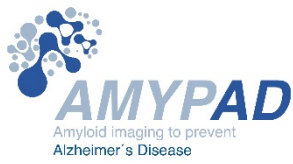


# **AMYPAD PNHS Parent Cohort Data Dictionary**

**Version 0.1, November 2019**



**AMYPAD Consortium**

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## Glossary of Terms

## Overview of Parent Cohorts

Cohort	Center / Sponsor	Principal Investigator	Reference(s)	Start Date	Recruiting?	Expected enrollment into AMYPAD PNHS
<b>EPAD LCS</b> (European Prevention of Alzheimer's Dementia Longitudinal Cohort Study)	University of Edinburgh	Craig Ritchie <a href="mailto:craig.ritchie@ed.ac.uk">craig.ritchie@ed.ac.uk</a>	<a href="http://www.ep-ad.org">www.ep-ad.org</a>  Study protocol: <a href="http://dx.doi.org/10.1136/bmjopen-2017-021017">http://dx.doi.org/10.1136/bmjopen-2017-021017</a>  Rationale paper: <a href="https://doi.org/10.1016/S2215-0366(15)00454-X">https://doi.org/10.1016/S2215-0366(15)00454-X</a>	May 2016	Yes	N>1000

Cohort	Center / Sponsor	Principal Investigator	Reference(s)	Start Date	Recruiting?	Expected enrollment into AMYPAD PNHS
<b>EMIF-AD PreclinAD – Twin60++ Study</b> (European Medical Information Framework – Alzheimer's Disease)	Amsterdam UMC, location VUmc	Pieter Jelle Visser <a href="mailto:pj.visser@amsterdamumc.nl">pj.visser@amsterdamumc.nl</a>	Study Design and Baseline Cohort: <a href="http://dx.doi.org/10.1186/s13195-018-0406-7">http://dx.doi.org/10.1186/s13195-018-0406-7</a> EudraCT: 2014-000219-15	November 2014	No	N=190

Cohort	Center / Sponsor	Principal Investigator	Reference(s)	Start Date	Recruiting?	Expected enrollment into AMYPAD PNHS
<p><b>ALFA+</b> (Alzheimer's and Families imaging sub-study)</p>	<p>Barcelonaβeta Brain Research Center</p>	<p>Oriol Grau <a href="mailto:ograu@barcelonabeta.org">ograu@barcelonabeta.org</a></p>	<p>Rationale and Study Design: <a href="http://dx.doi.org/10.1016/j.trci.2016.02.003">http://dx.doi.org/10.1016/j.trci.2016.02.003</a>  EudraCT: 2015-004474-15</p>	<p>March 2016</p>	<p>No</p>	<p>N=200</p>

## EPAD LCS

### Inclusion criteria

Due to the variety of Parent Cohorts (PCs) for EPAD LCS, some research participants will be e.g. memory clinic patients without dementia, while others will be e.g. PC participants without dementia from the general population. The variety of PC settings will ensure that the EPAD LCS probability-spectrum population can cover the entire continuum of probability for AD dementia development.

- Age at least 50 years, checked and recorded at Screening (Visit 1) only, as well as fulfilling the criteria set by the balancing committee.
- Fulfils the criteria set by the Balancing Committee [BC]
- Able to read and write and with minimum 5 years of formal education, checked and recorded at screening (Visit 1) only.
- Willing in principle to participate in the EPAD Proof of Concept (PoC) trial subject to further informed consent
- Have a study partner or can identify someone willing in principle to be a study partner

### Exclusion criteria

- Research participants who fulfil diagnostic criteria for any type of dementia (e.g. National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's Disease and Related Disorders Association [NINCDS-ADRDA] for AD; Lund Criteria for fronto-temporal dementia [FTD], McKeith Criteria for dementia with Lewy bodies [DLB], National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherche et l'Enseignement en Neurosciences [NINCDS-AIREN] Criteria for Vascular Dementia)
- CDR  $\geq 1$  at screening (Visit 1)
- Known carriers of a Presenilin (PSEN) PSEN1, PSEN2 or APP mutation associated with Autosomal Dominant AD or any other neurodegenerative disease
- Presence of any neurological, psychiatric or medical conditions associated with a long-term risk of significant cognitive impairment or dementia including but not limited to pre-manifest Huntington's disease, multiple sclerosis, Parkinson's disease, Down syndrome, active alcohol/drug abuse or major psychiatric disorders including current major depressive disorder, schizophrenia, schizoaffective or bipolar disorder.

- Any cancer or history of cancer in the preceding 5 years (excluding cutaneous basal or squamous cell cancer resolved by excision and localised prostate cancer in male subjects)
- Any current medical conditions that are clinically significant and might make the subject's participation in an investigational trial unsafe, e.g., uncontrolled or unstable disease of any major organ system; history within the last 6 months of any acute illness of a major organ system requiring emergency care or hospitalization, including re-vascularisation procedures; severe renal or hepatic failure; unstable or poorly controlled diabetes mellitus, hypertension, or heart failure; malignant neoplasms within the last 5 years (except for basal or squamous cell carcinoma in situ of the skin, or localized prostate cancer in male subjects); any clinically relevant abnormalities in blood parameters included in local Trial Delivery Centre routine assessments; severe loss of vision, hearing or communicative ability; or any conditions preventing co-operation or completion of the required assessments in the trial, as judged by the investigator
- Any contraindications for MRI/positron emission tomography (PET) scan
- Any contraindications for Lumbar Puncture at visit 1.
- Any evidence of intracranial pathology which, in the opinion of the Investigator, may affect cognition, including but not limited to brain tumours (benign or malignant), aneurysm or arteriovenous malformations, territorial stroke (excluding smaller watershed strokes), recent haemorrhage (parenchymal or subdural), or obstructive hydrocephalus. Participants with a MRI scan demonstrating markers of small vessel disease (e.g. white matter changes or lacunar infarcts) judged to be clinically insignificant, or microbleeds are allowed.
- Participation in a clinical trial of an investigational product (CTIMP) in the last 30 days. Participation in a non-CTIMP or an observational arm of a CTIMP is not considered an exclusion criterion. Co-enrolment in the Amyloid Imaging to Prevent Alzheimer's Disease (AMYPAD) Prognostic and Natural History Study (PNHS) is not considered to fall under this exclusion criteria.
- Diminished decision-making capacity/not capable of consenting at screening visit
- Unable to comply with protocol requirements in the opinion of the investigator

### Data Provided

- Demographics

Date of birth (subject to local regulations)

Age

Sex

Ethnicity (subject to local regulations)

Education

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Handedness  
Marital status  
Family history of AD

- Cognition & Clinical Functioning

MMSE  
CDR  
Dementia diagnosis  
RBANS List Learning & Story Memory (Verbal Episodic Memory)  
RBANS Figure Recall (Verbal Episodic Memory)  
RBANS Figure Copy & Line Orientation (Visuospatial/Constructional)  
RBANS Picture Naming (Language)  
RBANS Semantic Fluency, Digit Span, Coding (Attention/Executive Functioning)  
Dot Counting (Working Memory)  
Flanker (Choice reaction time and set-shifting)  
Favourites Learning, Delay & Recognition (Paired Associate Learning)  
Four Mountains Task (Allocentric Space)  
Supermarket Trolley Virtual Reality (Egocentric Space)

- Questionnaires

Amsterdam IADL  
Sleep (Pittsburgh Sleep Quality Index)  
Anxiety (STAI)  
Depression (GDS)

- Genetics

APOE genotype  
(others may be available at a later stage)

- BioSamples / Fluids

CSF A $\beta$ , t-tau, p-tau, NfL, TREM2, neurogranin  
Urine  
Blood  
Saliva

- Medical examination / Risk Factors

Medical history (stroke, diabetes, hypertension, hypercholesterolemia, myocardial infarction, chronic ischemic heart disease, chronic obstructive pulmonary disease, asthma, depression, rheumatoid arthritis, any cancer, general anesthesia after age of 50, head injury assessed with BISQ, MCI, other)  
Body height



Body weight  
Hip-waist circumference  
Smoking  
Alcohol consumption  
Drug abuse/misuse  
Diet (HATICE questionnaire)  
Physical activity  
Life events (brief questionnaire based on SNAC)  
Self-rated health and fitness  
Physical examination (neurological, blood pressure and pulse)  
Current Medication

- Imaging (MR)

Core MR Imaging

3D T1w  
3D T2  
FLAIR

Available variables: GCA, PCA, MTA, micro bleeds, lacunes, Fazekas score, stroke and hemorrhages

Advanced MR Imaging (sub-set of subjects)

3D-SWI or 3D-T2\*  
DTI  
ASL  
rs-fMRI

## EMIF-AD PreclinAD

### (Twin 60++)

Participants have been recruited from the Netherlands Twin Registry (n=100 monozygotic twin pairs).

#### Inclusion criteria

- Age 60-100 years
- Telephone Interview for Cognitive Status modified (TICS-m) >22
- Geriatric Depression Scale (GDS) (15 item) <11
- Consortium to Establish a Registry for Alzheimer's Disease (CERAD) 10 word list immediate and delayed recall (> -1.5 SD of age adjusted normative data)
- Clinical Dementia Rating (CDR) scale of 0 with a score on the memory sub domain of 0

#### Exclusion criteria

- Clinical diagnosis of mild cognitive impairment or probable AD
- Severe head trauma, with loss of consciousness
- Brain tumour (past, present)
- Schizophrenia, bipolar disorders, or recurrent psychotic disorders
- Stroke resulting in physical impairment
- Neurodegenerative disorders (e.g. Huntington disease, cortical basal degeneration, multiple system atrophy, Creutzfeldt-Jacob disease, primary progressive aphasia, Parkinson's disease)
- Epilepsy, currently using antiepileptic drugs (AEDs)
- Brain infection (e.g. herpes simplex encephalitis)
- Cancer with terminal life expectancy
- Known B12 vitamin deficiency without treatment
- Uncontrolled diabetes mellitus
- Known thyroid disease without treatment
- History of recreational drug use
- Alcohol consumption: >35 units per week
- Physical morbidity or illness which will not permit attendance at visit sessions
- Contraindication for MRI (e.g. metal implants, pacemaker etc.)

- Medications that may impair cognition, at the discretion of the investigator, e.g.:
  - High dose benzodiazepine
  - Lithium carbonate
  - Antipsychotics including atypical agents
  - High dose antidepressants
  - Parkinson's disease medicines

### Data Provided

- Demographics

Age

Sex

Education (Years & Verhage score)

Handedness

Marital status

Family history of AD

- Cognition & Clinical Functioning

MMSE

CDR

National Adult Reading Test (NART, NLVT in Dutch)

Rey Complex Figure Copy & Delayed

Visual Association Test (VAT)

Visual Short Term Memory Test (VSTM)

Face-name Associative Memory Exam (F-NAME)

WAIS III Digit Span Forward & Backward

Rey auditory verbal learning test (RAVLT)

Verbal Fluency

Graded Naming Test (GNT)

Trail Making Test A & B

WAIS-R Symbol Digit Symbol Substitution Test

CERAD 10 Word List

CANTAB

- Questionnaires

Amsterdam IADL

Depression (GDS)

Functional Activities Questionnaire (FAQ)

Amsterdam instrumental Activities of Daily Living (iADL) scale

Subjective Memory Complaints Clinical and Cognitive Complaints Index (CCI)

Health related Quality of Life (hQoL) questionnaire (Short form 12)

Neuropsychiatric Inventory Questionnaire (NPI-Q)

Mayo Sleep Questionnaire (MSQ)

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Berlin Questionnaire for sleep apnea  
Physical activity scale for the elderly (PASE)  
Cognitive abilities questionnaire

- Genetics

APOE genotype

- BioSamples / Fluids

CSF A $\beta$  (38, 40, 42), t-tau, p-tau, BACE-1, Neurogranin

Urine

Blood

Plasma

Serum

Saliva

DNA

RNA

- Medical examination / Risk Factors

Medical history

Body height

Body weight

BMI

Resting blood pressure

Pulse

Neurological examination

Heart rate

Grip strength

Hip-waist circumference

Smoking

Diabetes

Alcohol consumption

Drug abuse/misuse

Physical activity

Current Medication

- Imaging (MR)

3D T1w

FLAIR

3D-SWI or 3D-T2\*

DTI

ASL

rs-fMRI

Available variables: GCA, PCA (L & R), MTA (L & R), microbleeds, lacunes (number and presence BG), Fazekas score, stroke and hemorrhages, WMH load

- Imaging (PET)

Dynamic [<sup>18</sup>F]flutemetamol PET (0-30min, 60min break, 90-110min)

## ALFA+

ALFA+ is a sub-study of the ALFA parent cohort, where inclusion criteria includes being 1) cognitively normal, 2) Spanish and/or Catalan-speaking persons, 3) aged between 45 and 74 years, that 4) agreed with the study procedures and tests, and were able to 5) involve a close relative for the volunteer's functional evaluation. Exclusion criteria were MMSE <26, MIS <6, SF < 12, TO-BTII <68, CDR >0, as well as the presence of major psychiatric disorders (DSM-IV-TR) or diseases that could affect cognitive abilities, severe auditory and/or visual, neurodevelopmental and/or psychomotor disorders, or significant diseases that could interfere with cognition, neurological disorders, brain injury that could interfere with cognition, and family history of AD with suspected autosomal dominant pattern.

### Inclusion criteria

- Subjects that have previously participated in the 45-65/FMP2012 study
- Age between 45-65 years at the moment of the inclusion in the 45-65/FMP2012 study
- Long-term commitment to the study: baseline and follow-up visits. Potential participants have to agree to undergo all procedures described in the protocol.

### Exclusion criteria

- Cognitive impairment: to be included the participant must show no signs of objective cognitive impairment.
- Any significant systemic illness or unstable medical condition which could lead to difficulty complying with the protocol.
- Any contraindication to any test or procedure at time of the study inclusion
- Family history of monogenic AD.
- Not willing to undergo one or more of the tests and procedures described in the protocol.

### Data Provided

- Demographics

Date of Birth

Age

Sex

Ethnicity

Education

Handedness

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Marital status

Family history of AD

- Cognition & Clinical Functioning

MMSE

CDR

Verbal Fluency

Free and Cued Selective Reminding Test (FCSRT)

WAIS-IV (Digit Span, Digit Sequencing, Visual Puzzles, Matrix, Coding)

Test de acentuacion de palabras (TAP, based on NART)

Memory Binding Test (MBT)

WMS-IV Logical Memory

Trail Making Test A & B

Flanker Test

WMS-IV Visual Span

5 Digit Test

RBANS Line Orientation

Picture Sequence Memory Test

Spanish Face-Name Test (S-FNAME)

- Questionnaires

Depression (GDS)

HADS

Pittsburgh Sleep Quality Index

Amsterdam instrumental Activities of Daily Living (iADL) scale

- Genetics

APOE genotype

- BioSamples / Fluids

CSF A $\beta$ , t-tau, p-tau

Plasma

Serum

DNA

- Medical examination / Risk Factors

Medical history (diabetes, cerebellar vascular accident, cholesterol, myocardial infarction, chronic ischemic infarct, depression, cancer, operations, head injury, etc)

Body height

Body weight

Resting blood pressure

Neurological examination

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Hip-waist circumference  
Smoking  
Alcohol consumption  
Drug abuse/misuse  
Physical activity  
Current Medication

- Imaging (MR)

Core MR Imaging

3D T1w  
3D T2w  
3D FLAIR  
3D-SWI  
DTI  
ASL  
rs-fMRI

Available variables: GCA, PCA, MTA, micro bleeds, lacunes, Fazekas score, stroke and hemorrhages, WMH load, Koedam, Wahlund)

- Imaging (PET)

Static [<sup>18</sup>F]flutemetamol PET (90-110min post injection)