

Trial Nation
Clinical Trials Denmark



DANISH DEMENTIA
RESEARCH CENTRE

CENTER FOR DEMENTIA

A network of Danish memory clinics

Your clinical research partner within Alzheimer's
disease and other dementia diseases.

Trial Nation Dementia

a network of Danish Memory Clinics

Trial Nation Dementia is a network of Danish memory clinics with experience in clinical research with investigational medicinal products in Alzheimer's disease, Huntington's disease and other neurodegenerative disorders.

The network was established in 2018 based on a preexisting research network of memory clinics initially developed in a large randomized controlled national multicenter clinical trial on physical exercise in patients with mild Alzheimer's disease (ADEX).

The five memory clinics successfully collaborated on and completed this complex intervention trial with 200 patients^{1,2}, which has further developed and strengthened their capacity for conducting clinical drug trials.

As members of the world-wide observational study on Huntington's disease, the Enroll-HD study³ (<https://enroll-hd.org>), three of the memory clinics also have extensive experience with systematic longitudinal outcome assessments in patients with Huntington's disease, which has contributed to widening of the target group of patients in the network.

The main purpose of Trial Nation Dementia is to facilitate clinical trials regarding pharmacological interventions and application of new medical technology in the diagnosis and treatment of neurodegenerative cognitive disorders.

Trial Nation Dementia offers one point of contact to the network.

For coordinated request to all clinics please contact:

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Overview of Trial Nation Memory clinics

Table 1: DANISH MEMORY CLINICS PARTICIPATING IN TRIAL NATION DENMARK	REGION
Danish Dementia Research Centre, Dept. of Neurology, Rigshospitalet, University of Copenhagen	Capital Region of Denmark
Dementia Research Centre, Dept. of Neurology, Zealand University Hospital	Region Zealand
Dementia Clinic Dept. of Neurology, Odense University Hospital, Odense & Svendborg	Region of Southern Denmark
Dementia Clinic, Dept. of Neurology, Aarhus University Hospital	Central Denmark Region
Dementia Clinic, Dept. of Neurology, Aalborg University Hospital	The North Denmark Region



Patients

A wide range of neurodegenerative disorders

The memory clinics in the Trial Nation dementia network have access to patient cohorts with a wide range of disorders, including:

- Alzheimer's disease
- Vascular dementia
- Dementia with Lewy bodies
- Parkinson's disease with dementia
- Frontotemporal dementia.
- Mild cognitive impairment, including prodromal Alzheimer's disease
- Subjective cognitive decline
- Huntington's disease
- Spinocerebellar ataxia
- Hereditary spastic paraparesis

Large well-characterized cohorts

The routine extensive diagnostic work-up and biomarker-based diagnostic workflow in early phase neurodegenerative disorders, enables the memory clinics to have access to well-characterized patient cohorts from which participants for clinical trials can be recruited.

According to the national quality registry for diagnostic evaluation of dementia, DanDem¹, 9.000-10.000 patients with cognitive symptoms or dementia are referred annually to Danish memory clinics. About 50% of them are referred to the 5 memory clinics in Trial Nation Dementia network.

Alzheimer's disease

Approximately 35% of all referred patients are diagnosed with Alzheimer's disease dementia and 20% with Mild Cognitive Impairment (including prodromal Alzheimer's disease).

Patients with Mild Cognitive Impairment and Alzheimer's disease are seen on follow-up during a variable length of time in the participating memory clinics.

Huntington's disease

Defined by the Danish Health Authority, the management of patients with Huntington's disease is a specialized function centralized in 3 neurological departments in Denmark (Aarhus University Hospital, Odense University Hospital and Copenhagen University Hospital - Rigshospitalet) who see in total approximately 500 patients with symptomatic Huntington's disease, including approximately 100 individuals with presymptomatic Huntington's disease on a regular basis.

Many of these participate in the Enroll-HD study, a worldwide observational study for Huntington's disease families. Thus, recruitment to drug trials may be based on access to detailed information on patients in the database.

All 3 sites with Huntington's disease patients have access to state-of-the-art molecular genetics laboratories with experience in the genetic diagnostic procedures.

¹ <https://www.rkkp.dk/kvalitetsdatabaser/databaser/dansk-klinisk-kvalitetsdatabase-for-demens>

Trial experience and capacity

Based in clinical neurology, participating memory clinics have up to 25 years of experience in conducting clinical trials from more than 40 phase I-IV studies, with the inclusion of more than 300 patients with various neurodegenerative disorders.

We have a successful track record for timely delivery of high-quality data from clinical trials. For more information see table 1.

Trial participants diagnosed in a specialized clinical setting with trained staff

Trial participants are mainly recruited from the cohorts of patients already on the memory clinic lists. The majority of the staff responsible for the recruitment of patients and for the conduction of clinical trials have clinical experience from memory clinics and trial experience from previous clinical trials.

Biomarker based diagnoses with frequent use of lumbar puncture

All memory clinics in the network are based in neurology, and assessment of brain imaging biomarkers as well as lumbar puncture is used

on a routine basis in patients referred for diagnostic work-up of cognitive impairment.

Access to state-of-the art brain imaging techniques

All memory clinics in the network have access to MRI and FDG-PET on site, and some have also access to amyloid- and tau-PET.

Low screening failure rate

Due to the access to well-characterized patient cohorts, and the extensive experience in managing patients with Alzheimer, Huntington's disease and other neurodegenerative disorders, the network has a relatively low screen failure rate compared to international standards, with a median around 30 %, for previous and current trials.

High retention rate

As most patients are already in contact with the memory clinics, patient cooperation can be taken into account in the recruitment process, leading to a relatively high retention rate (70 % - 100 %).

Overview of Trial Nation Dementia clinics

Table 2:

Access to investigations

Clinic	Patients	Phase	CSF biomarkers	MRI	FDG PET	Amyloid PiB-PET	Tau PET	PET MRI	Gene testing	Contact
Danish Dementia Research Centre Dept. of Neurology Rigshospitalet University of Copenhagen	AD, DLB, FTD, HD, MCI, PDD, VAD, SCD, SCA	Phase I, II, III, IV Incl. FiH.	+	+	+	+	+	+	+	Director of Clinical Trial Unit, consultant neurologist Kristian Steen Frederiksen kristian.steen.frederiksen@regionh.dk For Huntington's Disease: Consultant neurologist Lena Hjermand lena.elisabeth.hjermand.01@regionh.dk
Dementia Research Centre, Dept. of Neurology, Zealand University Hospital	AD, DLB, FTD, MCI, PDD, VAD, SCD	Phase II, III, IV	+	+	+	(+)	(+)	(+)	+	Consultant neurologist, Ass. Professor, Peter Høgh pjh@regionsjaelland.dk
Dementia Clinic Department of Neurology, Odense University Hospital, Odense & Svendborg	AD, DLB, FTD, HD, MCI, PDD, VAD	Phase II, III, IV	+	+	+	+		+	+	Neurologist Berit Dall Sørensen berit.dall.sorensen@rsyd.dk For Huntington's Disease: Professor, Consultant neurologist Morten Blaabjerg morten.blaabjerg1@rsyd.dk
Dementia Clinic, Dept. of Neurology, Aarhus University Hospital	AD, DLB, FTD, MCI, PDD, VAD, SCA	Phase II, III, IV	+	+	+	+	+	+	+	Consultant neurologist Hanne Gottrup hannegott@rm.dk
Dementia Clinic, Dept. of Neurology, Aalborg University Hospital	AD, DLB, FTD, (HD), MCI, PDD, VAD	Phase III, IV	+	+	+				+	Consultant neurologist Karsten Vestergaard k.vestergaard@rn.dk

Note: AD = Alzheimer's disease; CSF = cerebrospinal fluid; DLB = Dementia with Lewy bodies; FDG PET = fluorodeoxyglucose Positron Emission Tomography; FTD = Frontotemporal Dementia; HD = Huntington's disease; MCI = Mild Cognitive Impairment; MRI = Magnetic Resonance Imaging; PDD = Parkinson's Disease Dementia; PiB = Pittsburgh compound B; VAD = Vascular Dementia; SCA = Spino Cerebellar Ataxia; SCD = Subjective Cognitive Decline.

"+" = method available in-house; "(+)" = method available via collaboration with other hospitals.

Harmonized diagnostic criteria

The memory clinics constituting the Trial Nation Dementia network collaborate on:

- A uniform set of diagnostic criteria for specific neurodegenerative disorders (see table 3).
- Standardized analysis of blood and cerebrospinal fluid (CSF) – compliant with the Alzheimer’s Association quality control program for CSF biomarkers.

- harmonization initiatives and clinical rater training at annual network meetings
- Preferred minimum set of rating scales in relation to diagnostic work-up and regular clinical reassessments.

The clinics have experience with several other instruments and scales as well (see table 4).

Table 3: DIAGNOSTIC CRITERIA USED IN CLINICAL PRACTICE

Diagnosis	Diagnostic criteria
Dementia	National Institute of Aging and Alzheimer’s Association (NIA-AA) workgroup criteria (2011) ^{4*}
Mild Cognitive Impairment	Winblad criteria (2004) ⁵
Mild Cognitive Impairment due to Alzheimer’s disease	National Institute of Aging and Alzheimer’s Association (NIA-AA) workgroup criteria (2011) ^{6*}
Alzheimer’s disease dementia	National Institute of Aging and Alzheimer’s Association (NIA-AA) workgroup criteria (2011) ^{4*}
Vascular dementia	The International Society for Vascular Behavioral and Cognitive Disorders (VASCOG) criteria (2014) ⁷
Dementia with Lewy bodies	Fourth consensus report of the DLB Consortium (2017) ⁸
Behavioural variant frontotemporal dementia	Revised diagnostic criteria for the behavioural variant of frontotemporal dementia (2011) ⁹
Language variants frontotemporal dementia	Classification of primary progressive aphasia and its variants (2011) ¹⁰
Huntington’s disease	Diagnostic Criteria for Huntington’s Disease Based on Natural History (2014) ¹¹

* Centers also have experience with the NIA-AA 2018 AD criteria

Table 4: CLINICAL OUTCOME MEASURES USED IN CLINICAL PRACTICE

Outcome	Scale
Global function	Clinical Dementia Rating (CDR) ¹²
Cognition	Mini-Mental State Examination (MMSE) ¹³ Rowland Universal Dementia Assessment (RUDAS) ¹⁴ Addenbrook Cognitive examination (ACE) ¹⁵
Activities of daily living	Disability Assessment for Dementia (DAD) ¹⁶ Functional Assessment Questionnaire (FAQ-IADL) ¹⁷
Mood	Geriatric Depression Scale 15 items (GDS-15) ¹⁸ Major Depression Inventory (MDI) ¹⁹
Neuropsychiatric symptoms	Neuropsychiatric Inventory - questionnaire (NPI-Q) ²⁰
Motor Symptoms in Huntington's disease	Unified Huntington's Disease rating scale - movement (UHDRSm) ²¹

Updates regarding Trial Nation Dementia are posted on:

- www.trialnation.dk
- www.linkedin.com/in/trialnation

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