Dementia in Italy and the Rome Region

Dementia is the most significant clinical emergency affecting the elderly population. Due to the aging population, the prevalence of dementia has reached near-epidemic proportions, with 12 million people affected across Europe. According to the latest Censis report, there are approximately 1.2 million people living with dementia in Italy, half of whom are affected by Alzheimer's disease. It is noteworthy that fewer than 50% of these patients receive care from specialized centers. This places Italy in line with the European average in terms of dementia prevalence, but below average when it comes to access to specialized care.

Currently in Italy, the prevention and treatment of dementia are structured across multiple levels, but the system remains highly heterogeneous. This is mainly due to the decentralized and regionalized structure of the National Health Service (SSN). While there are national guidelines and plans—such as the 2014 National Dementia Plan (PND)—their implementation is left to individual Regions, resulting in significant territorial disparities in the provision of services, especially between the North and South of the country.

The main preventive actions focus on:

1. Raising awareness and informing the public about modifiable risk factors (lifestyle, diet, physical activity, cardiovascular disease control).
2. Early detection of cognitive symptoms through so-called "memory visits" or "Memory Clinics" (available only in some regions).
3. Non-pharmacological prevention initiatives promoted by associations, local health authorities (ASLs), and municipalities, such as cognitive stimulation groups, mental exercise courses, or social workshops for the elderly.

However, structured primary prevention at the public health level is still limited, and much depends on local projects or exceptional funding.

On the treatment front, the SSN provides:

- Clinical diagnosis at Centers for Cognitive Disorders and Dementia (CDCD), which may include neurologists, geriatricians, psychologists, and neuropsychologists.
- Pharmacological therapies (particularly cholinesterase inhibitors or memantine for Alzheimer's).
- Psychosocial interventions, cognitive rehabilitation, and family support.
- Home-based or semi-residential services (such as Alzheimer's day care centers).

Again, coverage and quality of service provision vary greatly by region, depending on financial resources, local political priorities, and the availability of social and healthcare networks. Each Region has broad autonomy in planning and organizing healthcare services, resulting in disparities in access, waiting times, quality of services, and significant variability in diagnostic and treatment pathways with no effective standardization.

This creates major challenges for implementing a uniform national strategy for dementia prevention and treatment, hinders equitable access to healthcare and therapeutic opportunities, complicates the collection of consistent data (impacting clinical research and the effectiveness of predictive models), and necessitates localized, personalized interventions that are harder to coordinate centrally.

To improve the situation, it would be advisable to:

- Strengthen coordination between the State and Regions.
- Encourage digitalization and sharing of clinical data.
- Support specialized training for professionals, especially in more vulnerable areas.
- Promote integrated social and healthcare models throughout the national territory.

There is a widespread belief that dementia is a natural and expected consequence of aging. This assumption is incorrect, because if detected early and supported with preventive measures and symptomatic care, the more severe and disabling aspects of the disease can be delayed. Timely diagnosis is essential for activating prevention and symptomatic treatment strategies. In this context, early diagnosis of dementia is crucial, as it enables accurate planning and implementation of interventions aimed at improving the quality of life (QoL) for affected individuals.

The identification of modifiable risk factors depends on the availability of healthcare professionals with integrated knowledge, age-appropriate care programs, and territorial approaches based on multidisciplinary specialized services for both prevention and diagnosis of dementia.

The rapid aging of the population poses a major challenge for European society and economy, as aging is associated with an increase in chronic diseases, mental disorders, disabilities, and frailty. Living longer and healthier is becoming an increasingly important reality. Current research shows that pathological processes associated with neurodegenerative diseases, such as Alzheimer's disease (AD), can begin decades before clinical symptoms appear. The prodromal stage of dementia is often marked by mild cognitive impairment (MCI), a condition involving cognitive decline greater than expected with normal aging, but not yet significantly interfering with daily activities. Additionally, subjective cognitive decline (SCD), characterized by a self-perceived reduction in cognitive abilities without detectable neuropsychological deficits, also presents a risk of progression to dementia. Unfortunately, SCD is often underestimated, and there are currently no reliable biomarkers to predict its clinical progression.

The Gemelli Memory Clinic

The *Memory Clinic*, directed by Professor Camillo Marra, was established with the goal of creating a synergistic effort to bring together, under unified management, the various competencies from the neurological and geriatric fields involved, thus creating pathways and preferential channels to meet the growing demand for diagnosis and care related to dementia-related conditions.

Most patients who come to the Memory Clinic are referred by their general practitioner, who, in cases of suspected cognitive impairment (detected using simple screening tools such as the CP–COG), can direct the patient to specialized centers (such as the Memory Clinic of the Gemelli University Hospital), where a comprehensive assessment is conducted to determine the type and severity of dementia.

The primary aim of the Memory Clinic's dedicated unit is to provide patients with suspected dementia rapid diagnostic access through priority admission to initial neuropsychogeriatric assessments. Within the Memory Clinic, several healthcare professionals (neurologists, geriatricians, psychologists, cognitive rehabilitation specialists, and speech therapists) work together, offering their expertise at various stages of the patient's clinical journey.

In addition to the initial neuropsychogeriatric visit, patients undergo full neuropsychological testing to evaluate cognitive functions. Based on the resulting cognitive profile, further assessments are conducted, including blood tests and cerebrospinal fluid analysis (to study tauopathy, amyloidopathy, neurodegeneration, and neuroinflammation), as well as neuroimaging tests (such as brain MRI, amyloid PET, and FDG-PET). The clinic develops therapeutic plans for dementia patients, offers geriatric and neuropsychological follow-up visits (every six months for patients with mild cognitive impairment or established dementia, and annually for those with subjective cognitive decline), and encourages participation in research focused on preclinical and prodromal stages of dementia. The clinic also provides genetic counseling for familial forms of dementia (limited to early-onset cases), cognitive rehabilitation programs, and speech therapy for specific language and memory disorders that may benefit from targeted interventions.

The program aims to promote early diagnosis and management of dementia through the use of advanced technologies and innovative procedures. At the same time, it seeks to standardize care while addressing social inequalities and situations of socio-health vulnerability and fragility.

The ultimate objective is the rationalization of services and the implementation of work methodologies based on the appropriateness of the services provided. In this way, the Gemelli Clinical and Care Pathway provides a concrete response to the objectives set by the National Dementia Plan.

Timely access to early diagnosis of dementia is central to implementing preventive interventions and appropriate therapeutic and care measures. Neuropsychological assessments and neuroimaging, complemented by biological and genetic testing for familial forms of the disease, now allow for very early diagnosis with an accuracy exceeding 95%.

A recent study (conducted in collaboration with Gemelli Generator and Eli Lilly) at the Center for Cognitive Disorders and Dementia (CDCD) of the Fondazione Policlinico Universitario Agostino Gemelli IRCCS in Rome, analyzed retrospective clinical data from a large cohort of patients with cognitive decline. The total sample included 533 individuals, divided into two temporal sub-cohorts: the first, from 2017–2019, included 271 patients; the second, from 2021–2023, included 262 patients. Both cohorts showed a slight female predominance, with a median age at first evaluation of 77.1 years in the earlier cohort and 71.4 years in the more recent one—suggesting earlier access to services in the initial stages of cognitive decline.

Data were collected from anonymized medical reports (from outpatient visits and day hospital admissions) and structured hospital records, with a maximum follow-up of three years for each patient. In total, more than 2,100 clinical contacts were analyzed, allowing for a detailed understanding of diagnostic, therapeutic, and functional evolution over time.

Basic demographic variables were collected for each patient (such as gender, date of birth, and education level), along with clinical data extracted through automated natural language understanding (NLU) techniques. Diagnoses—both initial and final—were mapped across a broad spectrum of cognitive conditions, and then reclassified into four main groups: Alzheimer's disease (AD), mild cognitive impairment (MCI), other diagnoses (such as frontotemporal disorders, parkinsonism, psychiatric disorders, etc.), and diagnoses to be determined (TBD).

The analysis also included key functional and cognitive autonomy scales: the Mini-Mental State Examination (MMSE), Activities of Daily Living (ADL), and Instrumental Activities of Daily Living (IADL), enabling the evaluation of the severity and progression of cognitive decline over time.

A central aspect of the study was the detailed reconstruction of the diagnostic pathway, which included the use of instrumental examinations and biomarkers. Frequently used diagnostic tools included MRI, CT scans, PET scans (FDG and amyloid), EEG, and cerebrospinal fluid (CSF) analysis. Notably, the use of biomarkers evolved significantly: in the 2017–2019 cohort, only 5.9% of patients received a biologically based diagnosis through CSF analysis, while this figure rose to 96.4% in the more recent cohort—highlighting a marked change in clinical practice and greater integration of biological diagnostic criteria.

The study also documented the use of pharmacological therapies, extracted from clinical records and grouped into 15 categories, as well as the presence of relevant comorbidities such as hypertension, diabetes, dyslipidemia, atrial fibrillation, and other chronic conditions. These data support a rich clinical characterization, useful for predictive studies and risk stratification.

Finally, a longitudinal analysis was conducted on patients with multiple clinical contacts to assess changes in cognitive scores (MMSE) and diagnostic evolution. The integration of structured and unstructured data, combined with the use of text mining and NLP techniques, makes this dataset particularly suitable for advanced data mining analyses and the development of clinical AI models.

In summary, the data collected in the study represent a rich and structured resource that offers the opportunity to explore the real-world progression of cognitive decline, assess the impact of new biomarkers and diagnostic tools, and identify predictive patterns useful for personalizing diagnostic and therapeutic pathways.

The COMFORTAGE Project

The *COMFORTAGE* project brings together a multidisciplinary team of medical and technical experts to build a pan-European framework based on integrated, community-based, and person-centered approaches to prevent, monitor, and manage dementia and frailty. COMFORTAGE aims to develop and implement advanced algorithms for the prevention, diagnosis, intervention, and treatment of dementia and frailty by adopting a holistic approach that considers all aspects of elderly life—including physical, mental, and social well-being—to design and utilize assistive technologies that promote health and age-friendly environments.

In this context, *Pilot 4*, conducted by the Gemelli University Hospital (FPG), will specifically investigate the role of blood biomarkers, genetic factors, and risk factors in developing personalized prevention and intervention strategies for cognitive decline. Emerging evidence suggests that modifying lifestyle-related factors—such as diet, physical activity, and cardiovascular health—can significantly reduce the impact of dementia in older adults. Furthermore, neuropathological changes associated with Alzheimer's disease, such as amyloid deposition, occur years before clinical symptoms appear and can be detected in the early stages of the disease.

Our pilot will build upon this data, collected at baseline and after a two-year period, combining advanced diagnostic techniques (comprehensive neuropsychological assessments, blood tests for amyloidosis, tauopathy, neurodegeneration, and neuroinflammation; connectivity analysis through functional MRI and high-density EEG) with personalized intervention strategies (nutritional plans, physical activity programs, cognitive training, and control of cardiovascular and metabolic risk factors) to delay or prevent the onset of dementia—thus contributing to the overall goals of the COMFORTAGE project.

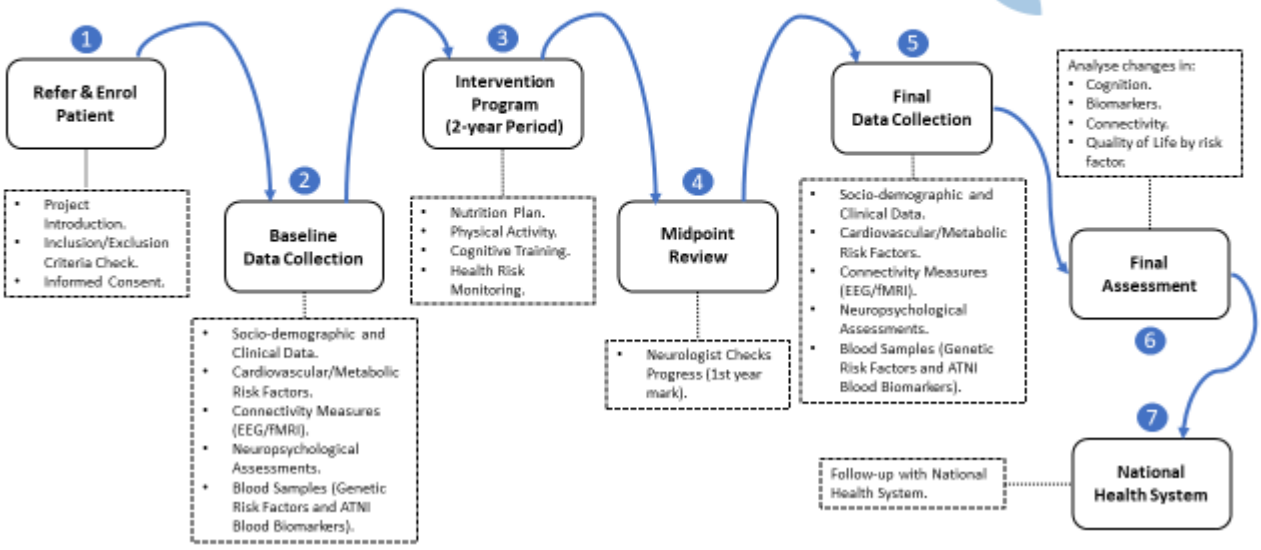
The underlying hypothesis of this pilot is that by integrating clinical, biological, genetic, and connectivity markers, it is possible to identify individuals at higher risk of progression from Mild Cognitive Impairment (MCI) or Subjective Cognitive Decline (SCD) to dementia. Early identification of at-risk individuals will allow for the creation of personalized prevention plans, which may include nutritional interventions, exercise programs, cognitive training, and the monitoring and management of metabolic and cardiovascular risk factors.

The primary goal of our pilot is to evaluate the differential impact of a two-year intervention on cognitive performance and quality of life (QoL) in individuals with SCD and MCI, stratified according to clinical, genetic, connectivity, and biomarker profiles. This objective aims to determine whether personalized intervention plans based on such stratifications lead to more significant improvements compared to standard approaches.

The study will include 100 individuals, divided into two distinct clinical categories: people with subjective cognitive decline and people with mild cognitive impairment, aged between 50 and 85 years. All recruited participants will undergo comprehensive initial assessments, including demographic variables (age, sex, education level), clinical variables (comorbidities, risk factors, family history of dementia, current medications, smoking and alcohol habits), neuropsychological assessments, and questionnaires to assess quality of life and other aspects of aging (e.g., Mini-Mental State Examination - MMSE, Clinical Dementia Rating Scale - CDR-SB, ADL and IADL, Neuropsychiatric Inventory - NPI, Pittsburgh Sleep Quality Index, and Cognitive Reserve Index - CRIq). Data will be collected at baseline (T0) and after two years of follow-up (T4).

At the end of these four years, new knowledge will be gained about the genetic, neurophysiological, and biological mechanisms that increase the risk of Alzheimer's disease. Personalized risk maps will be developed to identify individuals in the preclinical stage of dementia (without symptoms), and personalized preventive interventions will be implemented—potentially through new technological tools to support both patients and their families. The goal is to create a large European dataset to collect vast amounts of information that will enable more precise identification of those truly at risk and determine which non-pharmacological preventive interventions are most effective in slowing, delaying, or even halting the progression of dementia. The role of artificial intelligence in managing this big data will be crucial in defining algorithms for risk identification, disease prediction, and prevention.

COMFORTage


1
Refer & Enrol Patient
Project Introduction.
Inclusion/Exclusion Criteria Check.
Informed Consent.
2
Baseline Data Collection
Socio-demographic and Clinical Data.
Cardiovascular/Metabolic Risk Factors.
Connectivity Measures (EEG/fMRI).
Neuropsychological Assessments.
Blood Samples (Genetic Risk Factors and ATNI Blood Biomarkers).
3
Intervention Program (2-year Period)
Nutrition Plan.
Physical Activity.
Cognitive Training.
Health Risk Monitoring.
4
Midpoint Review
Neurologist Checks Progress (1st year mark).
5
Final Data Collection
Socio-demographic and Clinical Data.
Cardiovascular/Metabolic Risk Factors.
Connectivity Measures (EEG/fMRI).
Neuropsychological Assessments.
Blood Samples (Genetic Risk Factors and ATNI Blood Biomarkers).
Analyse changes in:
Cognition.
Biomarkers.
Connectivity.
Quality of Life by risk factor.
Final Assessment
6
7
National Health System
Follow-up with National Health System.