Progreessing on the identification of early stages of dementia and cognitive decline in Greece (Athens)

Presentation of the Cognitive Disorders Clinic of Aiginition Hospital and its role in the COMOFORTage project

The Cognitive Disorders Clinic of Eginitio Hospital operates under the auspices of the 1st Department of Neurology of the National and Kapodistrian University of Athens since 2004.

The Clinic work has a double focus: diagnosing and detecting cognitive decline detection and providing adequate care to people with cognitive decline due to neurodegenerative disease.

Dementia in Greece

In Greece, one-quarter of the population will be over 60 years old, and more than 450,000 already suffer from dementia-related diseases. According to Alzheimer Europe, the incidence rate of dementia in Greece (in % of the population) was 1.99% in 2018 and will reach 3.95% in 2050. This is the second highest rate in the EU, just after Italy.

A first Greek National Action Plan for Dementia was approved in March 2016 but it is only in 2023 that a bill was introduced to support an updated and more comprehensive plan. It aims to enable an effective treatment of dementia syndromes and improve the quality of life for people with dementia and their caregivers, support the prevention of dementia and the promotion of the population's health and focus on the implementation of cost-effective management measures for the dramatically increased number of people with dementia. The registration and classification of people with dementia in Greece and research on dementia are two important axes of this action plan. The bill

Who are the patients coming to the clinic ?

Patients are usually referred to the Cognitive Disorders Clinic. They are examined by a neurologist and they undergo a comprehensive neuropsychological assessment. If deemed necessary, patients are referred for blood tests, brain imaging with CT or MRI, lumbar puncture for measuring biomarkers, etc.

How is the follow-up of diagnosed patients organized in the clinic ?

People who do not face any serious cognitive decline but complain about their cognitive abilities are advised either to visit the Clinic again after 2-3 years or to participate in studies

performed by the Cognitive Disorders Clinic that focus in preclinical and prodromal stages of dementia.

People who are diagnosed with Mild Cognitive Impairment are advised to visit the Clinic again after ~12 months

People who are diagnosed with any type dementia are advised to visit the Clinic every 6 months in order to monitor their symptoms and prescribe the necessary medication.

Research is also part of the clinic's job.

The Clinic is actively contributing to the investigation of the epidemiology of dementia and cognitive disorders in Greece and the factors associated with dementia prevalence and incidence. The prevention of the preclinical and prodromal (when the first symptoms are experienced) stages of dementia is of particular interest and hence the clinic has participated to many Observations and Clinical Studies. Studying dementia is complex and require to collect data over a long period of time.

The important number of patients Followed in the clinic also allows thus to take an active role in many clinical trials for dementia drugs development. This has given the opportunity to many people with Mild Cognitive Impairment and/or dementia to participate in such trials and thus contribute to scientific research and benefit from new treatments.

Towards an early detection and better understanding of dementia

The development of dementia includes a preclinical and a prodromal (when first symptoms appear) stage that both may last many years (even decades) before diagnosis of dementia. The prodromal stage- also known as mild cognitive impairment (MCI)- is characterized by mild cognitive decline (that may affect complex attention, executive function, learning and memory, language, perceptual-motor control, and social cognition). This decline is noticeable and superior to the expected average for a person of this age. However, this decline is not severe enough to affect a person's daily life. The preclinical stage of dementia refers to the period where there are measurable changes in the brain or/and other biomarkers, but no noticeable symptoms of cognitive decline. Some of the brain changes that occur during the preclinical stage are already documented. However, researchers and clinicians are eager to identify other biomarkers that may indicate this stage. Besides biomarkers, it is also important to further investigate if and to which extent genetics, lifestyle and health factors have a protective role against Alzheimer Disease progression. The goal is to understand the relative incidence weight of genetic predisposition and other factors and also to identify how different causative and protective factors interact. This objective is shared by all COMFORTage pilots.

What will be the key objectives of the pilot in COMFORTage ?

This study aims to identify at least **5 modifiable and non-modifiable risk factors documented** by biomarkers and other data, ranging from neuroimaging and neuropsychological data to lifestyle factors, that are possibly related to development of the early stages of dementia and cognitive decline.

Which data will the pilot be using?

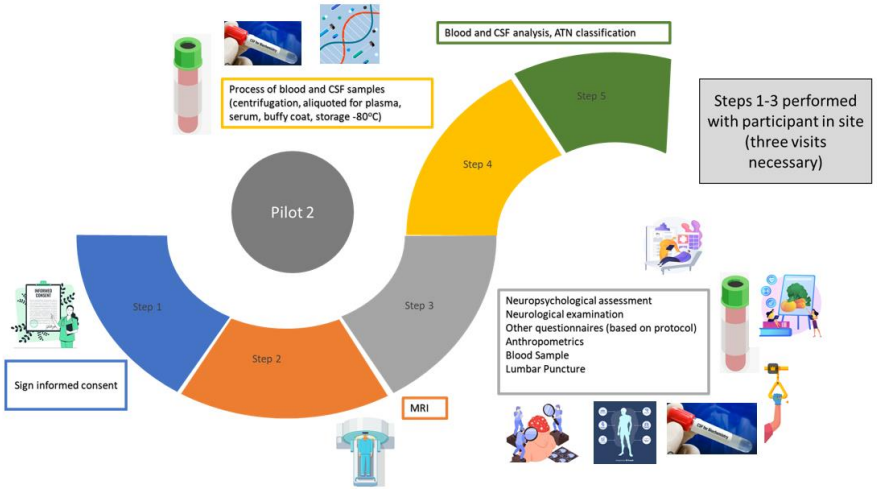
The COMFORTage pilot will be using two very large Greek studies databases which started before the project. Those data will be complemented with new data from patients enrolled during the project lifetime.

The Hellenic Longitudinal Investigation of Aging and Diet (HELIAD study) was a population-based, multidisciplinary, collaborative study designed to **estimate the prevalence and incidence of mild cognitive impairment, Alzheimer's disease and other types of dementia in the Greek population**. More generally it aimed at **evaluating the factors that contribute to the health status of older Greek people.** The sample consisted of community-dwelling older people (aged ≥65 years) from a suburb of Athens and an urban area in Greece, who were selected through random sampling from municipality registries. Volunteers participated in an extensive face-to-face evaluation with neurologists, trained neuropsychologists and dieticians, lasting approximately 2.0–2.5 hours per participant. The comprehensive assessment includes a neurological examination, a neuropsychological assessment, a dietary assessment and a collection of biomarkers (blood). All participants also completed questionnaires about their lifestyle (diet, sleep, physical activity, leisure time activities, etc) and any psychiatric symptoms. Complete neurological, psychiatric, functional, neuropsychological and dietary assessments were **repeated every 3 years** so that each participant is assessed multiple times. 2000 participants completed the baseline assessment, 1100 completed the 3-year follow-up and 300 who completed the 6-year follow-up. Based on the findings of this study we **have data for the prevalence and incidence of dementia in Greece but also valuable results on factors associated with development of dementia**. More details on this study can be found here.

The second one is still ongoing and aims to address several research questions concerning the **preclinical and prodromal stages of Alzheimer's disease**. The ALBION study is a longitudinal Biomarker Investigation Of Neurodegeneration. It thus explores potential markers for early detection, prediction, and primary prevention of dementia. Briefly, the **study's sample consists of middle-aged and older adults (≥40 years old) with subjective cognitive complaints and/or concerns about their future cognitive health**. They can be either cognitively normal or have at most mild cognitive deficits but clearly do not meet the criteria for dementia diagnosis. Each participant undergoes an extensive assessment including several demographic, medical, social, environmental, clinical, nutritional, neuropsychological determinants and lifestyle ((diet, sleep, physical activity, leisure time activities, etc) activities. In addition, during the baseline evaluation all participants undergo a MRI and a lumbar puncture is performed. Participants are evaluated bi-annually after their baseline assessment. Participants are followed-up every two years. Thus, so far, 250 people have completed the baseline assessment and 170 have completed at least one follow-up. More details on that study can be found here.

The new study started with COMFORTage has many similarities with ALBION study. Participants are above the age of 40 and are either cognitively normal or have mild cognitive deficits but **clearly do not meet the criteria for a diagnosis of dementia.** NKUA anticipates recruiting 40-50 participants/year.

How is the enrolment in the COMFORTage pilot organised ?

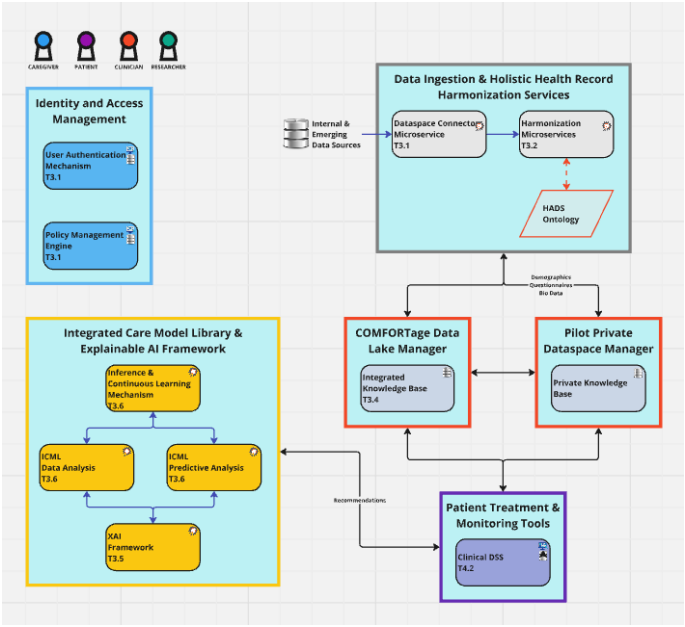


The figure shows the different steps for the data collection process and lists all data collected. One can immediately see the important diversity of information collected either through anamnesis and clinical examination, biomarkers or information provided by the patient himself through adequate tools, questionnaires and scales which have been agreed upon with the other COMFORTage pilots. Let's mention the evaluation of participants' everyday functioning and presence of any movement disorders. Physical strength of the upper extremities will also be estimated using a handgrip electronic dynamometer. The participants will be screened for depression, anxiety, and psychotic symptoms and a comprehensive battery of neuropsychological tests assessing all major cognitive domains. The blood samples collected will allow genomic DNA extraction and a close follow-up of important routine parameters. The Cerebrospinal fluid (CSF) and Magnetic resonance imaging data (MRI) collected will allow to categorize individuals based on the core Alzheimer disease (AD) fluid/imaging biomarkers, independently of cognition or clinical staging.

What will the COMFORTage platform bring to this pilot ?

Thanks to the COMFORTage AI based Virtual Health Platform, NKUA will have access to different and much more advanced techniques (compared to simple statistical analyses) to analyse the data gathered in the studies. Specifically, machine learning (ML) and artificial intelligence (AI) offer powerful tools for identifying biomarkers of dementia by leveraging large datasets and uncovering patterns that might be imperceptible to humans.

The clinicians will also have the opportunity to enhance their understanding of the disease and improve diagnostic precision. As shown in the figure For each enrolled patient, a digital twin will be created on the basis of all data collected on almost real time; this Digital Twin will trigger an AI-based decision support system which will provide the clinician with a predictive analysis cognitive decline risk. The ingestion of data of all pilots in the COMFORTage platform will also to enhance at a more general level diagnostic precision, streamline risk assessment, and support early intervention strategies. This will thus contribute to the development of early detection strategies and personalized care. The data gathered by the project are also meant to be reused by other studies: The implementation of the European Health Data Space provides a unique opportunity to create much more value with all data collected.



Conclusion:

The participation of the NKUA team in COMFORTage is a great opportunity to bring its work to identify risk factors and their interactions in a new dimension. The new knowledge acquired will allow to adapt the Greek strategy for Dementia and define more pertinent interventions targeting both primary and secondary prevention.