# Regulation of the stress-axis by vitamin D3 in subjects with multiple sclerosis; a double-blinded, randomized, placebo-controlled study

Published: 18-11-2013
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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Autoimmune disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON45180

**Source**
ToetsingOnline

**Brief title**
Vitamin D3 and the stress-axis in MS

### Condition

- Autoimmune disorders
- Demyelinating disorders

**Synonym**
Multiple Sclerosis; MS

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Universiteit Maastricht

**Source(s) of monetary or material Support:** Financiering vindt vanuit eigen middelen plaats;o.a. door financiering vanuit het Nationaal MS Fonds.

## Intervention

**Keyword:** cortisol, HPA-axis, Multiple sclerosis, Vitamin D3

## Outcome measures

### Primary outcome

We assess primarily the effect of vitamin D3 supplementation with a dose of

4000 IU/day (100µg/ day) for 16 weeks on the cortisol day curve.

### Secondary outcome

Furthermore, we assess the effect of the intervention on the slope of the

cortisol day curve, a dexamethason suppression test, the cortisone awakening

response, the CD4+ T cell cytokine profile and the HADS depression/ FSSS

fatigue score, and we assess descriptively to which extent vitamin D levels in

the serum are elevated, and assess whether the participant experience

side-effects.

# Study description

### Background summary

MS patients are at risk for developing depressive symptoms. Also, impaired vitamin D levels are associated with a higher risk of developing MS and with a more severe MS course. Our group observed a relationship between vitamin D status and the risk of developing depressive symptoms, suggesting an interaction between vitamin D and biological mechanisms affecting susceptibility to depression. Currently, we have two main hypotheses. Hypothesis A: Vitamin D regulates the hypothalamic stress axis in MS. Both MS patients and non-MS patients with a major depression have increased levels of circulating cortisol, due to hyper-reactivity of hypothalamic-pituitary-adrenal (HPA)-axis, also known as the stress axis. Previous research showed that vitamin D receptors in the brain are particularly expressed in the hypothalamus

and that vitamin D also may affect cortisolcorticotrophin releasing hormone (CRH)-positive cells. We postulate that vitamin D may regulate the release of CRH, and hereby is able to suppress the activity of the HPA-axis and protects MS patients for developing depressive symptoms in MS . Hypothesis B: Vitamin D affects T cell cytokine profile and hereby the odds of developing depression. In our previous studies, we showed that the cytokine profile of peripheral blood CD4+ T cells correlates with vitamin D status in MS patients and that vitamin D may promote T cell homeostasis in MS. Since both MS patients and non-MS patients with a major depression display increased circulating levels of pro-inflammatory cytokines and anti-depressants reduce those cytokines, an inflammatory component may contribute to the development or presence of depressive symptoms in MS , with whom vitamin D may interfere.

### Study objective

The main aim of this study is to assess hypothesis A, and we will perform an exploratory analysis on hypothesis B.

### Study design

This will be a randomized, double-blinded, placebo-controlled clinical study.

### Intervention

Patients have to take 100ug vitamine D3 solution a day for a period of 16 weeks.

### Study burden and risks

Patients have to take the vitamin D solution every day and have to visit the hospital 3 times for giving urine and blood samples. Also they have to collect several salivasamples at the start and the end of the study, covering 4 full days.
An elevation of serum calcium levels (hypercalcemia) has occasionally been described in patients supplemented with high doses of vitamin D. A severe hypercalcemia can give rise to complications as heart- and kidney faillure. However, the amount of vitamin D that we supplement, de frequency of monitoring and the exclusion of potential highrisk groups reduce this risk significantly.

## Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

- relapsing remitting multiple sclerosis (revised McDonald criteria 2005)
- female
- age >18 years
- premenopausal
- At start of study > 6 weeks in clinical remission of disease
- use of no immune-modulating treatments or the currently registered firstline immune modulating therapies (including Interferon-beta (1a or 1b), glatiramer acetate, dimethylfumarate, teriflunomide) or second-line immune modulating therapies (incl. fingolimod (Gilenya) and natalizumab (Tysabri)).

## Exclusion criteria

• Any contraindication to vitamin D according to Summary of Product Characteristics: Hypercalcaemia, hypervitaminosis D, nephrolithiasis, diseases or conditions resulting in hypercalcaemia and/or hypercalciuria (incl. primary hyperparathyroidism), severe renal impairment.
• Use of dexamethasone or other systemic glucocorticosteroids <2 months prior to first study

visit
• Supplementation of >=1000 IU/d (25µg) vitamin D2 or D3
• Medical history of disturbed vitamin D/ calcium metabolism other than low intake
• Present clinical (major)depression
• Present treatment with anti-depressants, benzodiazepines, or neuroleptics.
• Treatment with high-dose dexamethasone for MS exacerbation during study.
• Pregnancy or the intention to become pregnant during the study period.

# Study design

## Design

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|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Basic science |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 13-10-2014 |
| Enrollment: | 80 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | Vigantol Oil |
| Generic name: | Colecalciferol |

# Ethics review

Approved WMO

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|---|---|
| Date: | 18-11-2013 |
| Application type: | First submission |
| Review commission: | METC Z: Zuyderland-Zuyd (Heerlen) |
| Approved WMO Date: | 08-05-2014 |
| Application type: | First submission |
| Review commission: | METC Z: Zuyderland-Zuyd (Heerlen) |
| Approved WMO Date: | 09-10-2014 |
| Application type: | Amendment |
| Review commission: | METC Z: Zuyderland-Zuyd (Heerlen) |
| Approved WMO Date: | 19-08-2015 |
| Application type: | Amendment |
| Review commission: | METC Z: Zuyderland-Zuyd (Heerlen) |
| Approved WMO Date: | 09-02-2016 |
| Application type: | Amendment |
| Review commission: | METC Z: Zuyderland-Zuyd (Heerlen) |
| Approved WMO Date: | 24-03-2016 |
| Application type: | Amendment |
| Review commission: | METC Atrium-Orbis-Zuyd |

# 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 |
| --- | --- |
| EudraCT | EUCTR2014-000728-97-NL |
| ClinicalTrials.gov | NCT02096133 |
| CCMO | NL45995.096.14 |