# Subjective Cognitive Impairment Cohort, a focus on the earliest changes leading to Alzheimer*s disease.

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The primary objective of the SCIENCe project is to establish a prospective cohort of patients with subjective complaints, to study the earliest brain changes ultimately leading to cognitive decline and dementia due to AD. Specific research questions...

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Dementia and amnestic conditions |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON53088

**Source**
ToetsingOnline

**Brief title**
SCIENCe

### Condition

- Dementia and amnestic conditions

**Synonym**
Preclinical Alzheimer's disease; first symptoms of Alzheimer's disease

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Amsterdam University Medical Center, VU Universty Medical Center
**Source(s) of monetary or material Support:** Gieskes Strijbis Fonds welke een subsidie heeft gegeven voor het SCIENCe project aan het Alzheimercentrum Amsterdam;afdeling

neurologie van het Amsterdam UMC;locatie VUmc

## Intervention

**Keyword:** biomarkers, preclinical Alzheimer's disease, prognosis, subjective memory complaints

## Outcome measures

### Primary outcome

Clinical progression, i.e. progression to a clinical diagnosis of MCI or

dementia.

### Secondary outcome

- Decline in cognitive functioning on neuropsychological testing (i.e. memory,

language, visuospatial functioning, attention, executive functioning etc).

- Decline in daily functioning as measured using the Amsterdam IADL

questionnaire

- Amyloid-positivity (as measured using CSF biomarkers and/or amyloid-PET) as

an endophenotype for AD.

# Study description

### Background summary

Background
Alzheimer*s disease (AD) is the most common cause of dementia and has been coined one of the grand challenges of this century. There is no curative therapy available. This may have several causes. First, AD is a complex disease. A narrow focus on one aspect of the disease will not result in an answer. In addition to addressing the roles of amyloid-beta and tau, the main pathological hallmarks of AD, we must also take into account other factors, such as lifestyle factors and brain connectivity. Second, when patients have reached the clinical stage of dementia, the disease process has gradually unfolded in the course of 15 to 20 years.1 Even when we would be able to stop or modify the disease process, this would hardly help, as the damage in the

brain is already irreversible in the dementia stage. In other words, to find an effective therapy, we have to focus on the very earliest stages of the disease.

In vivo measurement of AD pathology
The amyloid cascade hypothesis, the most prominent hypothesis concerning the etiology of AD, is built around the assumption that deposition of the protein amyloid-beta 1-42 (A*42) in so-called plaques is among the initial brain changes associated with AD. The deposition of amyloid-beta subsequently triggers a cascade of events, including development of tau inclusions (tangles), synaptic loss, neurodegeneration, cognitive decline and eventually dementia due to AD. For a long time, amyloid-beta and tau could only be demonstrated at autopsy, hampering progress in AD research. The novel techniques to measure Alzheimer pathology in vivo (using CSF biomarkers or PET-scan) have opened op new avenues for Alzheimer research. Both CSF biomarkers and amyloid PET-tracers distinguish AD patients from controls with relatively good accuracy. In addition, both types of markers have prognostic value for the development of dementia in patients with MCI. These developments have led to the inclusion of these markers in the new research criteria for diagnosis of both dementia and MCI due to AD.

**Study objective**

The primary objective of the SCIENCe project is to establish a prospective cohort of patients with subjective complaints, to study the earliest brain changes ultimately leading to cognitive decline and dementia due to AD.

Specific research questions which will be addressed include:
In patients with subjective complaints,
1. What are the trajectories of cognitive decline?
2. Do the known Alzheimer markers amyloid-PET and CSF biomarkers predict clinical progression?
3. Which (combinations of) imaging markers predict clinical progression?
4. Can we identify genetic markers that predict clinical progression?
5. Can we identify new markers in CSF and/or blood that predict clinical progression?
6. Is the immunophenotype isolated from blood predictive for clinical progression?
7. Is the gut microbiome predictive for clinical progression?
8. Do lifestyle factors (including physical and mental activity, smoking and diet) predict clinical progression?
Newly identified imaging, genetic and CSF/blood/microbiome markers (question 3-7) will be studied taking into account preclinical AD stages as defined by amyloid-PET or CSF biomarkers.

**Study design**

SCIENCe is a prospective cohort study. We will include patients who have visited our diagnostic screening and subjects with memory complaints from the register www.hersenonderzoek.nl. The duration of follow up will initially be twelve years. A schematic overview of the study is provided in Figure 1 (see page 10 of the protocol v1.9, November 2021).

The value of the cohort lies in the extensive phenotyping of participants and the long duration of follow-up. The current protocol will serve as an *umbrella protocol*. We hope and expect that in time we will obtain funding for enlarging the cohort and extending follow-up. In addition, we expect additional sub-studies to be added in the future. These studies will share the well characterized SCIENCe cohort as a constant factor.

**Study burden and risks**

When patients participate in SCIENCe, they will undergo an additional neuropsychological test battery focusing on memory function and a series of questionnaires focusing on behavioural symptoms and lifestyle factors (estimated time: one hour), additional blood will be drawn (paxgene tube, for RNA; 10 min, under protocol P2017.315), and they will be offered the possibility to participate in the PET sub study (separate protocol; P13-256). In addition, patients will be invited for an annual follow-up visit (visit medical doctor, neuropsychologist and research nurse; 2.5 hours). The risks associated with participation are negligible and follow-up is organized in much the same way as our clinical follow-up. When there is clinical progression, patients have the benefit of the possibility to re-enter clinical follow-up.

# 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

- Label of subjective memory complaints (i.e. no diagnosis of dementia, mild cognitive impairment, psychiatric or neurological disorder explaining cognitive complaints).
- Signed informed consent projects P2005_160, P2000_211, P2016_061 or P2016_409.
- Age * 45 year.

## Exclusion criteria

- Insufficient knowledge of Dutch language.
- Major psychiatric disorder, such as psychosis, schizophrenia, severe personality disorder or depression with vital signs, abuse of alcohol or other substances.
- Neurological disorder such as Parkinson*s disease, symptomatic stroke, mental retardation.
- Acquired Immune Deficiency Syndrome (AIDS) or Human Immunodeficiency Virus (HIV).

# Study design

## Design

**Study type:** Observational invasive

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|---|---|
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |

| | |
|---|---|
| Primary purpose: | Basic science |

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 02-06-2014 |
| Enrollment: | 500 |
| Type: | Actual |

## Ethics review

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|---|---|
| Approved WMO Date: | 12-05-2014 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 15-12-2014 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 22-12-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 21-03-2018 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 24-07-2019 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 25-11-2022 |
| 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 | NL47284.029.13 |