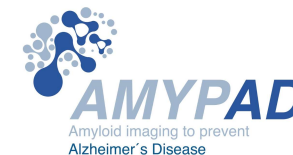# Methodological and Logistic Strategies for a Large Multi-Center β-Amyloid PET European Project: Amyloid Imaging to Prevent Alzheimer's Disease (AMYPAD)

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Background

'**Amyloid imaging to prevent Alzheimer's disease**' (AMYPAD) is a 5-year programme within the Innovative Medicines Initiative (IMI), a joint undertaking between the European Union and the European Federation of Pharmaceutical Industries and Associations (EFPIA).

AMYPAD will study the **impact of β-amyloid PET imaging** on:

- the **diagnosis and management** of Alzheimer's Disease (AD).
- the **natural history** of β-amyloid accumulation in the **pre-symptomatic** stage of AD,
- the selection of individuals for secondary **prevention trials**.

The AMYPAD project encompasses two studies:

1) The **Diagnostic and Patient Management Study** (DPMS) which aims at assessing the **impact of β-amyloid PET imaging on the clinical management** of individuals in the **spectrum from subjective cognitive decline (SCD) towards mild cognitive impairment (MCI) and in dementia of unclear aetiology** (WP3).

2) The **Prognostic and Natural History Study** (PNHS) that will be conducted to contribute to the Longitudinal Cohort Study (LCS) of the European Prevention of Alzheimer's Dementia (EPAD; http://ep-ad.org/) to better **understand the natural history of β-amyloid accumulation in the pre-symptomatic and prodromal stages of AD** (WP4) as well as **to improve disease modelling and treatment monitoring** (WP5).

Both studies will include determinations of brain amyloid load at baseline and mean change over 12-24 months as measured by PET with:

- [18F]flutemetamol (Vizamyl - GE Healthcare) and
- [18F]florbetaben (NeuraCeq - Piramal Imaging)

To contribute to these studies, a network of ~**20 European PET centres** aims to conduct a total of 6000 scans.

	Baseline PET	Repeat PET (2 yr)	Total Scans
Diagnostic & Management Study (WP3)	900	300	1200
Prognostic & Natural History Study (WP4)	3200	1600	4800
Total Subjects:	4100	1900	6000

Methods
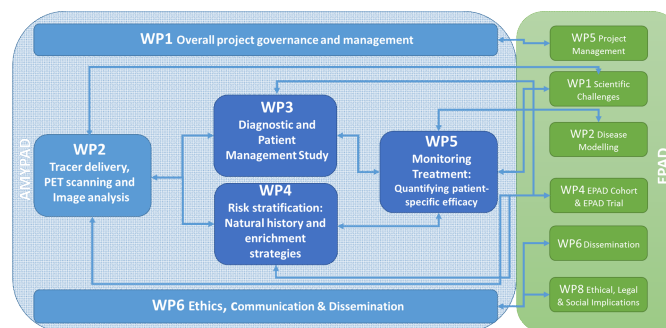
AMYPAD structure plan and relation to EPAD

AMYPAD's work package 2 (WP2) will support these goals by:

- Developing an **efficient tracer supply strategy**,
- Setting-up a **clinical imaging network**,
- Developing **image acquisition, quality control and quantification protocols**,
- Deploying a **centralized platform** for **image transfer, analysis and sharing**.

Since both NeuraCeq and Vizamyl will be used in AMYPAD, **standardization of β-amyloid load measurements** will be crucial to ensure **full comparability** of the project outcomes across tracers.

On top of this, specific sub-studies in WP2 will focus on:

1) Accurate determination of **β-amyloid change rates though dynamic PET** scanning
2) Further development of the **role of PET/MR for β-amyloid imaging**
3) **Refinement of β-amyloid quantification** methods by developing novel Partial Volume Correction and PET/MR Attenuation Correction methods
4) Identification of **lifestyle and environmental factors** affecting β-amyloid accumulation.
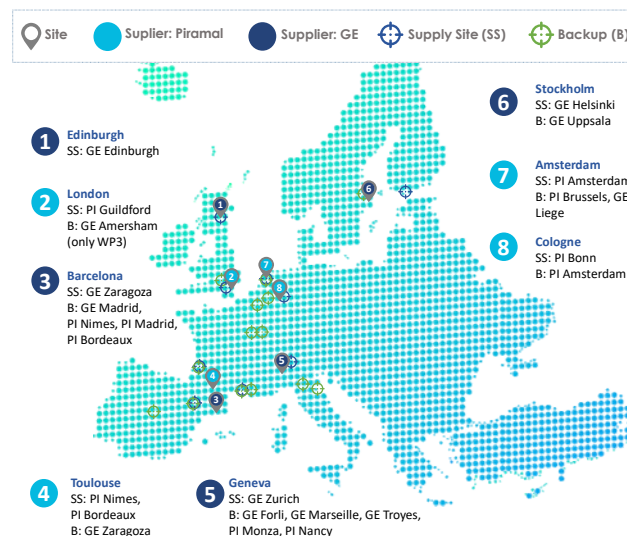
Results

At present, AMYPAD WP2 has:

1. Designed the **tracer distribution** strategy,
2. Setup the **clinical imaging network**,
3. Deployed the **centralized platform** for **image transfer and quantification**.

Outcomes in AMYPAD will be expressed in the **Centiloid scale** (Klunk *et al.* Alzheimers Dement. 2015) in order to ensure the full comparability across tracers and to enable generalization the results.
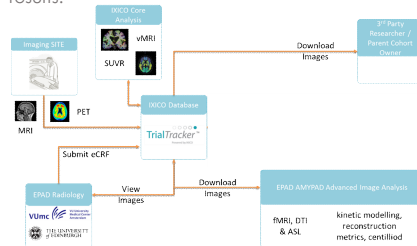
Database / data sharing workflow for the Prognostic & Natural History Study (the same holds for the Diagnostic & Patient Management Study, but without harmonized MRI scans)

1 Edinburgh
SS: GE Edinburgh

2 London
SS: PI Guildford
B: GE Amersham
(only WP3)

3 Barcelona
SS: GE Zaragoza
B: GE Madrid, PI Nimes, PI Madrid, PI Bordeaux

4 Toulouse
SS: PI Nimes, PI Bordeaux
B: GE Zaragoza

5 Geneva
SS: GE Zurich
B: GE Forli, GE Marseille, GE Troyes, PI Monza, PI Nancy

6 Stockholm
SS: GE Helsinki
B: GE Uppsala

7 Amsterdam
SS: PI Amsterdam
B: PI Brussels, GE Liege

8 Cologne
SS: PI Bonn
B: PI Amsterdam

Map: Tracer allocation and backup options for the 8 WP3/WP4 (Wave 1) participating centers

Conclusions

- AMYPAD will **improve our understanding** of the utility of β-amyloid PET imaging in **both clinical and research** contexts.
- Through WP2, AMYPAD will **develop novel acquisition and quantification methodologies** for β-amyloid PET imaging.
- The wealth of PET data acquired in the context of AMYPAD **will be reconciled with that collected by EPAD**
- As a fundamental goal of both projects, **all data will be made available** for the general scientific community.

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Academic partners

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