AMYPAD
Amyloid imaging to prevent Alzheimer´s Disease

AMYPAD Deliverable 4.8

Report on selection criteria for repeat imaging

Publishable Summary

Within the AMYPAD Prognostic and Natural History Study (PNHS), approximately 50% of enrolled participants will be invited to undergo a follow-up (repeat) imaging session in order to determine amyloid accumulation rates in the early phases of Alzheimer's disease. This deliverable describes the scientific considerations behind establishing a number of selection criteria to identify and invite a limited number of participants for follow-up, so that resources are invested in those who would provide the most relevant information regarding the disease's early stages.

First, the overall cohort enrollment has the particular goal to focus its recruitment to individuals at the beginning of the pathological cascade, i.e. those who are either at the cusp of developing amyloid pathology and/or those who have just initiated accumulating amyloid plaques. For that purpose, the team has suggested a target distribution of amyloid levels in the final AMYPAD PNHS cohort to be 20% amyloid negative subjects, 60% in a so-called "gray-zone" and 20% amyloid positive subjects. Similarly, when following individuals longitudinally, the goal is to make sure the majority of the "gray-zone" subjects do receive repeat imaging so that we can better understand these early phases. Therefore, the selection criteria for follow-up (repeat) imaging is directly related to the definition and operationalization of the "gray-zone" definition.

Currently, two main strategies are considered for defining a "gray-zone" of amyloid burden – i.e., a level of amyloid pathology that, while not sufficient to correspond to established cut-offs of pathology, does relate to an increased risk of disease progression. Data from internal and external scientific publications have been considered, and initially, the AMYPAD PNHS team has determined a lower cut-off for a gray-zone status of 12 Centiloids.

Finally, utilizing the Centiloid cut-off as well as other well-established risk factors (CSF $A\beta_{42}$ levels, age, family history and genetic risk), the team has determined selection criteria for each individual parent cohort from which AMYPAD PNHS can recruit. This cohort-specific criteria allows for the flexibility of balancing the overall cohort balance by e.g. entering different cohorts or restricting the recruitment from any particular source. Finally, the criteria established in this document and communicated to the parent cohorts are dynamic, so that the study leadership can regularly monitor the cohort balance and adjust the recruitment/selection according to emerging evidence.

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