Clinical Implementation of Amyloid Neurodegeneration and Tau testing in Primary Care.

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

Summary

ID

NL-OMON56307

Source
ToetsingOnline

Brief title
CANTATE-PC

Condition

- Dementia and amnestic conditions

Synonym
AD, Alzheimer's disease

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Alzheimer□s drug discovery foundation,Quanterix

Intervention

Keyword: Alzheimer's disease, Bloodbiomarkers, Diagnosis, Primary care

Outcome measures

Primary outcome

1)Working diagnosis of the general practitioner in terms of:

- Disease stage

- Suspected etiology

2) Plasma biomarkers for Alzheimer's disease.

Secondary outcome

1) Patient management decisions at baseline.

2) Working diagnosis (defined as etiology and diseases stage) after 6 months.

3) Patient/caregiver-reported cognitive complaints.

4) Global cognitive functioning.

5) Impairment in daily living.

6) Qualitative evaluation of unmet needs in primary care that can be fulfilled

by an AD blood test as defined by the practitioner.

Study description

Background summary

Cognitive complaints have a broad differential diagnosis. The challenge for the general practitioner or elderly care physician is to facilitate an optimal diagnostic trajectory, treatment and management for each patient. Blood-based biomarkers for Alzheimer*s disease and neurocognitive disorders in general may aid in this process. For example, Alzheimer*s disease (AD) is the most common form of dementia with roughly 200.000 persons suffering from the disease in the

Netherlands. An accurate diagnosis improves action ability for patients and caregivers and is therefore highly important. With the first disease-modifying therapy available in the United States and other treatments in the pipeline, the need for accurate and cost-effective detection of AD becomes critical.

Unfortunately, an accurate diagnosis in primary care is difficult. Early and atypical signs of AD often remain unrecognized by the GP or elderly care physician and other diseases may be mistaken for AD. The pathological hallmarks of the disease - amyloid and tau - are traditionally detected using either cerebrospinal fluid (CSF) or PET imaging techniques. These methods are invasive or very expensive and cannot be utilized in primary care. Moreover, in view of the foreseen increased demand for AD diagnostic testing, such testing in primary care is critical to meet the demand in a cost-effective way. This leaves a need for biomarkers that are both accurate and can be easily obtained. Based on well-defined recent prospective and retrospective cohort studies several blood-based biomarkers are on the brink of being able to fulfill this need.

The AD blood test is a fully automated singlemolecule array (Simoa) digital immunoassay panel intended for the quantitative measurement of biomarkers for AD, astrocyte dysfunction and neurodegeneration (for example Amyloid-Beta-40 (Aβ40), Amyloid-Beta-42 (Aβ42), Glial Fibrillary Acidic Protein (GFAP) and Neurofilament Light (NfL)). In addition, recent evidence from multiple cohorts suggests that p-tau isoforms are highly accurate detectors of AD pathology. Together, these markers combine the most promising blood biomarkers that is specific for AD and other neurodegenerative causes of cognitive complaints with the most sensitive immunoassay technology.

Clinically, the combination of Aβ42/40 and GFAP predict amyloid PET positivity with an area under the ROC curve of 88% (95% confidence interval 83-93%) when APOE*4 and age were included in the model. This is similar to the performance of combinations between Aβ42/40 and p-tau. In addition, NfL is increased in all forms of dementia, especially in frontotemporal dementia, thus enabling us to detect other forms of dementia than AD. Cut-points and their according sensitivity and specificity have recently been defined for the aforementioned AD plasma biomarker panel (Aβ40, Aβ42, GFAP, NfL and pTau-181) by Verberk et al (in preparation). Also, age and disease specific reference values for NfL have been defined in studies before. Precision results of these biomarkers are acceptable with average intra-assay CV*s ranging from 6-15% and average reproducibility between runs between 6.5 % CV and 16% CV for Aβ40, Aβ42, GFAP and NfL.

Current evidence is restricted to highly selected cohorts. The aim of this study is to take first steps towards development of a prediction model based on blood-based biomarkers for AD in primary care, tailored to the specific needs of this setting.

Study objective

The objective of this study is, to detect potential uses of plasma biomarkers in primary care, by
(a) To investigate if plasma biomarkers are associated with working diagnosis in primary care.
(b) To ascertain if diagnosis and patient management differ between patients with and without plasma evidence of underlying AD.
(c) To explore associations between plasma biomarkers and (1) the nature and severity of cognitive complaints, (2) global cognitive performance and (3) functioning in iADL.
(d) To qualitatively identify scenarios in which plasma biomarkers can improve current care.

Study design

Observational study with a single invasive measurement (venipuncture).

Study burden and risks

The benefit for participating in this study is the contribution to making the diagnostic process of AD and other neurocognitive disorders in primary care more reliable, cost-effective and easier. Eventually, this study will contribute to improvement of patient care, diagnostics and prognostics. Moreover, improvement of diagnostics can benefit patients with AD receiving accurate treatment without delay and in the future, receiving disease modifying therapy.We aim to make the diagnostic process of neurocognitive disorders more reliable and easier in primary care and thereby intent to contribute to limiting the healthcare costs in the course of this disease. The group of patients with cognitive complaints who present to primary care stand to benefit from this research, but the participants themselves will not. Risk on the other hand, is negligible. Risk associated with blood draw is minimal and consists of risk of a hematoma and a small infection risk at the puncture site. The CANTATE-PC test Battery consists of clinical and tests and questionnaires that have been widely implemented in the AD research field. Each researcher that visits participants has the experience and knowledge on how to conduct these test with minimal risks.

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

1) Present to primary care with cognitive complaints or behavioral change. Either the patient him/herself, a caretaker / relative, the GP or elderly care physician needs to be concerned.
2) Adequate fluency in Dutch to understand the informed consent and complete questionnaires.

Exclusion criteria

1) Age under 50.
2) Alcohol / drug abuse to such an extent that treatment would be advisable.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-11-2023
Enrollment:	400
Type:	Actual

Medical products/devices used

Generic name:	Quanterix Simoa Human Neurology 4-Plex E (N4PE) and pTau181 Assay
Registration:	No

Ethics review

Approved WMO Date:	22-09-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-05-2024
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	NL82220.000.23