



A European Medical Information Framework for Alzheimer's disease (EMIF-AD)

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Karolinska Institute
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EMIF: 2013-2018



❖ Vision:

- European hub for health care data intelligence, enabling new insights into diseases and treatments

❖ Three subprojects:

- EMIF-Platform
- EMIF-Metabolic
- EMIF-AD

❖ 56 partners from 14 European countries



❖ Aims

- Improve treatment opportunities for predementia AD by:
 - Discovery diagnostic and prognostic markers
 - Increased understanding AD pathophysiology
- Build infrastructure for reuse of data

Reuse cases



- ❖ Use existing data for analysis
- ❖ Use existing samples/scans for biomarker discovery
- ❖ Select individuals for research projects

Reuse cases



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 - Amyloid biomarker study
- ❖ Use existing samples/scans for biomarker discovery
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- ❖ Select individuals for research projects
 - PreclinAD study
 - EMIF-AD 90+ study

How to reuse data (FAIR)?



- ❖ Find existing data/samples/scans
- ❖ Accessible
- ❖ Interoperable
- ❖ Reusable

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 - EMIF-AD/EHR catalogue
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 - EMIF-AD/EHR catalogue
- ❖ Accessible
 - EMIF-AD participant selection tool and Switchbox
 - Jerboa/Octopus (EHR)
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- ❖ Reusable
 - EMIF-AD tranSMART data platform

Find: EMIF catalogue (emif-catalogue.eu)



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pj visser

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ELECTRONIC HEALTH RECORD DATA
15 entries
EMIF-EHR intends to explore how the massive data available in pan-European EHR systems can improve biomedical research.
[Leave](#) [More](#)
[OPEN](#)

ALZHEIMER'S DISEASE COHORTS
47 entries
The overall aim of EMIF-AD is to build an IF for studies on neurodegeneration in order to discover and validate AD biomarkers.
[More](#)
[OPEN](#)

EPAD
23 entries
EPAD aims to develop an infrastructure to undertake adaptive studies for early and accurate decisions on the development of drug candidates or combinations.
[More](#)
[OPEN](#)

EMIF catalogue: cohort meta-data



EMIF CATALOGUE / EMIF AD

Free text search EMIF AD

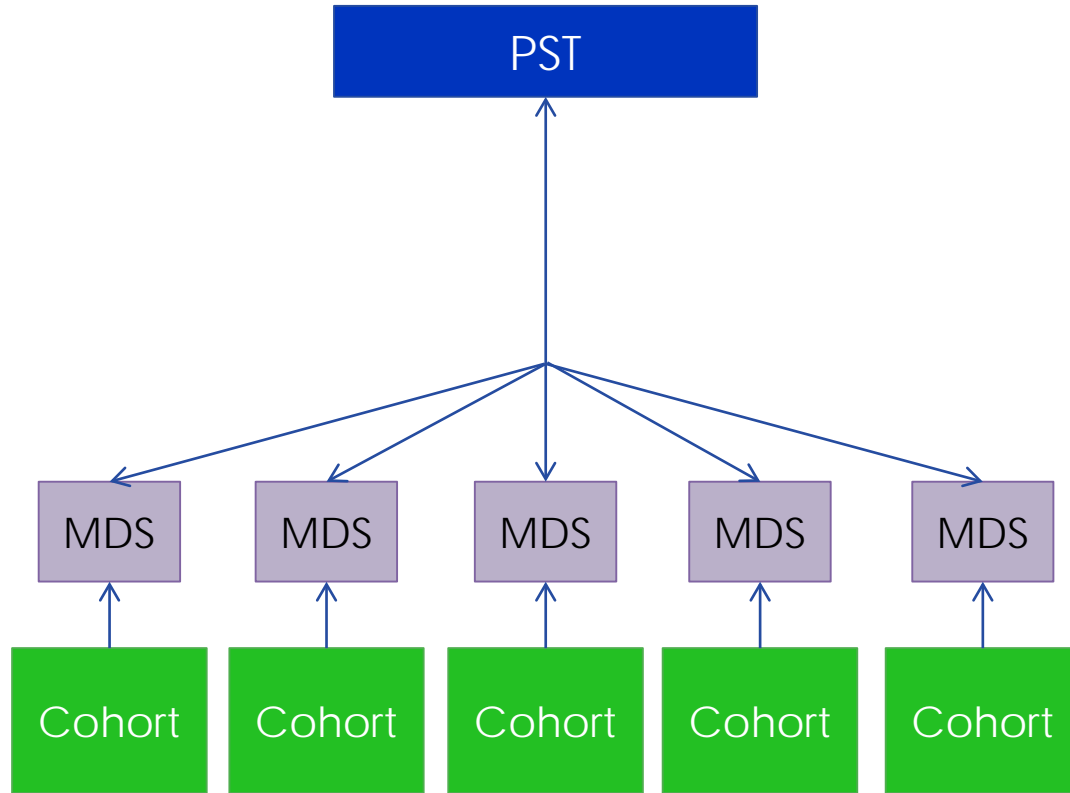
EMIF AD / All

Compare Export Print

Selected databases: 0

Acronym	Name	Institution name	Location	...	P...	Last update	Select
Filter	Filter	Filter	Filter	Filter	Filter	Filter	?
AddNeuroMed	AddNeuroMed, Innovative Medicines for Europe (Innomed)	Institute of Psychiatry, King's College London	City of London, Greater London, England, United Kingdom			2016-04-04	<input type="checkbox"/>
ADGEN	60 cohorts (56 pending) 471 registered users					2015-11-06	<input type="checkbox"/>
ADNI-1						2015-11-06	<input type="checkbox"/>
ADNI 2	Alzheimer's Disease Neuroimaging Initiative	University of California	San Francisco County, California, United States			2015-11-06	<input type="checkbox"/>
ADNI-GO	Alzheimer's Disease Neuroimaging Initiative	University of California	San Diego County, California, United States			2015-11-05	<input type="checkbox"/>
AgeCoDe	German Study on Ageing, Cognition, and Dementia in	University of Bonn	Germany	2003	1,338	2015-11-05	<input type="checkbox"/>

Assess: Participant selection tool



Participant selection tool



Total Subjects: 477

Participant Selection Variable Selection Request Form Status Tracker

All Subjects Summary Graph Summary Graph with attribute selection Attribute Breakdown

All Subjects

	IMI1	IMI2	IMI3	IMI4	IMI5	IMI6	IMI7	Total
Age at Enrollment in Study	0	0	0	0	0	23	49	72
APOE Genotype	35	29	30	311	0	23	49	477
Consent to Recontact Patient	0	0	0	0	0	0	49	49
CSF Amyloid Beta 42 - Date Last Observation	0	29	0	0	0	21	48	98
CSF Amyloid Beta 42 - Value Last Observation	0	29	0	0	0	23	49	101
Current Age	35	29	30	311	0	23	49	477
Diagnosis	35	24	30	0	0	23	49	161
Diagnosis - Last Date Recorded	35	0	0	0	0	23	45	103
Diagnosis Availability	35	24	30	0	0	23	49	161
Episodic Memory Value (normalized)	0	0	0	311	0	0	0	311
Last RAVLT value (normalized)	0	0	0	0	0	0	0	0
MMSE - Date Last Observation	35	29	30	0	0	22	44	160
MMSE - Value Last Observation	35	29	30	0	0	23	49	166
MMSE - Value Last Observation <=1 yr	0	0	0	0	0	0	0	0
MMSE Observation Count	35	29	30	0	0	22	49	165

Subject Selection

Save Load

Summary view

APOE Genotype [3 of 6] ✖

Select all Clear all

- e2/e2 [24]
- e2/e3 [104]
- e2/e4 [41]
- e3/e3 [2443]
- e3/e4 [997]
- e4/e4 [112]

Current Age [60 - 80] ✖

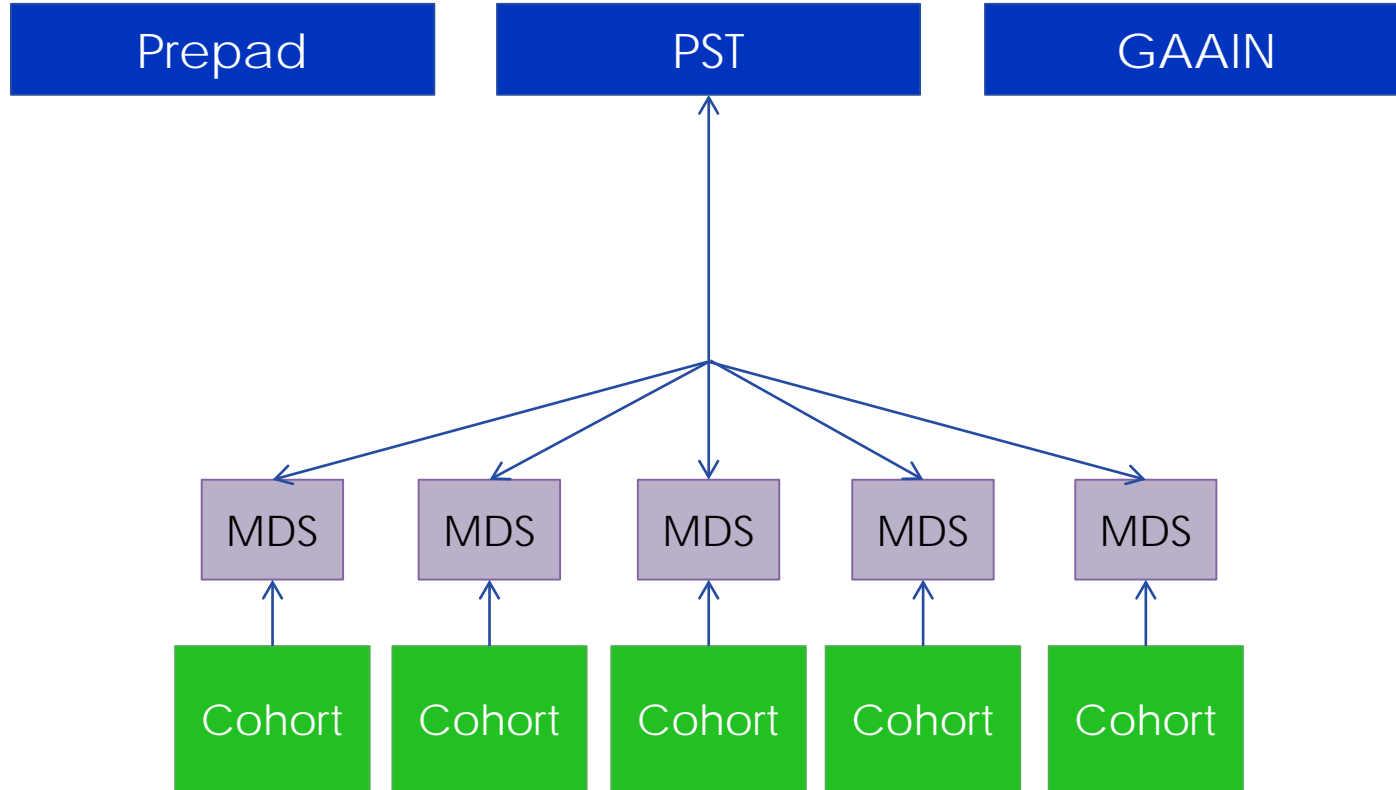
60 80

AND

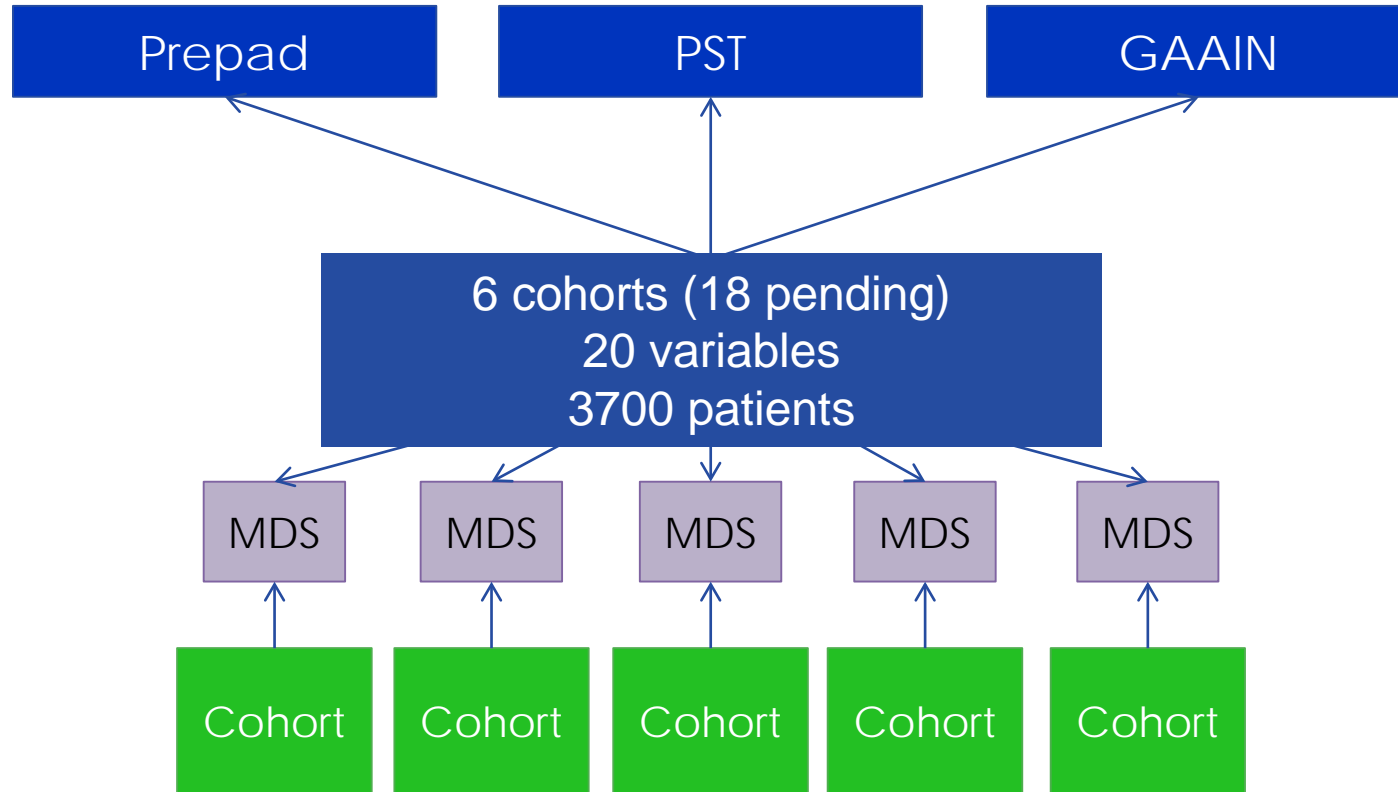
Filters



Participant selection tool



Participant selection tool



Reusable: EMIF-AD tranSMART platform



Active Filters and on Filter Clear

Navigate Terms

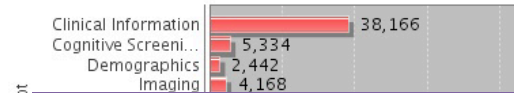
- Across Trials
- Private Studies
 - 1000 Study (1221)
 - AddNeuroMed (774)
 - Amsterdam (172)
 - Antwerp (150)
 - Descriva (881)
 - EDAR (332)
 - GAP (40)
 - Genoa (157)
 - Gothenburg (95)
 - IDIBAPS (164)
 - IMAP (144)
 - Lausanne (40)
 - Leuven (180)
 - Pharmacog (147)
 - SantPau (135)
- Public Studies

Comparison **Summary Statistics** Grid View Advanced Workflow Data Export Export Jobs Analysis Jobs Workspace

Analysis of concepts found in subsets

Analysis of ...\Private Studies\Private Studies\1000 Study for subsets:

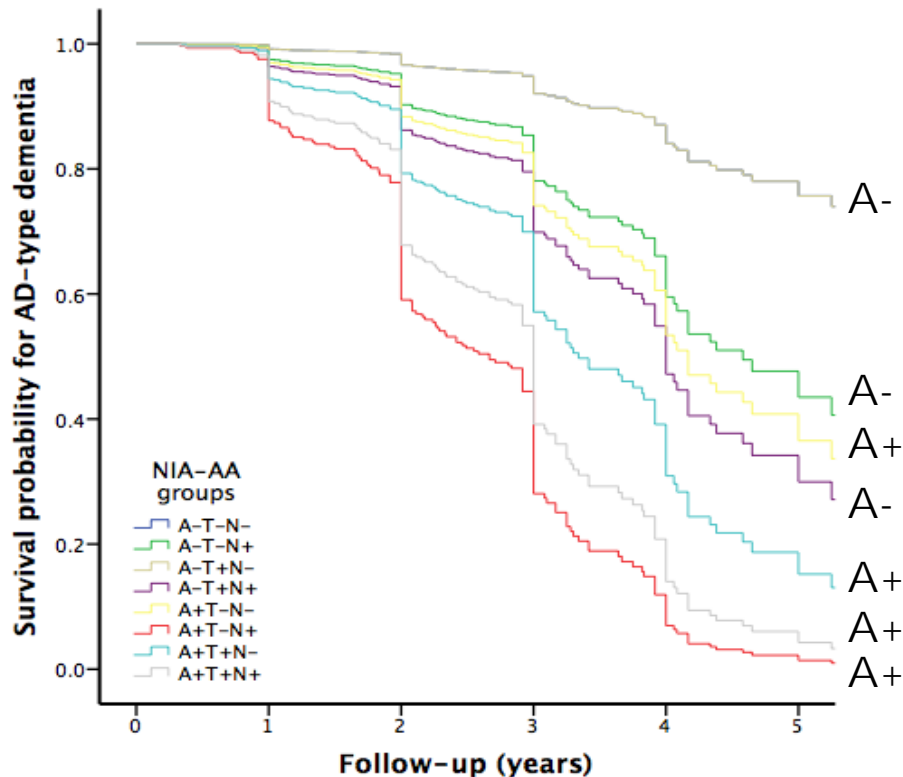
Subset 1



15 cohorts
3000 subjects
40 variables (subset omics)

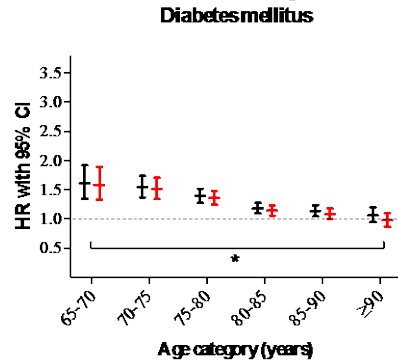
Category	Subset 1 (n)	Subset 1 (%n)
Clinical Information	38166	24.5%
Cognitive Screening Tests	5334	3.4%
Demographics	2442	1.6%
Imaging	4168	2.7%
Laboratory Test Results	16476	10.6%
Neuropsychological Examination	72179	46.3%
Pharmacogenetics Findings	3019	1.9%
Rating Scales	9028	5.8%
Study Information	3663	2.4%
Subject Characteristics	1304	0.8%
Total	155779	100%

Reuse existing cohort data: Validation NIA-AA 2018 framework



Risk for dementia in 700 participants with mild cognitive impairment from 6 cohorts as function of NIA-AA category

Reuse existing EHR data: predictors dementia

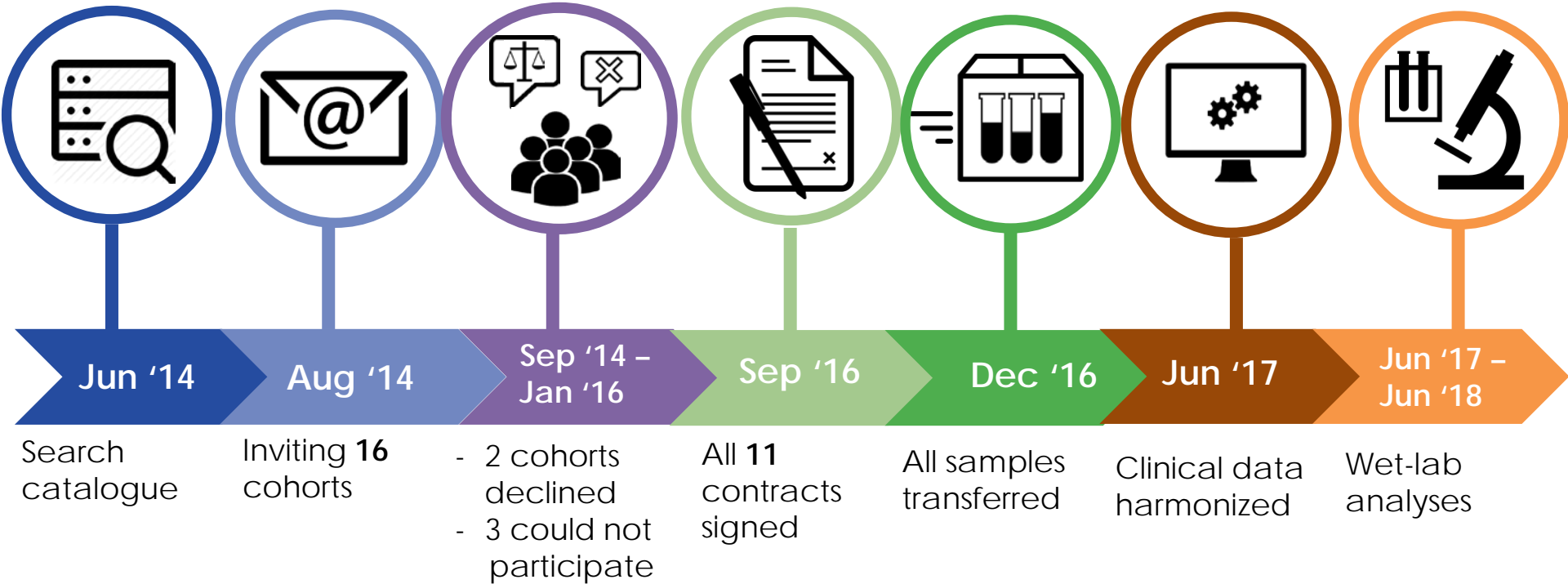


Reuse existing samples and scans

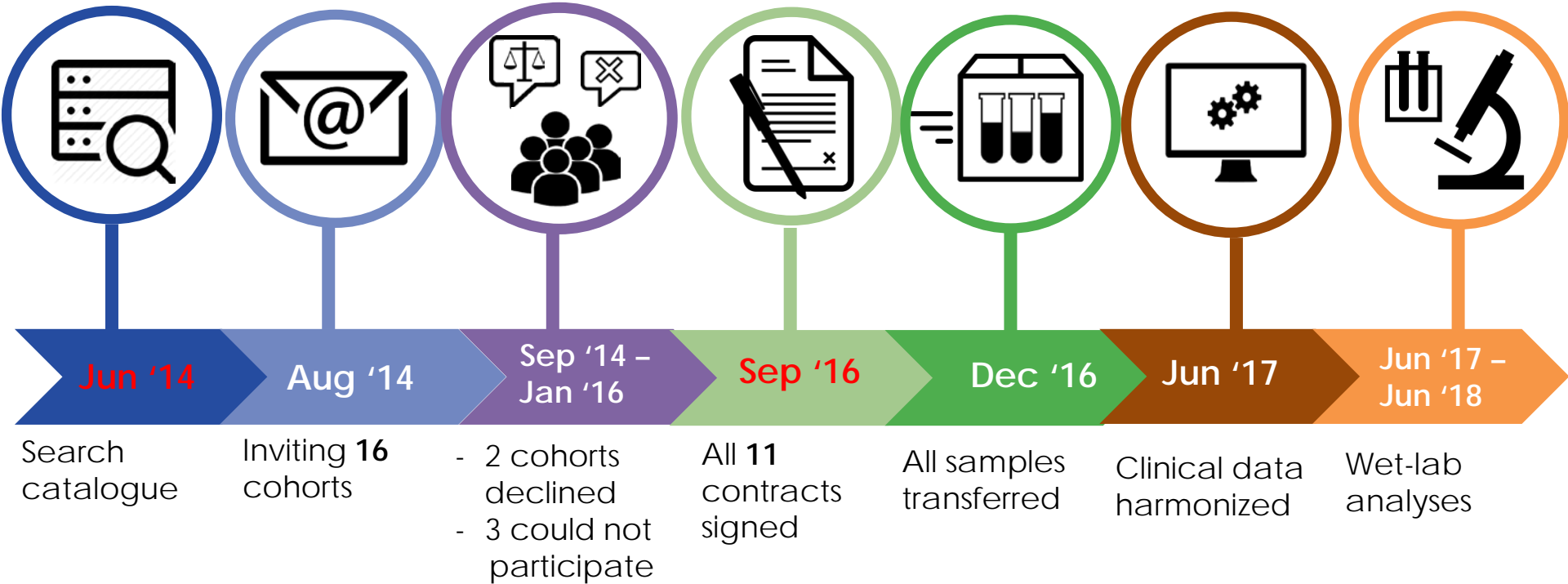


- ❖ EMIF-AD Biomarker Discovery Study
- ❖ Subjects (n=1220):
 - Normal cognition, MCI, AD-type dementia
 - Known amyloid status
 - Analysis
 - Plasma metabolomics and proteomics
 - Structural MRI
 - GWAS, EWAS, rare variants
 - CSF proteomics

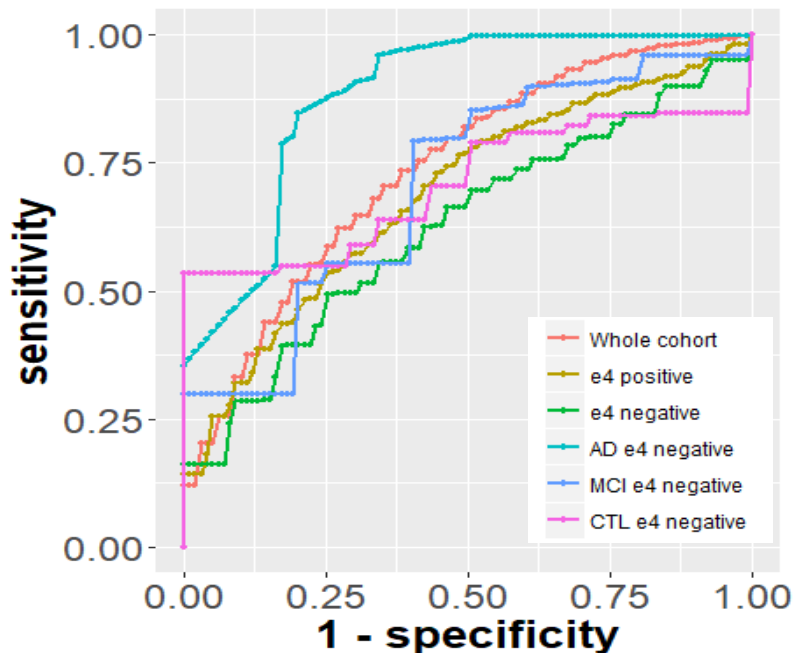
Biomarker Discovery Study timeline



Biomarker Discovery Study timeline



Prediction CSF A β ⁺ by multivariate untargeted plasma proteomics



	Features	AUC
Whole cohort	Age, gender, APOE ϵ 4 & 15 proteins	0.74
APOE ϵ 4 carrier	Age & 12 proteins)	0.64
APOE ϵ 4 non carrier	15 proteins	0.63
MCI APOE ϵ 4 non carrier	3 proteins	0.77
HC APOE ϵ 4 non carrier	14 proteins	0.74

Reuse: recruitment from existing cohorts

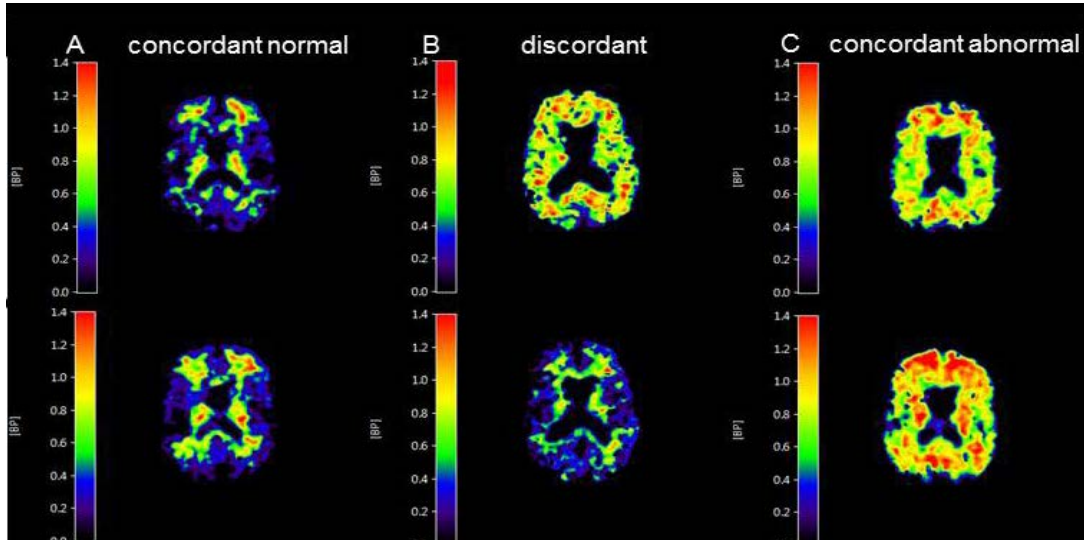


PreclinAD study (n=280)
VUmc: monozygotic twin pairs



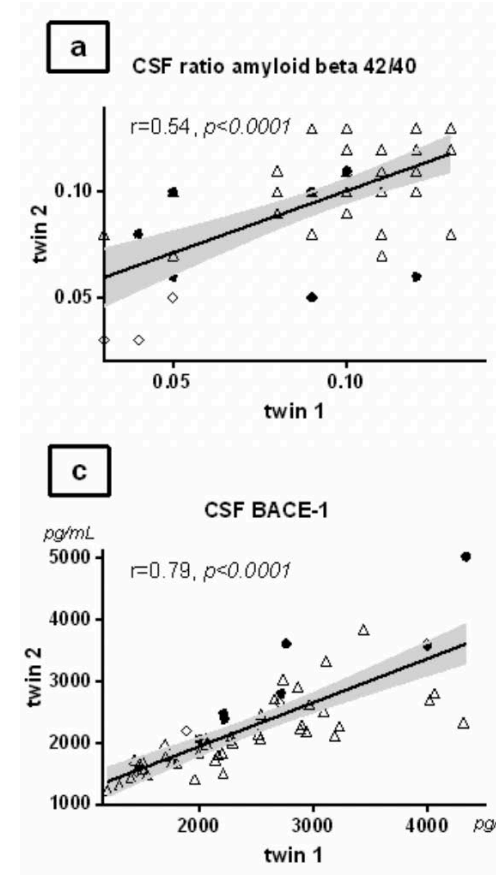
90+ study
(n=120)

PreclinAD twin study



Correlation within pair=0.55
n=200 (96 pairs)

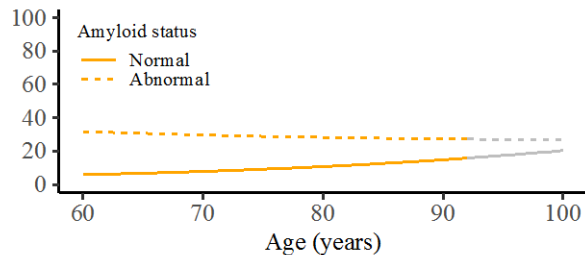
Konijnenberg et al submitted



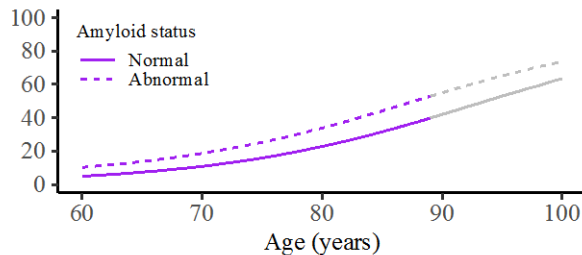
EMIF-AD 90+ study + preclinAD



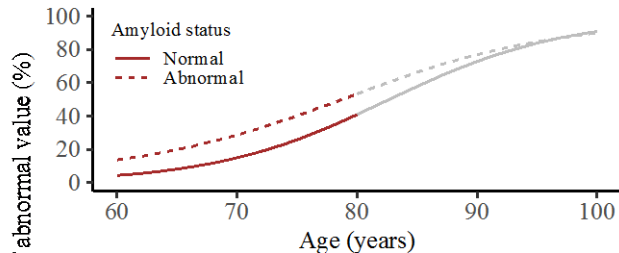
A. MMSE



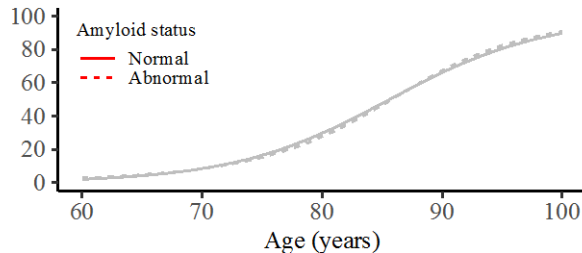
B. CERAD memory test



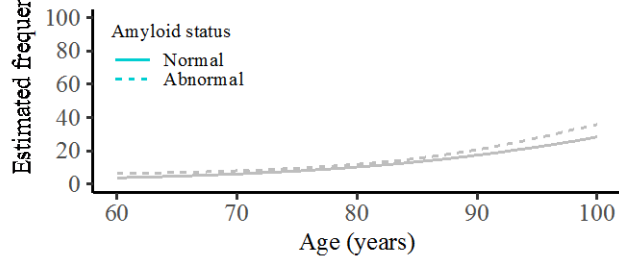
C. Digit Symbol Substitution Test



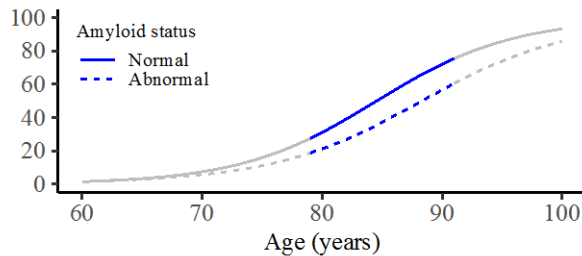
D. Hand grip strength



E. Skeletal muscle mass index



F. Hippocampal volume



Change of cognitive, imaging, frailty measures with age as a function of amyloid positivity

Legdeur et al in prep

Collaborations



- ❖ EPAD:
 - Prepad: selection research participants for EPAD cohort
 - EPAD catalogue
- ❖ ROADMAP
 - Selection cohorts for model validation
- ❖ AMYPAD:
 - Inclusion participants preclinAD in prospective study
- ❖ Aetionomy
 - Providing plasma proteomic and genomic data EMIF-AD MBD study
- ❖ DPUK:
 - Providing software catalogue and participant selection tool

Next steps



❖ EMIF-2

- Maintain and expand datasharing infrastructures
 - Host future IMI cohort data?
- Funding Janssen, Lilly, UCB
- Provide data analysis expertise
- Share infrastructures for use in other disorders
 - Multiple sclerosis and Parkinson's disease

- Stephanie Vos, Isabelle Bos, Karl Herholz, Stephan Carter, Rainer Hinz, Elles Konijnenberg, Anouk Den Braber, Jori Tomassen
- Gerald Novak, Mark Gordon, Sebastiaan Engelborghs, Jana Podhorna, Gayan Perera, Rob Stewart, Elizabeth Baker, Alejo Nevado-Holgado, Wenbo Tang, Preciosa Coloma, Lisa Ford, Nienke Legdeur, Maryam Badissi, Christian Schultheis, Rosemary Abbot, Hilkka Liedes
- Simon Lovestone, Johannes Streffer. Alison Baird, Cristina Legido-Quigley, Richard Dobson, Stephen Newhouse, Sarah Westwood, Anna Myers, Stuart Snowden, Malcom Ward, Lars Bertram, Kristel Slegers, Katie Lunnon, Henrik Zetterberg, Frederik Barkhof, Mara Ten Kate, Giovanni Frisoni, Alberto Redolfi,
- Piotr Lewczuk, Hilkka Soininen, Henrik Zetterberg, Kina Höglund, Maria Pikkarainen
- PI's data-cohorts: Philip Scheltens, Sebastiaan Engelborghs, Giovanni Frisoni, Rik Vandenberghe, José Luis Molinuevo, Anders Wallin, Alberto Lléo, Julius Popp, Pablo Martinez-Lage

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- Gerald Novak, Mark Gordon, Sebastiaan Engelborghs, Jana Podhorna, Gayan Perera, Rob Stewart, Elizabeth Baker, Alejo Nevado-Holgado, Wenbo Tang, Preciosa Coloma, Lisa Ford, Nienke Legdeur, Maryam Badissi, Christian Schultheis, Rosemary Abbot, Hilkka Liedes
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