ME/CFS research as well as research into related post-infectious fatigue syndromes (PIFS; e.g. long-COVID, Lyme*s disease, Q-fever). Such studies will undergo a separate ethics review.

Study design

Cross-sectional collection of samples and data from cases and controls

Study burden and risks

All procedures have a moderate risk and moderate burden.

Questionnaires: Burden is limited through online data collection that allows participants to self-pace. Patients can select to limit their involvement to filling out a core questionnaire set whereby the remainder of questionnaires are optional.

Physical assessments: All participants will be given the option to either come

into the clinic for these assessments or to be visited at home, limiting the patient burden of having to travel.

Blood draws: A minor burden exists for blood draws, which may cause discomfort and bruising at the injection site, and some participants may feel faint.

MRI: There are no major risks involved with MRI scanning. Well-trained personnel will perform neuroimaging acquisitions from all participants. Scanning may cause discomfort during scanning, and some participants may feel claustrophobic. Individuals who have difficulties to lie still, or have non-removable metal objects/materials (e.g. pacemakers) in their body will be excluded.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet the following criteria:
- The ability to provide informed consent.
- A willingness and ability to comply with all aspects of the protocol, including physical assessments and biospecimen collections.

In addition to the general inclusion criteria, ME/CFS patients must meet the following criteria:
- A diagnosis of ME/CFS with verification by a medical doctor (i.e., excluding alternative diagnoses). A diagnosis in this context implies meeting the case definitions as established according to (either/or) the CDC-94 criteria (also called the Fukuda criteria (4)), the Canadian Consensus Criteria (CCC) (3), the International Consensus Criteria (ICC) (21), or Institute of Medicine (IOM) (22) case definitions. These symptom definitions will be established in an interview and a physical assessment by well-trained personnel.

For MRI: - A willingness and ability to comply with all aspects of the MRI protocol.

In addition to the general inclusion criteria, clinical controls must meet the following criteria:
- A diagnosis of MS, Q-fever, long-COVID, or Lyme*s disease. With the exception of MS, if any of the clinical controls with Q-fever, long-COVID, or Lyme*s disease meet ME/CFS case definitions, they will be invited to join the study as an ME/CFS case.

Exclusion criteria

All participants:
- Taking immune modulatory drugs in the past 3 months;
- Having a serious medical condition that may explain ME/CFS-like symptoms, such as cancer, coronary heart disease, uncontrolled diabetes, chronic infection (hepatitis B and C, tuberculosis, HIV), inflammatory disorders, autoimmune diseases (e.g. rheumatoid arthritis, lupus, or polymyositis), severe COPD or other severe ongoing respiratory disease, severe anaemia, kidney failure, Addison*s or Cushing*s disease, or serious neurological disorder (e.g. Parkinson*s Disease);
- Excessive consumption of alcohol or recreational drugs as defined by a score > 2 on the CAGE-AID survey;
- Unwillingness to stop consumption of alcohol and recreational drugs for at least 48 hours prior to the study visit;

- A mood disorder or other psychiatric diagnosis, determined by asking if they have a mood disorder or other psychiatric diagnosis, and if they are taking medication for their diagnosis, prior to entering the study. As part of checking a potential participant*s eligibility for the study, they will be asked to fill in the Participant Health Questionnaire-2 to determine if they have a score of >= 3, indicating major depressive disorder;
- Pregnant or breastfeeding in the past 12 months;
- BMI >40;
- Age <18 or >65 years.

For MRI: -patients who are unable to lay still for scanning due to claustrophobia or severe back pain
- history of gross neurological pathology (strategic or lobar infarcts or stroke or neurotrauma) prior to enrolment (besides a serious neurological disorder)

In addition, for healthy controls and Multiple Sclerosis controls:
- No previous diagnosis of ME/CFS;
- Not meeting either of CDC94/CCC/ICC/IOM case definitions, according to the DePaul Symptom Questionnaire.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-10-2024
Enrollment:	2100
Type:	Actual

Ethics review

Approved WMO Date:	08-04-2024
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-06-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-10-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
CCMO	NL84795.018.23