Diagnosis and treatment of dementia and Mild Cognitive Impairment

When, what, where

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This document is aimed at family members and caregivers of people with dementia.
It contains information derived from the Guideline “Diagnosis and Treatment of Dementia and Mild Cognitive Impairment,” based on rigorous analysis of recent scientific publications made by experts in the field of dementia: social workers, biologists, dietitians, educators, physical therapists, geriatricians, nurses, speech therapists, general practitioners, neurologists, neuropsychologists, social workers, psychiatrists, psychologists, psychiatric rehabilitation technicians, occupational therapists, as well as representatives of family members and caregivers of patients, epidemiologists and methodologists.

The version for professionals is the Guideline “Diagnosis and Treatment of Dementia and Mild Cognitive Impairment,” published in January 2024. It is associated with the interactive diagnostic care pathway intended for health professionals, decision-makers and family members/caregivers.

1. Diagnosis

Dealing with dementia is a complex challenge starting from the **diagnosis**. To access care and support, people with dementia need first and foremost to receive a diagnosis. A **timely, accurate and specific** diagnosis enables the access to dedicated care pathways and appropriate support involving the person and their family at all stages of the disease.

Dementia can be caused by various clinical conditions, which are classified into different nosological entities based on specific diagnostic criteria. A common feature of the different forms of dementia is the **progressive decline** of cognitive functions associated with a variety of psychobehavioral disorders. The progressive decline can involve different domains, such as memory, attention, visuospatial functions, executive functions, and language, in various combinations.

Dementia progressively interferes with a person's **critical and judgmental ability**, with a gradual loss of autonomy in the activities of their life, variable from case to case. Dementia affects not only the individual but also their family members, influencing their emotional connections and social relationships. The greatest burden in all phases of the disease primarily involves those who directly care for the patient, such as informal caregivers, but also health professionals.

Diagnosis of Mild Cognitive Impairment

Mild Cognitive Impairment (MCI) is a condition characterized by **mild involvement** of one or more cognitive domains, with independence in **functional skills preserved**. It is important to note that the condition of MCI does not necessarily progress to dementia. People diagnosed with MCI may remain **stable**, show **regression** and return cognitively intact, or **progress** to dementia.

The diagnosis of MCI, in a specialist clinical setting, is currently supported only by **clinical criteria**. No validated biomarker is available for the differential diagnosis of MCI in this clinical setting. The use of cerebrospinal fluid and neuroimaging biomarkers for the diagnosis of MCI is currently limited to research purposes (including clinical trials). MCI is a condition defined by clinical, cognitive, and functional criteria that requires, for its definition, the clinical judgement of a specialist.

2. General Practitioner role

The **general practitioner (GP) represents the first contact** with the person reporting cognitive and behavioural changes and his family members. Family and medical history, the clinical interview, and some initial diagnostic tests can guide the GP in defining the initial suspicion of dementia.

The **clinical interview** involves both people suspected of having cognitive decline and their close family members/caregivers, who can provide valuable information. An appropriate **initial assessment** should include a physical examination during which the GP makes a global assessment of the person in relation to his or her basic clinical parameters (vital signs), nutritional status, motor functions, ability to maintain attention during the examination, and ability to express themselves. Other conditions and diseases should also be considered that might affect cognitive assessment and support the suspect of dementia, such as sensory deficits (visual and hearing impairment), depressive disorders, delirium, and use of anticholinergic drugs or other psychotropic medications. Within this initial diagnostic approach, the use of a validated **cognitive test** that is both accurate and quick to administer is essential. The initial primary care assessment aims to confirm the suspect of dementia or cognitive deficit, but also to exclude secondary and potentially reversible causes of cognitive decline that might be due to medical reasons or other neurological conditions.

3. Specialist role

Suggesting the clinical **suspicion of dementia** in a primary care setting allows for quickly addressing the subsequent, more complex diagnostic process at the Centres for Cognitive Disorders and Dementia (CCDD). Confirmation of the suspected pathology and a refined differential diagnosis of dementia forms are the aim of CDCD's diagnostic process and are essential for the timely planning of targeted interventions.

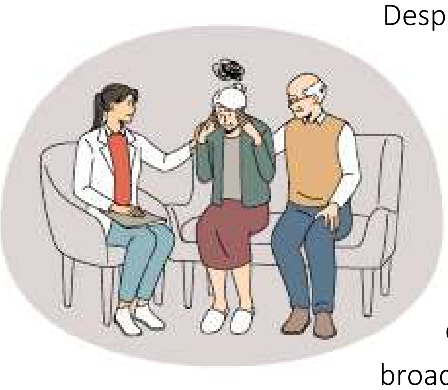
The **diagnosis of primary dementia** currently remains eminently clinical. It is based on the confirmation of cognitive deficit detected by targeted neuropsychological assessments, and it is guided by specific and standardized diagnostic criteria.

The **diagnostic process** for dementia in a specialist setting, such as memory clinics (e.g., Centres for Cognitive disorders and dementias) needs to be planned as a sequence, and tailored to each person, based on the ability of the tests adopted in each phase to correctly define the diagnosis. The decision to include further tests in the diagnostic process should be programmed gradually when a further support is needed to clarify diagnostic uncertainties and perform a differential diagnosis to define a specific subtype of dementia. In cases where reaching a diagnosis is more difficult, clinicians can consider the use of all tests that can provide a relevant diagnostic support.

4. What happens after the diagnosis? (After diagnosis)

Dementia is a progressive condition that is not only responsible for a strictly cognitive deficit, but also primarily or secondarily of several other psycho-behavioural symptoms including anxiety, depression, and personality disorders. Dementia highly affects the quality of life of both people and their caregivers.

The diagnostic process has **three phases:** the phase immediately preceding diagnosis, the phase communicating the diagnosis, and the phase immediately after diagnosis. These phases are crucial steps in defining supportive interventions.



Despite the lack of evidence, the Guideline (GL) underlined the importance of supporting the issues characterizing the lives of people with dementia and their caregivers in this crucial step of the diagnostic process. Therefore, the GL includes a recommendation to consider **counselling** both before and after a diagnosis of dementia to individuals and their caregivers. This takes into account the importance of consistent care as the disease progresses beyond the initial diagnosis, necessitating broader support services.

Dementia and delirium

Delirium is a neuropsychiatric disorder with an acute onset mainly characterized by a "disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) accompanied by reduced awareness of the environment". These symptoms can be associated with alterations in memory, orientation, language, visuospatial abilities, and perception.

The diagnosis of delirium is complex. Delirium can be due to an underlying medical condition whose suspicion can be supported by medical history, clinical examination, and blood tests. Delirium can be due to intoxication or substance withdrawal. Some older people with delirium has an underlying undiagnosed dementia, while some others show an excellent recovery of symptoms, without any evidence of an underlying cognitive decline at a subsequent evaluation. However, people with dementia have a significantly higher risk of delirium, and people who experience delirium at any time have a higher risk of dementia.

5. Care models

Due to the complexity of its clinical picture, **dementia represents a public health challenge**. It involves cognitive functions and behaviour and entails the loss of ability to manage the most common activities of daily life and a progressive loss of autonomy in all functions, even the simplest ones.
Patient care for people with dementia is complex, starting from formulation and communication of the diagnosis, which directly involves the person and their family, and continuing with all the phases characterizing the course of the disease.
The clinical picture of the person with dementia is, by its nature, susceptible to modifications that can also be unpredictable. These modifications require timely adaptation of the care plan structure and an interdisciplinary approach.

It is important to consider that **each individual may have their own disease trajectory** in relation to any comorbidities and related polypharmacological therapies. Some pre-existing clinical conditions, whether of an internal or psychiatric nature, place the person in a particular fragile state. It is also possible that the pharmacological treatment the patient takes for a pre-existing pathology turns out to be inadequate by the time a condition of cognitive decline develops.

People with dementia and their caregivers experience different environments and engage with multiple professionals, especially during transitions between care settings, such as moving from their own homes to residential or hospital facilities. During these transitions, it is essential to guarantee **continuity of care** in terms of treatments, communication between reception facilities, and adequate management of the consequences that such changes could have on the psychophysical well-being and quality of life of the person with dementia and the caregiver. There is a need for more appropriate and targeted care models and coordination of care, capable of intercepting the individual needs, skills and competencies of the person and the caregiver (e.g. how well the latter is able to use technological tools) in the environment in which they live, and improving clinical conditions and quality of life. Furthermore, these strategies must support the physical and mental well-being of the caregivers in consideration of the fact that this has repercussions on the person assisted.

Care planning

People with dementia often present complex clinical pictures that need to be considered when planning care. It is important to include people with dementia in a care and support plan starting immediately after diagnosis to ensure their ability/possibility to plan for future care. It is useful to identify a **care coordinator** to overcome difficulties in the communication among health and social care professionals involved in the care process.

Providing families and caregivers with adequate information on **available services** and how to access them is crucial for people with dementia. Their family members or caregivers should be specifically addressed and supported in identifying where and from where they can receive **information** throughout each stage of the disease.

Post diagnosis review

Specific strategies aimed at **monitoring** people with a diagnosis of cognitive deficit (MCI or dementia), could help the person and their family members or caregivers preserve or improve cognitive functions, functional abilities, and quality of life.

Caregiver involvement

It is essential to involve family members or caregivers and, where possible, people with dementia in supporting and **decision making**, sharing and reviewing care and support plans, defining times and methods for updating, and documenting any changes in care goals and needs.

Support and inform caregivers

Caregivers are essential resources for both people requiring care and healthcare professionals, who have a close relationship with them. The time they dedicate to caregiving allows them to acquire an **intimate knowledge** of the people they care for and to be able to provide useful information.

Caregivers’ burden and quality of life are extremely relevant factors that should be monitored in time to allow for timely interventions to reduce the former and ensure the latter as high/long as possible, also considering that caregivers of people with dementia are at risk of depressive disorders.

Caregivers can request information on services to which they are entitled and how to access them, such as a formal assessment of their needs, including their mental and physical health, short breaks and other respite services.

The World Health Organisation has identified the development of support and training programmes for caregivers and family members of people with dementia as a priority action.

Staff training

Due to the complexity of dementia and its consequences on the lives of both people with dementia and their caregivers, managing people with dementia can be an extremely challenging process. Adequate training of the staff caring for people with dementia can be essential for the **early or timely identification** of emerging needs and the subsequent definition of an appropriate intervention strategy. In this context, the definition of training programmes for family members and caregivers, formal and informal, assumes a strategic role.

6. Drugs for Alzheimer's dementia

The **history of drug trials** aimed at finding a therapy that modifies the course of Alzheimer's dementia is more than 30 years long.
The principle that has driven the research is the so-called amyloid cascade hypothesis, according to which the central event in the neurodegeneration characteristic of the disease would be the accumulation in specific brain areas of aggregates of abnormal proteins, amyloid β plaques and tangles neurofibrillary tangles of hyperphosphorylated Tau protein.
The only categories of drugs for the management of currently available authorized by regulatory authorities for the treatment of Alzheimer's disease are **acetylcholinesterase inhibitors** and **memantine**.

Acetylcholine is one of the most important neurotransmitters in the nervous system. Its action at the central nervous system level is crucial for memory and learning. For this reason, it has been hypothesized that a drug that inhibits the enzyme acetylcholinesterase, which degrades acetylcholine, could improve cognitive function in people with dementia.
The acetylcholinesterase inhibitor drugs on the market (donepezil, galantamine and rivastigmine) are subject to strict prescription regulations. They are recommended as monotherapy for the treatment of mild to moderate Alzheimer's dementia only after appropriate assessment by a neurologist, geriatrician or psychiatrist with specific expertise.

Memantine, on the other hand, acts by blocking the receptors of another substance, **glutamate**, excess of which may contribute to the manifestation of cognitive symptoms and the progression of neurodegeneration. Monotherapy treatment with memantine is an option for people with moderate Alzheimer's dementia who cannot tolerate treatment with acetylcholinesterase inhibitors or have contraindications to them and for people with severe Alzheimer's dementia.
Based on medical expert judgement, memantine may also be considered in addition to treatment with acetylcholinesterase inhibitors in cases of moderate and severe disease.

Doctors at the Centres for Cognitive Disorders and Dementia (CCDD) monitor persons taking these drugs with the support of the General Practitioner.

New pharmacological treatments: monoclonal antibodies

To date, there are no commercially available drugs capable of slowing down or blocking the progression of Alzheimer's disease. Over the past two decades, enormous economic efforts have made it possible to develop highly innovative therapies with the aim of modifying the natural history of the disease (Disease-Modifying Therapies, DMTs). In the United States, the Food and Drug Administration (FDA) approved three monoclonal antibodies directed against different forms of β amyloid, aducanumab, lecanemab, and donanemab.
In Europe, the European Medicines Agency (EMA) is currently evaluating for the marketing of lecanemab and donanemab, drugs that have shown the ability to bind and remove fibrillar forms of β amyloid. In clinical trials, these drugs have been shown to be effective in removing amyloid plaques in the brain identified by amyloid PET examination.
Both treatments, however, led to only minimal improvements in cognitive ability and functional capacity, underlining the dissociation between the biological aspect and the clinical symptom.

These three drugs, like other monoclonal antibodies in previous studies, have caused a significant increase of adverse events, in particular brain alterations identifiable by MRI. These alterations (defined as **Amyloid Related Imaging Abnormalities**, ARIA), although often asymptomatic, can cause headaches, confusion and falls and in some studies have led to severe, even fatal, ischaemic and hemorrhagic brain events.

These aspects are of great concern, not only from a clinical point of view, but also for patient management and monitoring, especially since, at present, long-term effects are unknown.

7. Non-pharmacological interventions

The term "non-pharmacological interventions" refers to the entire spectrum of interventions that **do not include the use of drugs** (e.g., rehabilitation, psychosocial interventions, and/or the use of dietary supplements).

A non-pharmacological approach may improve and/or maintain the cognitive functions of people with dementia, allowing the person to continue to perform their occupations and address behavioural symptoms.

Various factors can impact cognitive impairment, requiring tailored interventions based on the person’s specific needs. Treatment needs also differ depending on the stage of disease. Treatments in the initial stages aim to preserve cognitive functions and stimulate the use of compensatory strategies. As the disease progresses, individualized interventions can contribute to maintaining independence and managing everyday functions.

Offering group activities can create opportunities for socialization, peer support, and engagement. Furthermore, creative and leisure activities can promote the well-being of people living with dementia at every stage of the disease.

Non-pharmacological interventions for cognitive symptoms in dementia

Activities offered to promote well-being and autonomy must be targeted to the **individual preferences** of the person.

Several studies emphasize the usefulness of both **aerobic and nonaerobic exercise** in support the treatment of cognitive symptoms. Other evidence-based interventions are **music therapy**, **reminiscence therapy**, based on the elderly person's natural propensity to recall their past, and **occupational therapy** aimed at support functional abilities in people with mild to moderate dementia. **Cognitive rehabilitation** can be useful for supporting functional abilities in people with mild to moderate dementia, while cognitive training is recommended for the treatment of cognitive disorders in people with mild Alzheimer's dementia.

Non-pharmacological interventions for cognitive symptoms in MCI

In people with MCI, **cognitive training** has been shown to be effective in treating cognitive symptoms, while **cognitive rehabilitation** appears to be useful in both treating cognitive symptoms and in maintaining autonomy.

Participation in **art therapy** interventions and music therapy has been shown to be helpful in improving cognitive symptoms and reducing depressive symptoms and anxiety.

Physical exercise helps to maintain autonomy (e.g. dancing) to reduce depressive symptoms.

Finally, participation in recreational activities (e.g. cards and board games) improves cognitive functions and reduces depressive symptoms.

Nutritional interventions

To date, **no evidence** is available to support the use of nutritional supplements (e.g., with vitamin E, folic acid, or specific formulas) in the absence of documented deficiencies, nor to support the use of ginseng, ginkgo biloba, huperzine A and other herbal compounds, antioxidants such as omega-3 selenium and sodium oligomannate, or ketogenic diets.

8. Non-cognitive symptoms

Non-cognitive symptoms of dementia comprise a wide spectrum of conditions and significant **behavioural changes**, including aggression, anxiety, apathy, agitation, depressive disorders, delusions, hallucinations, and sleep disorders. In some types of dementia, neuropsychiatric symptoms can be present during the earlier stages of the disease and be typical of the clinical picture. However, most people with dementia present them during the course of the disease. Neuropsychiatric symptoms deeply affect the overall **well-being and quality of life** of people with dementia and their caregivers, along with direct and indirect costs. Their management is challenging for healthcare professionals and requires specific training and expertise.

The clinical assessment of neuropsychiatric symptoms of dementia should be aimed at identifying potential medical, psychological, and environmental **causes or triggers**. As a first approach, it is therefore necessary to carefully and specifically assess possible causes of distress for the person with dementia, particularly pain, delirium, treatment inappropriate and inadequate care, which support a condition of distress, agitation, aggression, sleep disturbances, and more generally other mental and behavioural disorders that fit into the framework of cognitive disorders. It is important to consider the challenges that people with dementia may experience in communicating potential physical or environmental sources of distress/discomfort. The first line of treatment should include **psychosocial and environmental interventions** to be continued also after drugs prescription.

In clinical practice, the **pharmacological management** of these symptoms is based on the use, according to specialist judgement, of psychotropic agents such as antipsychotics, mood stabilizers, antidepressants, anxiolytics and hypnotics. However, the use of these medications in people with dementia is limited, and sometimes not approved by regulatory agencies due to their controversial risk-benefit profile.

9. Intercurrent illness and frailty

Most people with dementia live with other **chronic conditions**. Comorbidities, multimorbidity and frailty are frequently reported in clinical practice and are associated with a higher risk of disability and death and a lower quality of life.

Acute conditions such as pain, falls, loss of mobility, delirium, and urinary tract infections are common in frail individuals, whether or not they have comorbid dementia. These conditions can worsen overall health and quality of life for these individuals, and also increase the burden of care for their caregivers.

People with dementia experience **pain** like any other cognitively unimpaired person. However, assessing pain in people with dementia can be extremely difficult due to their inability to communicate their discomfort both on their own accord and upon request from caregivers or health professionals. This leads to an increased risk that people with dementia might be undertreated, thus receiving inappropriate or inadequate pain medications rather than being overtreated. This issue requires reaching a compromise that should be based on best clinical practices.

What to do in case of hospitalisation?

The process of caring for people with dementia should be carefully planned, taking into account the potential for significant and sometimes erratic changes in the clinical condition due to acute events requiring hospitalisation and **timely adjustment** to the already complex care plan.

Within the **transition** between care settings, and especially in cases of people with dementia experiencing clinical emergencies requiring hospitalization, a more accurate **medicine optimization** is required, including transferring information on current prescriptions for pre-existing conditions, and the need for new treatments. This would optimise the risk/benefit profile, accounting for the unique frailty condition of people with dementia. Therefore, caring for people with dementia should include a careful assessment of the main manifestation of the index conditions, but also a careful consideration of those coexisting conditions that contribute to the clinical complexity and the individual care needs.

10. Palliative care

The World Health Organization (WHO) defines palliative care as "an approach that improves the quality of life of patients and their families who are facing problems associated with life-threatening illness (...)" and states that "it prevents and relieves suffering through the early identification, correct assessment and treatment of pain and other problems, whether physical, psychosocial, or spiritual." The WHO also underlines that "palliative care does not replace your usual care: it can be provided alongside regular medical care" and that "palliative care is not a luxury, it is essential" and "should be available and affordable to each and every person who needs it" (WHO 2020)[1]. Documents focusing on palliative care and end of-life care often lack precise and complete reference to the specific conditions of people with dementia.

One critical issue concern **when to initiate palliative care** in people with dementia. The course and characteristics of dementia, along with the individual clinical variability, require considering a flexible approach, accounting for the individual needs emerging from each disease trajectory. This condition, in fact, does not allow the definition of a specific period identifiable as the start of the end-of-life phase. This difficulty in identifying the end-of-life phase, and thus knowing when to initiate a palliative care approach, can increase the variability in quality of care and access to palliative care for people with dementia.

This also suggests considering planning in advance the steps of the care process to facilitate the transition of the clinical condition, allowing for the most important element, which is **involving people with dementia and their caregivers in decision-making**. In particular, the process should account for each individual situation, underlining the importance, towards the end of life, of following the processes of **advance care planning** with people with dementia, and that their caregivers respect the principles of **best-interest** decision-making, especially in case the individuals with dementia are incapable of deciding for themselves. The complexity of advance care planning and its adequate application starts from the identification of the most appropriate time to start sharing and discussing this topic with people with dementia and their caregivers.

It is essential to offer palliative and end-of-life care that is flexible and tailored to the physical, emotional and environmental needs in line with the cultural, spiritual or religious attitudes of the person with dementia, recognising their personal and social identity. Palliative care should start early in the course of the disease.

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[1] WHO. Palliative care. Last update august 2020. Available at: https://www.who.int/news-room/fact-sheets/detail/palliative-care

11. Costs

In the context of the Guideline on the diagnosis and treatment of dementia and Mild Cognitive Impairment, understanding the costs associated with the management and treatment of people with dementia in Italy could help decision-makers in developing and prioritizing policies and interventions for both the person and their caregivers. Understanding the costs associated with a specific condition or disease allows for the proper allocation of healthcare resources, enabling efficient implementation of health policies within budgetary constraints.

The economic analysis developed to support this Guideline aims to provide an updated overview, considering available data sources, of the current management of patients with dementia in Italy from an organizational and economic perspective.

In the Italian context, the total expenditure for treating and managing people with dementia was approximately €23.6 billion, with 63% being covered by their families. Clinicians and all those involved in the care relationship must address ethical problems carefully, with attention to participation and preservation of the dignity and rights of the most vulnerable individual and all the people involved.

12. Ethical aspects

The bioethical reflection needs an increasingly rigorous and effective synergistic approach. The commitment of the numerous professionals involved in governance and clinical practice in the dementia sector represents the desire to build an institutional, cultural, and scientific path aimed at developing a fair system of care, taking charge, and protecting patients, with particular attention to the relationship between socioeconomic conditions and inequalities in health status. The complex and multifaceted issues that need to be addressed are manifold and already arise from primary prevention, which is an essential and, also from a public health point of view, imperative issue.

No less important, in the context of the therapeutic alliance, is the theme of the approach to treatment and palliative care. There is still little data in Italy concerning the application of Law no. 219 of 2017, which has harmonized all the requirements on consent in the medical field, placing a strong emphasis on the protection and promotion of the individual's autonomy and self-determination. The approach proposed by this law implies the involvement of people affected by diseases in decisions that concern them from the very early stages of the illness, as well as a paradigm shift from the disability model to the valorisation of residual skills and abilities.

Where to find information

Observatory Dementia website: https://www.demenze.it/

National Dementia Plan documents:
https://www.demenze.it/it-schede-5-piano_nazionale_demenze

Guideline on Diagnosis and treatment of dementia and Mild Cognitive Impairment. National Institute of Health, 2024 (English version):
https://www.demenze.it/it-schede-18-documentazione_sulle_demenze

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