AMYPAD
Amyloid imaging to prevent
Alzheimer´s Disease

# AMYPAD

## Amyloid Imaging to Prevent Alzheimer's Disease

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www.amypad.eu

# Amyloid Imaging to Prevent Alzheimer's Disease

Part of Innovative Medicines Initiative (IMI) program, a joint undertaking between the European Union and the European Federation of Pharmaceutical Industries and Associations (EFPIA)

A 5-year programme with a budget of €27.3M distributed across a total of 15 partners.

**Academia**

VU University Medical Center Amsterdam

Université de Genève

The University of Edinburgh

UCL

Karolinska Institutet

barcelonaβeta Brain Research Center

Hôpitaux de Toulouse

University of Cologne

Radboudumc

**EFPIA**

GE Healthcare

Janssen

Life Molecular Imaging

**Patient organisation**

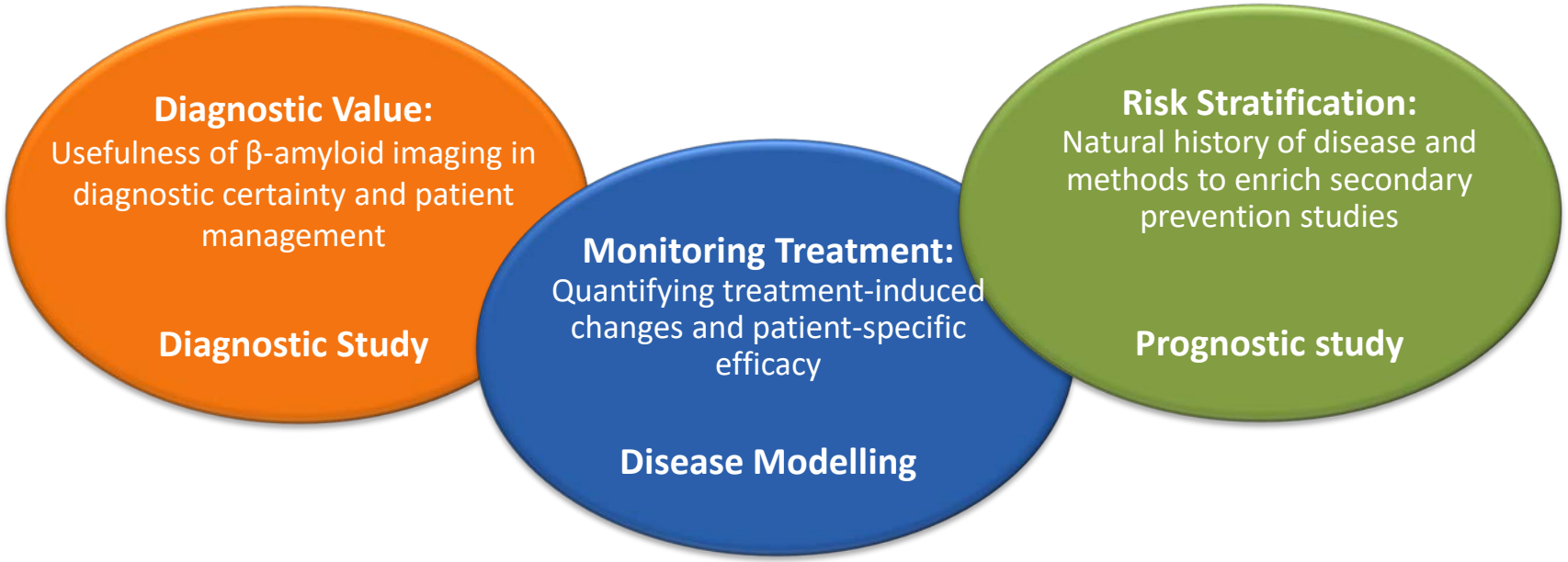
Alzheimer Europe

**SMEs**

IXICO

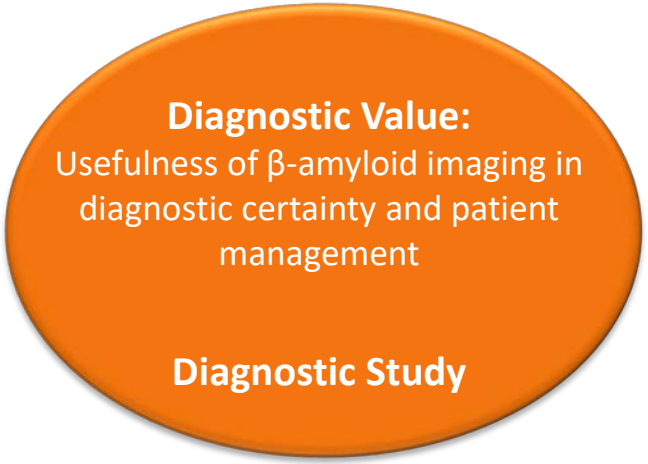
SYNAPSE

# Two studies to deliver on objectives




| Study/objective | Cohort | Baseline PET | Follow-up PET | Total scans |
|---|---|---|---|---|
| Diagnostic | Memory clinic | 900 | 300 | 1200 |
| Prognostic | Natural history | 2000 | 1000 | 3000 |
| Disease Modelling | All subjects | 2900 | 1300 | 4200 |

# Diagnostic & Patient Management Study




**Aim:** to determine the impact of amyloid PET imaging on diagnostic thinking in the workup of patients with SCD-plus, MCI, and dementia

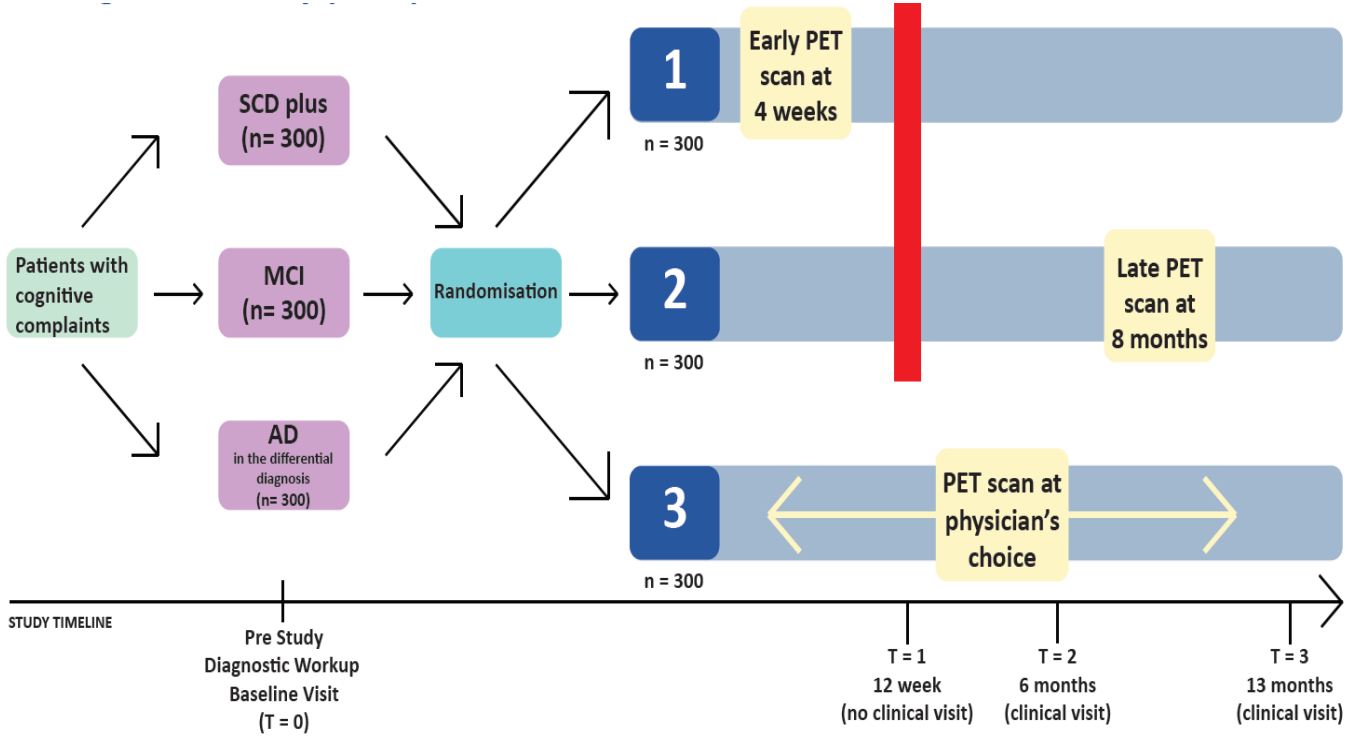
**Primary objective**: To test the hypothesis that an etiologic diagnosis with very high confidence (≥90%) is reached **earlier** if amyloid PET imaging is performed early in the diagnostic workup

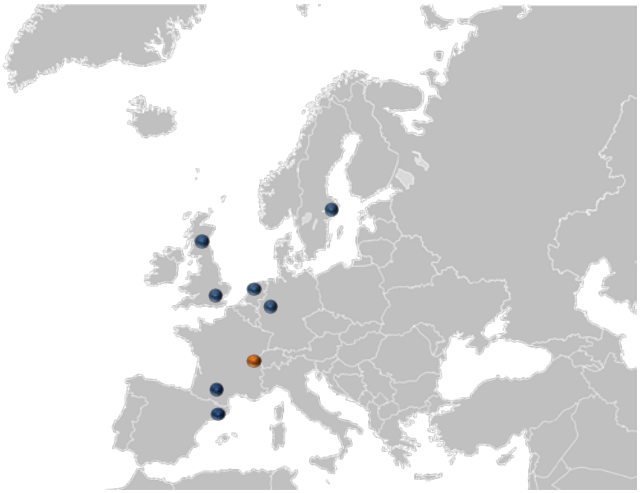
**Secondary objectives**: diagnosis and confidence, patient management, HTA, quantitative PET

**Novel features:** randomized design & inclusion of SCD-plus

# Randomization, SCD value & cost-effectiveness

## *(Across Europe, n=900)*



**Randomised design**

Close adherence to clinical practice

Less observer bias (e.g. IDEAS, ABIDE)

Longitudinal observations

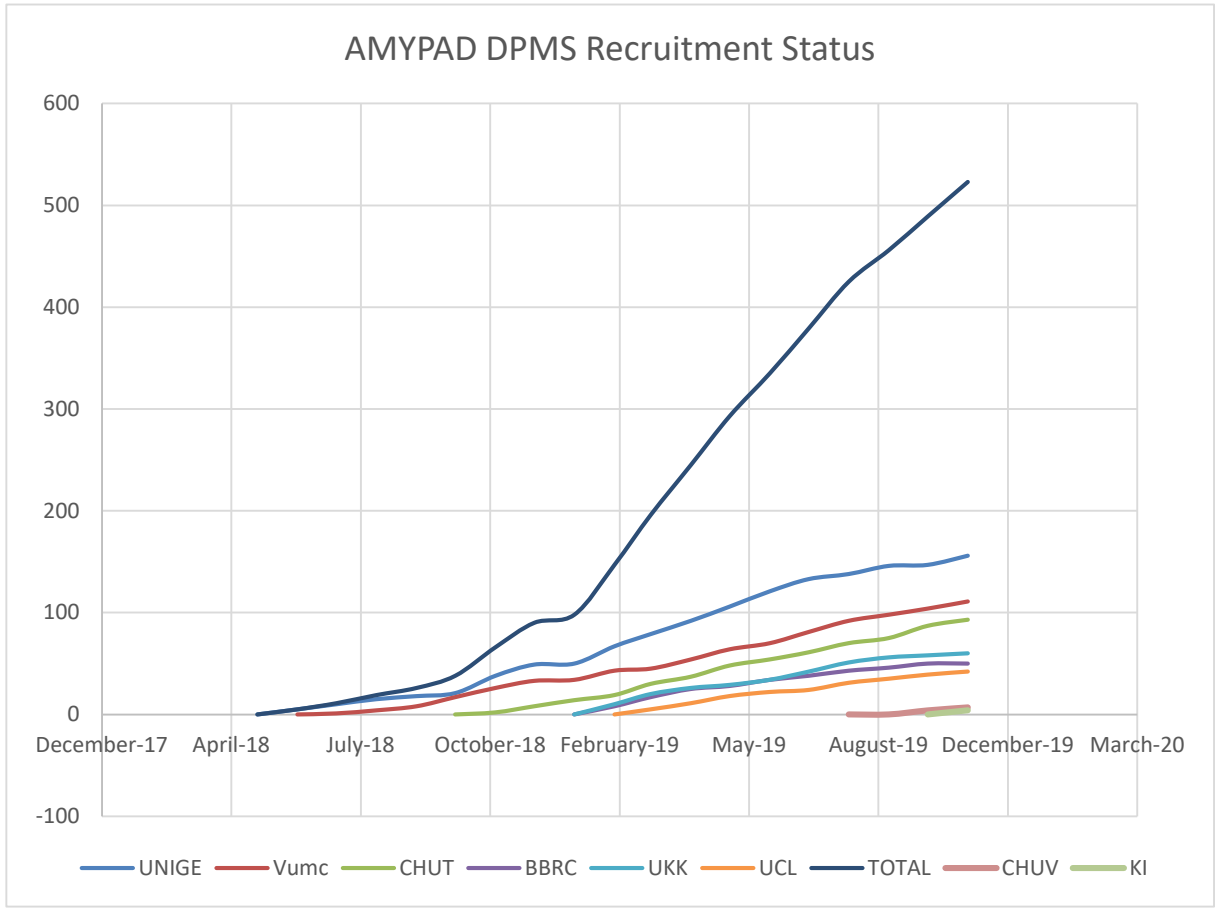
**Recruitment status**: 523 randomized

**EudraCT NUMBER: 2017-002527-2**

# For who and when is it valuable? Is it cost-effective?

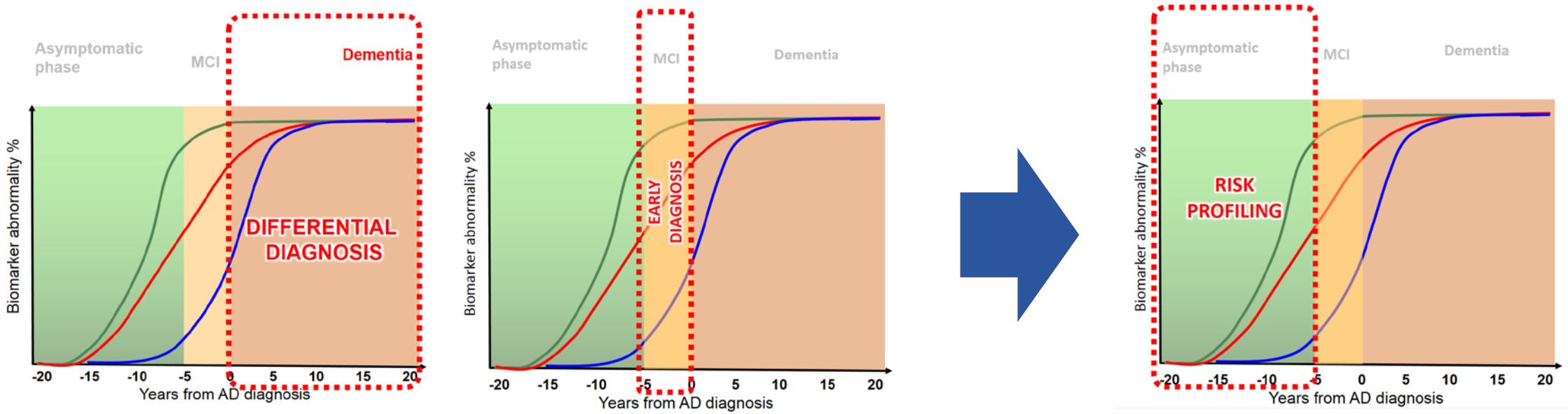
| Secondary endpoints | | | |
|---|---|---|---|
| **Diagnosis and Confidence** | **Patient Management** | **Health Economics Outcomes** | **Quantitative Imaging** |
| Time to communicate an etiological diagnosis | Patients randomised to DMD or other AD clinical trials | Impact of patient reported outcomes (eg coping skills) | Analysis of local image read results |
| Changes in etiological diagnosis over time | Change in patient management plans | Cost of diagnostic work up to high confidence Dx | Measurement of SUVr and Centiloid units across tracers and patient subgroups |
| Changes in diagnostic confidence over time | | Differences in use of medical resources | Comparison of global & visual read results to quantitative measures across tracers & subgroups |
| Likelihood patients symptoms due to AD over time | | Subject withdrawals/costs | **Early Arm will get 2nd scan**: measurement of longitudinal change |
| Changes over time in use of amyloid in free choice arm | | | |

# Recruitment ongoing, balancing strata




| Site | SCD | MCI | Dementia |
|---|---|---|---|
| UNIGE | 33 | 81 | 33 |
| VUmc | 20 | 37 | 45 |
| CHUT | 26 | 40 | 19 |
| BBRC | 24 | 22 | 2 |
| UKK | 5 | 34 | 19 |
| UCL | 10 | 23 | 5 |
| CHUV | 0 | 4 | 0 |
| KI | 0 | 0 | 0 |
| **TOTAL** | **119** | **240** | **123** |

# From early diagnosis to secondary prevention



# Prognostic and Natural History Study


**Aim:** to understand the role of amyloid PET imaging in predicting progression within each domain of a so-called AD risk probability spectrum

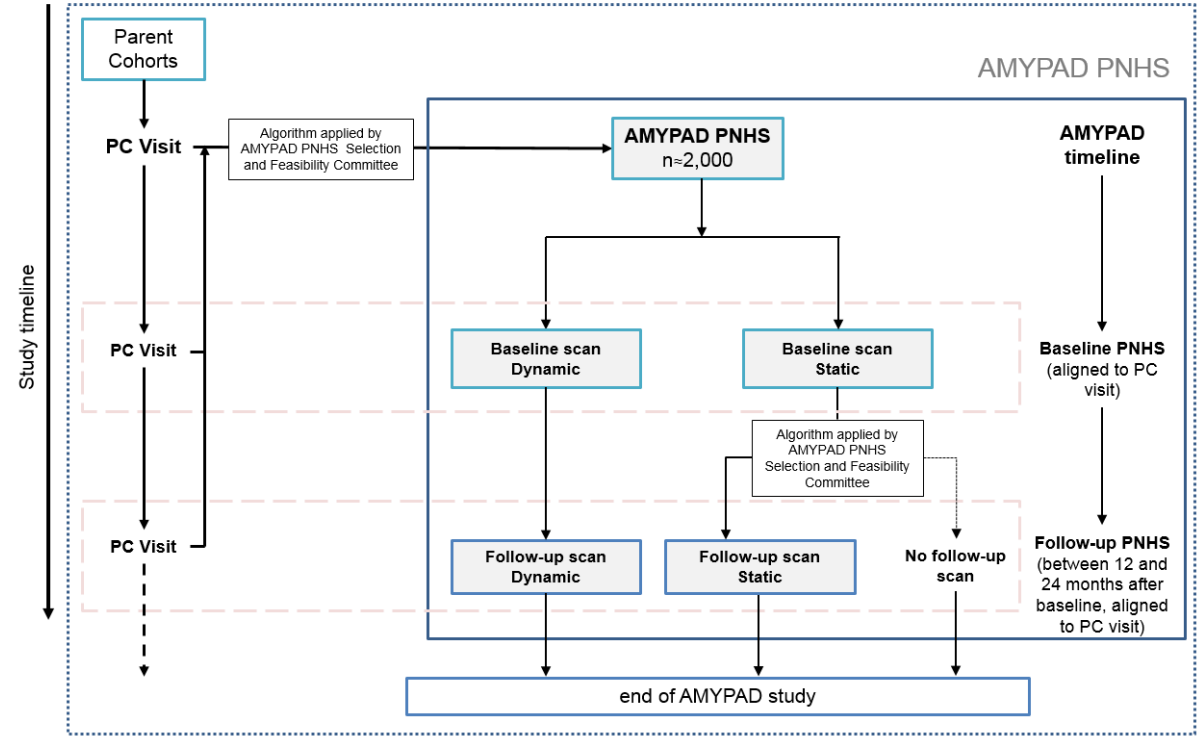
**Primary objective**: quantitatively assess amyloid burden using PET to complement the extensive assessment of Parent Cohorts and enable risk assessment and updated disease models

**Secondary objectives**: determine and assess the utility of rate of amyloid accumulation, CBF proxy measures, advanced PET analyses and several risk factors in predicting cognitive and other AD-related decline

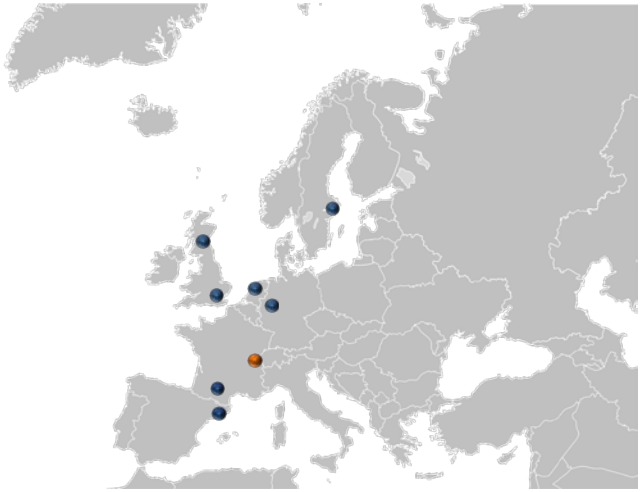
**Novel features:** dynamic & quantitative PET, adaptive inclusion, effective resource utilization and collaborative framework

# Large scale amyloid PET in preclinical/prodromal AD

## Parent Cohorts for PNHS




**Recruitment status**: 319 enrolled



- ✓ ***~ 20 sites across Europe***
- ✓ ***2,000 cognitively unimpaired subjects***
- ✓ ***Focus on "gray-zone" of amyloid build up***

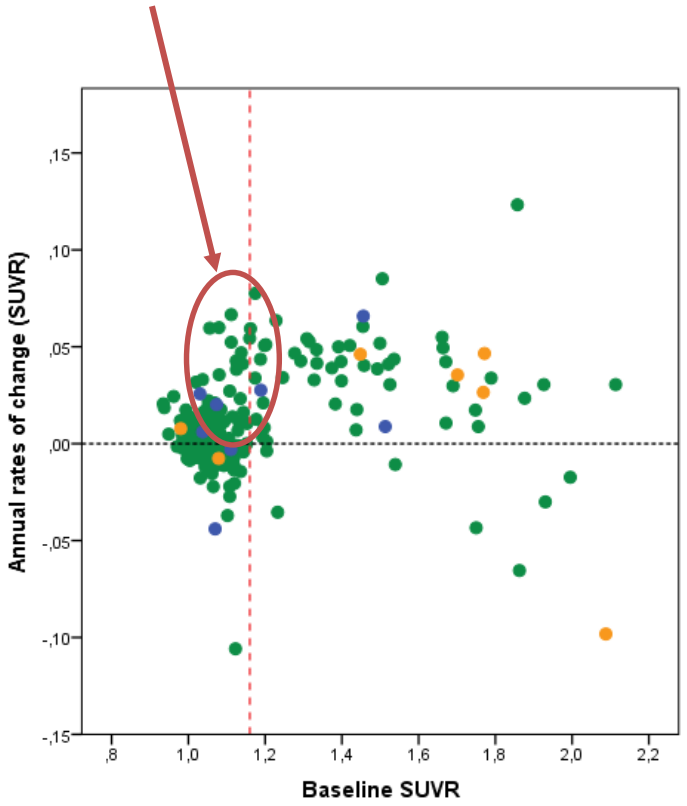
**Study design**

*Dynamic scans* as preference

*Longitudinal PET* in at least 50%

# Focus on “gray-zone” of amyloid build up

Initial amyloid accumulation, even **prior** to current abnormality thresholds




Parent Cohorts for PNHS
*Available biomarkers*

*Select 80% of target subjects based on risk factors available (20% at random):*

- *Previous PET/CSF*
- *Age*
- *APOE4 status*
- *Family history*
- *etc*

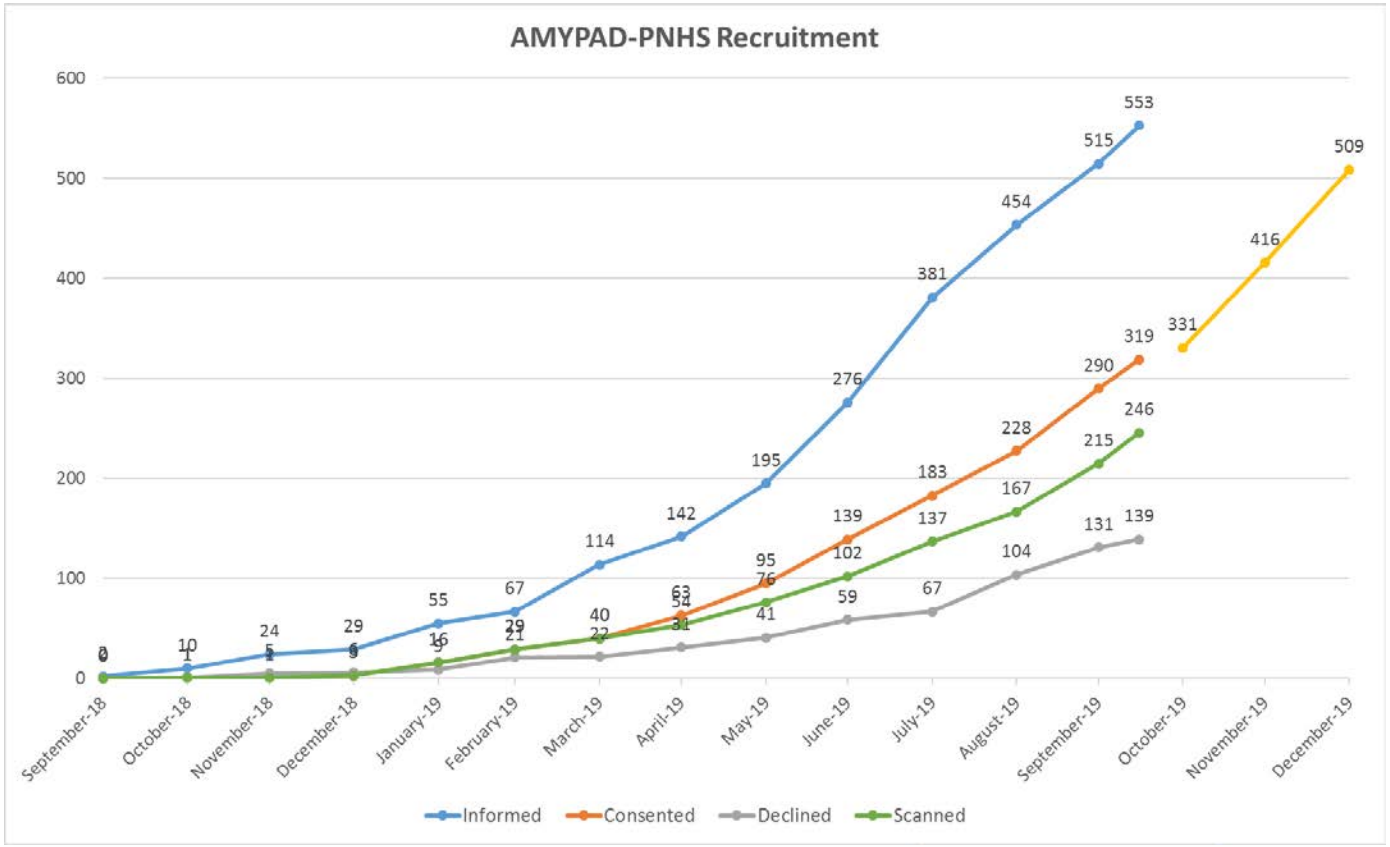
AMYPAD PNHS Scan #1

*Re-select enrolled participants for follow-up (50%) based on:*

*previous info + AMYPAD PNHS scan results*

AMYPAD PNHS Scan #2

# Ongoing recruitment of participants and Parent Cohorts




| Cohort | # participants | Inclusion (expected) |
|---|---|---|
| EPAD | >1500 | October 2018 |
| EMIF-AD | 190 | May 2019 |
| ALFA+ | 200 | November 2019 |
| F-PACK | 180 | Q4 2019 |
| GAP | 150 | Q1 2020 |
| FACEHBI | 130 | Q1 2020 |
| BIOFINDER | 350 | Q2 2020 |
| Others? | - | - |

# Earlier and etiological diagnosis & improving risk profiling

## Early diagnosis (AMYPAD Diagnostic Study)

- Positive and negative predictive value in real-life setting
- Actual change in management
- Cost-effective implementation and reimbursement possibilities

## Natural history and risk stratification (AMYPAD Prognostic Study)

- Value of quantitative PET in preclinical/prodromal AD
- Who is at most risk of developing dementia and when can we intervene
- How can we best measure the impact of treatment

# Thank you



The project leading to this application has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 115952. This Joint Undertaking receives the support from the European Union's Horizon 2020 research and innovation programme and EFPIA