# The utility of blood-based biomarkers for Alzheimer*s disease in memory Clinic

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We aim to identify the utility of blood-based biomarkers for AD. Our first objective is to determine percent agreement between plasma biomarkers and clinical diagnosis set in a memory clinic. In summary: testing the agreement between plasma...

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| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Cranial nerve disorders (excl neoplasms) |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON51700

**Source**
ToetsingOnline

**Brief title**
Blood-based biomarkers in AD

### Condition

- Cranial nerve disorders (excl neoplasms)

**Synonym**
cognitieve impairment, Dementia

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Medisch Centrum Leeuwarden
**Source(s) of monetary or material Support:** Medisch Specialistisch Bedrijf/Verenigd Collectief Leeuwarden

## Intervention

**Keyword:** Alzheimer, Biomarkers

## Outcome measures

### Primary outcome

The main outcome measure is:

1) Agreement will be calculated between plasma biomarkers for AD and clinical diagnosis at baseline and at follow up (1 year).

Working diagnosis

Diagnoses of probable AD will be made according to the core clinical criteria of the National Institute on Aging-Alzheimer*s Association (NIA-AA) workgroups.

### Secondary outcome

Information for descriptive statistics, if present, will be collected (Disease stage, reported cognitive complains, impairment daily living, cranial MRI result and CSF results). There are no other secondary outcomes.

# Study description

### Background summary

Alzheimer*s disease (AD) is one of the major healthcare challenges of this century. In the Netherlands, an estimated >270,000 individuals suffer from dementia, mostly the AD type. This number will continue to rise, exceeding half a million by 2040. There is no cure for AD yet and the care given focuses on the last stage of this disease, resulting in a compromised quality of life.

Research has shown that AD develops in the course of 20 to 30 years. Preventive strategies are being developed to delay or stop progression to AD. In this perspective, early stages of AD offer an opportunity for treatment and prevention.

However, in patients, cognitive complains are usually present at least 1,5 year before AD diagnosis. And commonly diagnosis is set in hospital using neuropsychological test batteries and diagnostic tools (like MRI, CSF, or PET). This results in delay and expensive care. To reduce healthcare costs the diagnostic course need to be changed. As a consequence, there is an urgent need for low*invasive and affordable techniques.

Blood biomarkers (BB) have been developed which can detect early AD pathophysiological changes 5-9. Pathological, extracellular amyloid beta (Abeta) and intracellular Tau are the hallmarks in brains of AD patients 4. Individuals with these pathological changes are at increased risk to develop dementia. For this reason, they are important to investigate. Can blood biomarkers be used in the diagnostic process ?

Recently, Amyblood 4-plex is developed, an AD blood test. This is a fully automated single molecule array (Simoa) digital immunoassay panel intended for the quantitative measurement of amyloid-beta-40 (Aβ40), amyloid-beta-42 (Aβ42), Glial Fibrillary Acidic Protein (GFAP) and Neurofilament Light (NfL). Together with p-tau 181, these biomarkers combined are the most promising AD blood biomarkers 11. Till now, these markers have being investigated only in tertiary centres and are not yet in use in GP or MC.

These measurements are low invasive and affordable to pre-screen patients. We hypothesise that if this method is implemented in the early diagnostic course, fewer individuals will be forwarded toward memory clinics. This will eventually result in fewer invasive and/or expensive testing and in an earlier diagnosis. This delivers treatment opportunities in an early phase of the disease.

The goal of this study is to investigate the agreement between the blood test and the clinical diagnosis (golden standaard). This will hopefully lead in early identification of AD patients. Which will result in lower care costs, and it will open opportunities for early diagnosis.

## Study objective

We aim to identify the utility of blood-based biomarkers for AD. Our first objective is to determine percent agreement between plasma biomarkers and clinical diagnosis set in a memory clinic.

In summary:
testing the agreement between plasma biomarkers and working diagnosis

## Study design

Enrolment of subjects: Using digital referrals, GPs send patients with possibly underlying cognitive problems to the memory clinic of the Medisch Centrum

Leeuwarden for further investigation. When a referral is received, patients will be approached by phone to set an appointment at the memory clinic. This moment will be used to ask an informed consent and to ask if the patient is willing to participate with this study. After signing the informed consent, blood biomarkers will be collected during routine blood drawn as part of standard clinical care of patients visiting the memory clinic. The patients will eventually be seen by the treating geriatrician/neurologists and care as usual will be given. The results of the blood biomarkers will be blinded for the treating geriatricians/neurologists. Patients will be enrolled for one year (target is 400 samples) and will be followed up for at least 1 yar months.

Dementia assessment (care as usual): All participants will receive a dementia screening/assessment at the Medisch Centrum Leeuwarden. It will include a clinical history, a medical and neurological examination, and screening laboratory tests. Screening using a neuropsychological assessment will be performed by the geriatrician. If needed a magnetic resonance imaging (MRI) of the brain or cerebrospinal fluid (CSF) will be performed. Diagnoses of probable AD and MCI will be made according to the core clinical criteria of the National Institute on Aging-Alzheimer*s Association (NIA-AA) workgroups. The neuropsychological assessment consist of the MMSE, Clock drawing test (Shulmanscore 1993), Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE-N), and the Zarit Burden Interview (ZBI).

Analysis of blood samples: Whole blood samples drawn following clinical best practices, will be collected. Plasma samples will be stored and eventually transported on dry ice for analysis at the Clinical Neurochemistry Laboratory, AMC, location VUmc. AD biomarkers, amyloid-beta-40 (Aβ40), amyloid-beta-42 (Aβ42), Glial Fibrillary Acidic Protein (GFAP) and Neurofilament Light (NfL will be measured on the Simoa HD-X instrument using in-house (Department Clinical Chemistry, VUmc) developed and validated assay. Plasma p-tau181 is measured using with the assay delivered by Simoa HD-X instrument (Quanterix) as described bij Karikari, Lancet Neurology 2020.

**Study burden and risks**

We aim to make an AD diagnosis more reliable and easier. Members of the group that is included in the current study will benefit from this research, but the participants themselves will not. Risk on the other hand, is negligible. Blood draw is already taking place for most participants and taking one additional tube will not add to patient risk. Risk associated with blood draw itself is minimal and consists of risk of a hematoma and a small infection risk at the puncture site.

# 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

The patient has to have cognitive complaints or behavioral change and has to be referred from the GP to the memory clinic.

## Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
1) age under 50
2) known alcohol abuse in the past or present
3) Incapacitated patients

# Study design

## Design

**Study type:** Observational invasive

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Diagnostic |

## Recruitment

NL

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| Recruitment status: | Completed |
| Start date (anticipated): | 04-04-2023 |
| Enrollment: | 400 |
| Type: | Actual |

# Ethics review

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| Approved WMO Date: | 16-11-2022 |
| Application type: | First submission |
| Review commission: | RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden) |
| Approved WMO Date: | 13-08-2024 |
| Application type: | Amendment |
| Review commission: | RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden) |

# 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 | NL81775.099.22 |