

# Dutch Multiple sclerosis study (DMSS)

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1. Disability & Quality of life (descriptive nature, primary analyses) Change in patient-reported outcome variables in overall group (MS diagnosis) and subgroups (CIS, RRMS, SPMS, PPMS) from baseline to 8-year follow-up • Change in...

<b>Ethische beoordeling</b>	Positief advies
<b>Status</b>	Werving gestopt
<b>Type aandoening</b>	-
<b>Onderzoekstype</b>	Observationeel onderzoek, zonder invasieve metingen

## Samenvatting

### ID

NL-OMON22564

### Bron

NTR

### Verkorte titel

Not applicable

### Aandoening

Multiple sclerosis

## Ondersteuning

**Primaire sponsor:** Nationaal MS Fonds Industrieweg 130C 3044 AT Rotterdam 010 - 591 98 39 info@nationaalmsfonds.nl Curavista bv Markt 9 4931 BR Geertruidenberg Tel: 0162 520 964 info@curavista.nl MS4 Research Institute Dr. Peter Joseph (Sjef) Jongen Ubbergseweg 34 6522 KJ Nijmegen The Netherlands

**Overige ondersteuning:** See sponsors

## Onderzoeksproduct en/of interventie

## Uitkomstmaten

### Primaire uitkomstmaten

The primary study outcomes are disabilities (MSIP-Disability) and disability perceptions (MSIP-

## Toelichting onderzoek

### Achtergrond van het onderzoek

MS is a chronic disease of the central nervous system, in which immune-mediated inflammation or degeneration leads to loss of myelin and axons. In most patients disease course is initially characterized by relapses and remissions: relapsing remitting MS (RRMS). After the first relapse patients are diagnosed as Clinically Isolated Syndrome (CIS) suggestive of MS. In CIS and RRMS immune activity and inflammation are the major pathophysiological processes, which may be positively influenced by disease-modifying treatment (DMT). In most patients with RRMS the disease course changes into secondary progression (SP), a phase that is characterized by slow increase of disability and disappearance of relapses. In about 10-15% of MS patients symptoms start and develop slowly without relapses (primary progression, PP). In PPMS and SPMS the continuous slow increase in disability is thought to result from degenerative processes, that are not modified by DMT.

Data on the long-term changes in disability in patients with MS or CIS are fragmented. Prospective studies on long-term disability were performed in the Australia, USA, Canada, France and Italy. These studies were often limited to certain regions or to patients treated in academic centers. As a result, the findings cannot easily be generalized to patients in the Netherlands. Information on the patient-reported long-term disability in MS and CIS patients in the Netherlands is lacking. Likewise, prospective data on the long-term changes in disability perception and HR-QoL are limited, and virtually absent for patients in the Netherlands.

Data on the patient-reported long-term disability (Multiple Sclerosis Impact Scale) and quality of life (Multiple Sclerosis Quality of Life-54) in patients with MS or CIS in the Netherlands will significantly contribute to better understand the risk of Dutch patients to develop major levels of disability. In addition, the Expanded Disability Status Scale (EDSS) will be used to measure disability from a clinical point of view. In RRMS, SPMS and CIS patients data on long-term disability and self-reported adherence to DMT will enable to study relations between disease modifying treatment (DMT) and the risk to reach major levels of disability. In PPMS patients information on the long-term disability will provide essential data on the natural course of progressive MS in the Netherlands and are a reference for future treatments

### Doel van het onderzoek

#### 1. Disability & Quality of life (descriptive nature, primary analyses)

Change in patient-reported outcome variables in overall group (MS diagnosis) and subgroups (CIS, RRMS, SPMS, PPMS) from baseline to 8-year follow-up

- Change in disabilities [MSIP], corrected for demographic and disease characteristics

#### 1. H0: Disabilities [MSIP] remain constant over time between baseline and last follow-up

Ha: Disabilities [MSIP] change over time between baseline and last follow-up

And/or

2. H0: Disabilities [MSIP] remain constant from study enrolment and follow-up time depending on data

Ha: Disabilities [MSIP] change from study enrolment and follow-up time depending on data

- Change in disability perceptions [MSIP], corrected for demographic and disease characteristics

1. H0: Disability perceptions [MSIP] remain constant over time between baseline and last follow-up

Ha: Disability perceptions [MSIP] change over time between baseline and last follow-up  
And/or

2. H0: Disability perceptions [MSIP] remain constant from study enrolment and follow-up time depending on data

Ha: Disability perceptions [MSIP] change from study enrolment study enrolment and follow-up time depending on data

- Change in mental HRQoL [MSQoL-54], corrected for demographic and disease characteristics

1. H0: Mental HRQoL [MSQoL-54] remains constant over time between baseline and last follow-up

Ha: Mental HRQoL [MSQoL-54] changes (if mean change in score  $\neq$  MCID) over time between baseline and last follow-up

And/or

2. H0: Mental HRQoL [MSQoL-54] remains constant from study enrolment and follow-up time depending on data

Ha: Mental HRQoL [MSQoL-54] changes (if mean change in score  $\neq$  MCID) from study enrolment and follow-up time depending on data from baseline to MX

- Change in physical HRQoL [MSQoL-54], corrected for demographic and disease characteristics

1. H0: Physical HRQoL [MSQoL-54] remains constant over time between baseline and last follow-up

Ha: Physical HRQoL [MSQoL-54] changes (if mean change in score  $\neq$  MCID) over time between baseline and last follow-up

And/or

2. H0: Physical HRQoL [MSQoL-54] remains constant from study enrolment and follow-up time depending on data

Ha: Physical HRQoL [MSQoL-54] changes (if mean change in score  $\neq$  MCID) from study enrolment and follow-up time depending on data from baseline to MX

## 2. Disability & Quality of life (secondary analyses)

- Intra-individual HRQoL change in overall groups and subgroups

1. H0: Intra-individual change in HRQoL from baseline to last follow-up in subgroup 1a is equal to intra-individual change in HRQoL in subgroup 1b (e.g. male vs. female)

Ha: Intra-individual change in HRQoL from baseline to last follow-up in subgroup 1a is not

equal to intra-individual change in HRQoL in subgroup 1b (e.g. male vs. female)

H0: There is no interaction of subgroups on the within-subject change in HRQoL over multiple follow-up measurements between baseline and last-follow-up.

Ha: There is an interaction of subgroups on the within-subject change in HRQoL over multiple follow-up measurements between baseline and last-follow-up.

Specify subgroups (subgroup 1a vs. 1b (vs. 1c))

Sex: male vs. female: not equal

Duration disease: longer vs. shorter: not equal

Type MS: CIS, RRMS, SPMS, PPMS: not equal

Age: subgroups based on literature (e.g. MS Base)/ median

Degree of disabilities (each domain of MSIP): low vs. moderate vs. high, median: not equal

Degree of HRQoL: low vs. moderate vs. high: not equal

Treatment center: generic vs. specialized: not equal

Treatment center: South NL vs. North NL: not equal

Specialist education: year of education: not equal

Type DMD: first-line vs. second-line: not equal

Or

2. H0: mean HRQoL in subgroup 1a is equal to mean HRQoL in subgroup 1b at M0, M24, M48, M72, M96

Ha: mean HRQoL in subgroup 1a is not equal to mean HRQoL in subgroup 1b at M0, M24, M48, M72, M96

Specify subgroups (subgroup 1a vs. 1b (vs. 1c))

Sex: male vs. female: not equal

Duration disease: longer vs. shorter: not equal

Type MS: CIS, RRMS, SPMS, PPMS: not equal

Age: subgroups based on literature (e.g. MS Base)/ median

Degree of disabilities (each domain of MSIP): low vs. moderate vs. high, median: not equal

Degree of HRQoL: low vs. moderate vs. high: not equal

Treatment center: generic vs. specialized: not equal

Treatment center: South NL vs. North NL: not equal

Specialist education: year of education: not equal

Type DMD: first-line vs. second-line: not equal

- Comparison of HRQoL of study sample with Dutch population and/or other chronic diseases

1. H0: HRQoL is equal in patients with MS at study enrolment and the general Dutch population/ other chronic disease (incl. MS Base)

2. Ha: HRQoL is not equal in patients with MS and the general Dutch population other chronic disease (incl. MS Base) at study enrolment

H0: HRQoL is equal in patients with MS at X months at study enrolment and the general Dutch population/ other chronic disease (incl. MS Base)

Ha: HRQoL is not equal in patients with MS at X months at study enrolment and the general Dutch population other chronic disease (incl. MS Base)

Association between disease variables:

- Change in disabilities and change in disability perceptions

1. H0: Long-term increase in disabilities is not correlated with an increase in disability perceptions

Ha: Long-term increase in disabilities is correlated with long-term increase in disabilities perceptions ('response shift' due to adaptation to situation)

- Change in disabilities and change in HRQoL

1. H0: Long-term increase in disabilities is not correlated with long-term decrease in quality of life

Ha: Long-term increase in disabilities is correlated with the long-term decrease in quality of life ('response shift' due to adaptation to situation).

2. Increase in disabilities (perceptions) is preceded by decrease in quality of life

Descriptive: differences in QoL preceding the decrease in disabilities (perceptions)

- Increase in disabilities and relapses

1 H0: There is no association between number of relapses (Annualized Relapse Rate) and increase in disabilities.

Ha: There is an association between number of relapses (Annualized Relapse Rate) and increase in disabilities.

Lineaire regression: an extra relapse (onafhankelijke variabele), contributes to the increase in disabilities (dependent variabele)

- Change in assessment adherence and change in disabilities (perceptions)

1. H0: There is no association between early discontinuation of assessment and an increase in disabilities (perceptions) in the year before discontinuation

Ha: There is an association between early discontinuation of assessment and an increase in disabilities (perceptions) in the year before discontinuation

- Change in assessment adherence and change in HRQoL

2. H0: There is no association between early discontinuation of assessment and an increase in physical HRQoL in the year before discontinuation

Ha: There is an association between early discontinuation of assessment and an increase in physical HRQoL in the year before discontinuation

3. H0: There is no association between early discontinuation of assessment and an increase in mental HRQoL in the year before discontinuation

Ha: There is an association between early discontinuation of assessment and an increase in mental HRQoL in the year before discontinuation

3. Trends in treatment utilization, persistence and effectiveness (descriptive and change over time, primary analyses)

Trends in treatment utilization

- Trends in the prescription of first-line and second-line DMDs

o Time between diagnosis and prescription first-line DMD, prescription second-line DMD

o Time between first-line and second-line DMDs: differences between subgroups based on gender, EDSS, relapses

Descriptive: mean (SD)

- Prescription trends follow Dutch guidelines

## Qualitative discussion

### Effectiveness of first-line and second-line DMDs (RRMS and SPMS patients)

#### Descriptive:

- Frequencies on first-line DMD
  - o Number of relapses: Mean (SD)
  - o Disabilities and disability perceptions: Mean (SD)
  - o Mental and physical HRQoL: Mean (SD)
- Frequencies on second-line DMD
  - o Number of relapses: mean (SD)
  - o Disabilities and disability perceptions: Mean (SD)
  - o Mental and physical HRQoL: Mean (SD)
- Adherence (discontinuation) to DMD treatment and change in disabilities
  1. H0: Persistent (based on literature: e.g. >2 yrs) patients to DMDs for MS report equal amount of disabilities compared to non-persistent (<2yrs) patients  
Ha: Persistent (based on literature: e.g. >2 yrs) patients to DMDs for MS report less amount of disabilities compared to non-persistent (<2yrs) patients
  2. H0: Persistent (based on literature: e.g. >2 yrs) patients to DMDs for MS report equal amount of less mental HRQoL compared to non-persistent (<2yrs) patients  
Ha: Persistent (based on literature: e.g. >2 yrs) patients to DMDs for MS report less amount of less mental HRQoL compared to non-persistent (<2yrs) patients
  3. H0: Persistent (based on literature: e.g. >2 yrs) patients to DMDs for MS report equal amount of less physical HRQoL compared to non-persistent (<2yrs) patients  
Ha: Persistent (based on literature: e.g. >2 yrs) patients to DMDs for MS report less amount of less physical HRQoL compared to non-persistent (<2yrs) patients
  4. H0: There is no association between patients with stable disease over study period and treatment persistence  
Ha: There is an association between patients with stable disease over study period and treatment persistence
  5. H0: There is no relationship between patients with high disease activity and treatment persistence  
Ha: There is a positive relationship between patients with high disease activity and treatment persistence
- 4. Trends in treatment utilization, persistence and effectiveness (secondary analysis)
  - Time-to-first DMD and conversion to SPMS/ change in disabilities
    1. Relationship between time-to-first DMD, and increase in disabilities.  
H0: there is no association between time-to-first DMD and increase in disabilities  
Ha: there is an association between time-to-first DMD and increase in disabilities
    2. Relationship between DMD duration-disease duration ratio, and increase in disabilities.  
H0: there is no association between DMD duration-disease duration ratio and increase in disabilities  
Ha: there is an association between DMD duration-disease duration ratio and increase in disabilities

3. Negative relationship between time-to-first DMD and conversion to SPMS/ reaching clinical milestone of EDSS 4.0 and EDSS 6.

H0: there is no association between time-to-first DMD and conversion to SPMS

Ha: there is an association between time-to-first DMD and conversion to SPMS

H0: there is no association between time-to-first DMD and reaching clinical milestone of EDSS 4.0/ EDSS 6.0

Ha: there is a an association between time-to-first DMD and reaching clinical milestone of EDSS 4.0/ EDSS 6.0

## **Onderzoeksopzet**

At baseline the Multiple Sclerosis Impact Profile (MSIP), Multiple Sclerosis Quality of Life-54 items (MSQoL-54), Relapse Self-Report, and Medication and Adherence Inventory were completed by means of an online questionnaire, and the EDSS score was assessed by phone. At follow-up the MSIP, MSQoL-54 and Relapse Self-Report, are completed every 6 months. Monthly completion of Medication and Adherence Inventory is optional. The EDSS score was assessed in 2016, at variable follow-up time points. In 2021, EDSS score will be assessed again, this means for each patient at a different follow up.

## **Onderzoeksproduct en/of interventie**

Care as usual

## **Contactpersonen**

### **Publiek**

Maastricht University  
Ghislaine van Mastrigt

0638615631

### **Wetenschappelijk**

Maastricht University  
Ghislaine van Mastrigt

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## **Deelname eisen**

## Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- 1) Diagnosis of MS or Clinically Isolated Syndrome (CIS)
- 2) Willing and able to comply with the study protocol
- 3) Having access to the internet
- 4) Have given informed consent

## Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Not defined

## Onderzoeksopzet

### Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blinding:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

### Deelname

Nederland	
Status:	Werving gestopt
(Verwachte) startdatum:	01-03-2011
Aantal proefpersonen:	500
Type:	Werkelijke startdatum

## Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

**Wordt de data na het onderzoek gedeeld:** Nog niet bepaald

### Toelichting

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## Ethische beoordeling

Positief advies

Datum: 27-05-2021

Soort: Eerste indiening

## Registraties

### Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

### Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

### In overige registers

Register	ID
NTR-new	NL9520
Ander register (METOPP), Tilburg, The Netherlands	METC: Medical Ethical Assessment Research Patients and Test Subjects Registration number; M397; issue of an investigation not subject to the WMO, dated 1 March 2011

## Resultaten