

## GUIDELINE

# The Italian guideline on diagnosis and treatment of dementia and mild cognitive impairment

ELISA FABRIZI<sup>1,‡</sup>, ANTONIO ANCIDONI<sup>1,‡</sup>, NICOLETTA LOCURATOLO<sup>1</sup>, PAOLA PISCOPO<sup>2</sup>,  
FRANCESCO DELLA GATTA<sup>3</sup>, SIMONE SALEMME<sup>4,5</sup>, SARA MARIA PANI<sup>6</sup>, DOMITILLA MARCONI<sup>7</sup>,  
LUCA VIGNATELLI<sup>8</sup>, LUCIANO SAGLIOCCA<sup>9</sup>, PAOLO CAFFARRA<sup>10,11</sup>, PIERO SECRETO<sup>11,12</sup>, ANTONIO GUAITA<sup>11,13</sup>,  
ANDREA STRACCIARI<sup>11,14</sup>, NICOLA VANACORE<sup>1,11</sup>, ELEONORA LACORTE<sup>1</sup>, The Guideline Working Group<sup>§</sup>

<sup>1</sup>National Center for Disease Prevention and Health Promotion, Italian National Institute of Health, Rome, Italy

<sup>2</sup>Department of Neuroscience, Italian National Institute of Health, Rome, Italy

<sup>3</sup>Department of Neuroscience, Mental Health and Sense Organs (NESMOS), Faculty of Medicine and Psychology, Sapienza University of Rome, Rome, Italy

<sup>4</sup>Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy

<sup>5</sup>International School of Advanced Studies, University of Camerino, Camerino, Italy

<sup>6</sup>Department of Medical Sciences and Public Health, University of Cagliari, Monserrato, Cagliari, Italy

<sup>7</sup>Post Graduate School of Public Health, University of Siena, Siena, Italy

<sup>8</sup>IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

<sup>9</sup>Local Health Unit Salerno, Salerno, Italy

<sup>10</sup>Dementia Unit A.O.U. (Parma), Parma, Italy

<sup>11</sup>National Committee for Dementia of the Italian Ministry of Health, Rome, Italy

<sup>12</sup>Alzheimer Unit, Fatebenefratelli Hospital, San Maurizio Canavese, Italy

<sup>13</sup>Golgi Cenci Foundation, Abbiategrasso, Milan, Italy

<sup>14</sup>Cognitive Disorder Center, Neurology Unit, S.Orsola-Malpighi University Hospital, Bologna, Italy

Address correspondence to: Antonio Ancidoni, National Center for Disease Prevention and Health Promotion, Italian National Institute of Health, Viale Regina Elena 299, 00161 Rome, Italy. Email: [antonio.ancidoni@iss.it](mailto:antonio.ancidoni@iss.it)

‡Elisa Fabrizi and Antonio Ancidoni equally contributed to this work

§Acknowledgement of Collaborative Authorship: The Guideline Working Group comprises Paolo Caffarra, Antonio Guaita, Piero Secreto, Andrea Stracciari, Nicola Vanacore, Luciano Saggiocca, Luca Vignatelli, Petronilla Battista, Consuelo Borgarelli, Chiara Cerami, Annalisa Chiari, Massimo Corbo, Alfredo Costa, Maria Cotelli, Alessandra Dodich, Elisa Faè, Elisa Favaretto, Vincenza Frisardi, Lidia Fubini, Monica Gandelli, Donata Gollin, Daniele Imperiale, Claudio Ivaldi, Fabio Izzicupo, Alessandro Lanzoni, Valentina Lavermicocca, Margherita Lazzarino, Rosa Liperoti, Massimiliano Massaia, Giacomo Menabue, Maria Angela Molinari, Alessia Morelli, Anna Peruzzi, Fabrizio Piazza, Mario Possenti, Clara Ricci, Stefano Russo, Patrizia Spadin, Gianfranco Spalletta, Davide Zenaro, Antonio Ancidoni, Francesco Della Gatta, Elisa Fabrizi, Eleonora Lacorte, Nicoletta Locuratolo, Paola Piscopo, Ilaria Bacigalupo, Guido Bellomo, Marco Canevelli, Elena Carbone, Alessio Crestini, Eugenio Distaso, Ylenia Druda, Sabrina Esposito, Giorgio Fumagalli, Sandra Morelli, Alice Paggetti, Giulia Remoli, Roberto Rivabene, Simone Saleme, Francesco Sciancalepore, Martina Valletta, Nicola Veronese, Valerio Zaccaria, Daniela Coclite, Alice Fauci, Antonello Napolitano, Chiara Bini, Francesco Saverio Mennini, Paolo Sciattella, Alessandra Ceccarini, Zuzana Mitrova, Scilla Pizzarelli, Rosella Saulle, Sabina Gainotti, Carlo Petrini, Luciana Riva, Salvatore De Masi, Francesco Nonino, Maria Cristina Porrello, Gabriella Martelli

## Abstract

**Introduction:** Approximately 2 million people in Italy are currently living with dementia or mild cognitive impairment (MCI), and 4 million are involved as family members or caregivers. Considering the significant impact of dementia, the Italian Ministry of Health entrusted the Italian National Institute of Health (Istituto Superiore di Sanità) with the development of a guideline within the Italian National Guideline System (Sistema Nazionale Linee Guida, SNLG) on the diagnosis and treatment of dementia and MCI. The main objective was to provide evidence-based recommendations aimed at reducing the

variability and ensuring the appropriateness of clinical practices throughout the whole care process from identification and diagnosis to the end of life for people with dementia (PwD) or MCI and their families/caregivers.

**Methods:** The GRADE-ADOLOPMENT approach was used to adopt, adapt and update the guideline developed by the National Institute for Health and Care Excellence in 2018 (NG97). The methodology was based on the Methodological Handbook produced by the SNLG. A multidisciplinary panel of 29 experts and four representatives of family members/caregivers discussed and approved 47 review questions. Of these, 34 questions were adopted from the NG97, and 13 were new questions, including 10 questions referring to MCI. Systematic literature reviews were performed for each question, and a team of methodological and clinical experts qualitatively assessed and summarised results from included studies based on the GRADE approach. To facilitate the implementation and dissemination of the contents of this guideline, a care pathway and a leaflet dedicated to PwD or MCI and their families/caregivers were also developed.

**Results:** The literature review for this guideline included studies published up to November 2023. More than 1000 peer-reviewed publications were included, covering the following areas: (i) identification, diagnosis and post-diagnostic support; (ii) care models and care coordination; (iii) pharmacological interventions for cognitive symptoms; (iv) non-pharmacological interventions for cognitive symptoms; (v) non-cognitive symptoms, intercurrent illnesses and palliative care. The multidisciplinary panel discussed and approved 167 clinical practice recommendations and 39 research recommendations.

**Commentary:** Italy's first National Guideline on dementia and MCI addresses diagnosis, treatment and care within the National Healthcare System. It includes recommendations on pharmacological and non-pharmacological approaches, and emphasises tailored interventions, comprehensive cognitive assessment, staff training and palliative care. The guideline also underlines the need to involve PwD in decision-making and supporting caregivers throughout the entire course of the disease.

**Conclusions:** Structured strategies for the dissemination and implementation of the guideline will be defined within the Italian Fund for Alzheimer and other Dementias 2024–2026. An interactive care pathway and a leaflet dedicated to PwD and their carers are already available. The guideline will be updated starting January 2027, but early updates may be planned in case of breakthrough advancements.

*Keywords:* dementia; Alzheimer's disease; guideline; Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology; mild cognitive impairment; older people

## Key Points

- This is the first Italian guideline that makes evidence-based recommendations on the diagnosis, treatment and care for people with dementia and mild cognitive impairment and their caregivers.
- Thirty-four questions were adopted or adapted from the NICE guideline NG97 and 13 new review questions were added, including 10 on the diagnosis and management of people with mild cognitive impairment.
- The Italian guideline also included evidence synthesis and recommendations for new disease-modifying drugs.

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## Introduction

Italy is the second oldest country in the world, with nearly one-fourth of its population being  $\geq 65$  years [1]. Current estimates suggest that almost 2 million people in Italy live with dementia or mild cognitive impairment (MCI), and 4 million family members and caregivers are involved in caring for and supporting people with cognitive disorders [2] (Fig. 1). Developing an evidence-based guideline was essential to ensure the best quality of care for people with dementia (PwD) and MCI.

Here, we present the Italian guideline on the diagnosis and treatment of dementia or MCI (LG DEM). This guideline was developed as part of the activities of the Italian Fund for Alzheimer's and other Dementias (IFAD), which is, so far, the largest public health initiative on dementia in Italy

[6, 7]. The Italian Ministry of Health (MoH) dedicated 15 million euros to the 2021–2023 IFAD, of which >200 000 euros were dedicated to develop this guideline.

The MoH entrusted the Italian National Institute of Health (Istituto Superiore di Sanità, ISS) with coordinating the development of the guideline within the Italian National Guidelines System (Sistema Nazionale Linee Guida, SNLG). The primary objective was to provide recommendations based on the best and most updated evidence to reduce the variability of clinical practice, and to ensure the best quality of care throughout the whole care process from the diagnosis to the end of life.

A scoping review of available guidelines on this topic was performed. Among all available guidelines developed by public entities, only the guideline published in the UK by the National Institute for Health and Care Excellence (NICE) in

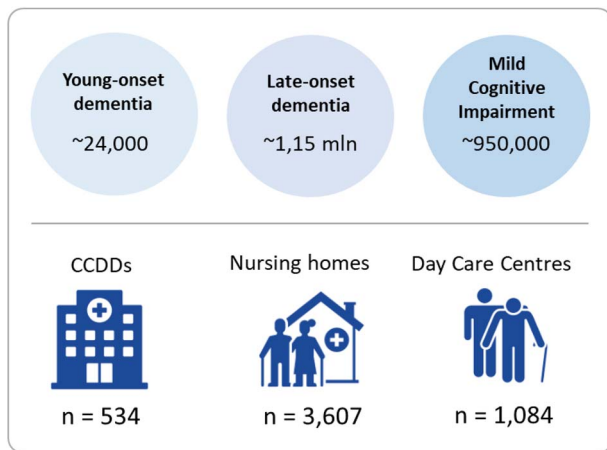


Figure 1. The Italian context: epidemiology of dementia and mild cognitive impairment and availability of dementia services. *Note:* the prevalence of dementia in Italy was estimated based on three epidemiological studies: Bacigalupo 2018 [3], Chiari 2021 [4] and Sachdev 2015 [5]; late-onset dementia (age > 65 years); young-onset dementia (age < 65 years). CCDDs, Centres for Cognitive Disorders and Dementias.

2018 (NG97) [8] was considered as comparable in terms of scope and objectives to the document planned by the IFAD. Therefore, the National Committee for dementia established by the IFAD agreed to adopt, adapt and update the NG97. The National Committee for dementia also agreed, due to the relevance of the topic, to include MCI in the scope of the guideline by defining new specific review questions.

This article summarises the key recommendations and contents of the Italian guideline on the diagnosis and treatment of dementia and MCI.

## Methods

The methodology of this guideline was based on the Methodological Handbook issued by the SNLG of the ISS [9] and on the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology [10]. The guideline Working Group (WG) included 81 members. The multidisciplinary panel included 29 experts from 17 health-care professions. Four representatives of family members and caregivers were also included to ensure consideration of their values, priorities and preferences.

The present guideline adapted and updated 34 Review Questions (RQs) from the NG97 and included 13 new RQs (Supplementary Table S1). Search strategies were updated to include literature published up to November 2023. The RQs were categorised by topic of interest and numbered from 1 to 24, with some questions being categorised as sub-questions, for a total of 47 RQs. The RQs were classified according to the five areas covered by the guideline (Fig. 2).

The draft version of the guideline was peer reviewed by two external reviewers using the AGREE (Appraisal of

Guidelines Research and Evaluation) Reporting Checklist and the AGREE II tool to assess its contents and methodology [11, 12]. In December 2023, the Full Guideline was released and made available on the SNLG website along with the interactive care pathway and a leaflet dedicated to PwD and their caregivers [13]. In July 2024, the English version of the Full Guideline, the care pathway and the leaflet were also published on the SNLG and Dementia Observatory websites [13, 14].

See Appendixes 1 and 2 in the Supplementary data for a detailed description of the Scope document and methodology adopted in this guideline.

## Results

### Systematic review of the literature

Database searches identified over 280 000 records for all included RQs. After removing duplicates and applying the predefined eligibility criteria, >1000 publications were included (see Appendix 3 in the Supplementary data), considering both the literature already included in NG97 and the studies identified by the update (see Supplementary Table S2).

Overall, 167 recommendations for clinical practice and 39 research recommendations were approved (Tables 1, 2, 3, 4, 5 and 6). Out of the 167 clinical recommendations, 101 were adopted from NG97, 44 were adapted to the Italian context and 61 were developed *de novo*.

### Identification, diagnosis and post-diagnostic support

#### Case-finding strategies

Dealing with dementia is a complex challenge starting from the diagnosis. The timely diagnosis of dementia is increasingly seen as a public health priority, with some reports indicating rates of underdiagnosis as high as 50% [15] or even higher [16]. This RQ aimed to assess the impact of strategies of case-finding on the frequency of correct diagnosis in people at a higher risk of cognitive decline and on the outcomes of people who receive a diagnosis. Definitions for case-finding, screening strategies, and early and timely diagnosis can be found in the Supplementary Table S3.

A single study was included by the NG97, and no studies were identified through the literature update. Case-finding approaches involve actively seeking cases in high-risk groups. The WG stressed that case-finding strategies follow a specific methodology, different from screening strategies, which are deemed as inappropriate.

Due to the lack of supporting evidence, no clinical practice recommendations were included and the WG agreed to add a research recommendation for further, high-quality studies exploring both case-finding strategies and subsequent interventions for people who receive a diagnosis of dementia.

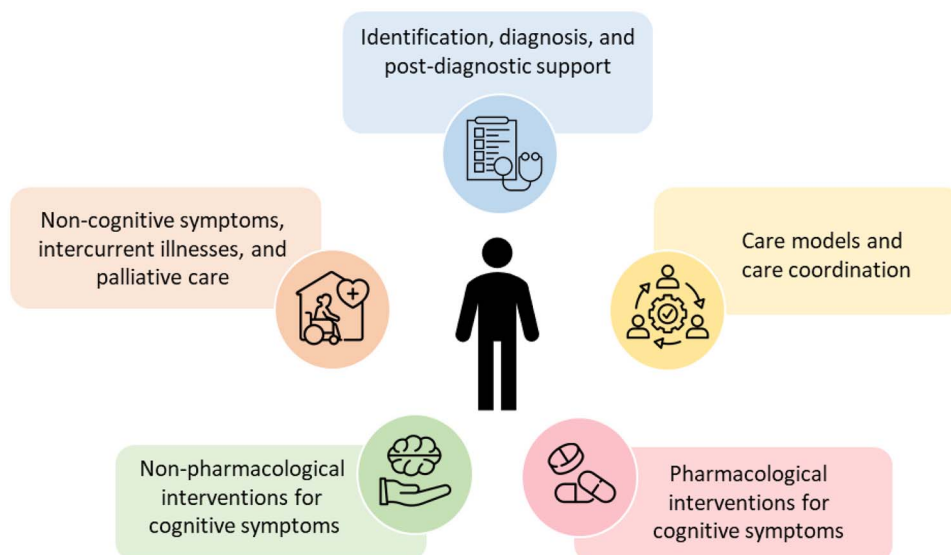


Figure 2. The five areas prioritised by stakeholders and covered by the guideline.

### Diagnosis and differential diagnosis of dementia and MCI

A timely, accurate diagnosis allows for targeted interventions and appropriate care for people with suspected dementia or MCI, as well as their caregivers [17]. Although most people prefer to be informed about their dementia diagnosis, it can cause emotional distress for both PwD and their families [18].

Four RQs were included: two from NG97 and two new ones. Two RQs addressed diagnostic studies evaluating the accuracy of tests used in non-specialist, primary care settings, while the other two focused on tests used in specialist settings. All the diagnostic tests considered in included studies are listed in the [Supplementary Table S4](#).

Overall, 10 studies (3 from the literature update) were included for non-specialist settings and 151 studies for specialist settings. The initial evaluation in a non-specialist setting should include medical history, physical examination, blood tests and Computer Tomography (CT)/Magnetic Resonance Imaging (MRI) to exclude potentially reversible or secondary causes of cognitive decline, and cognitive tests. In case of suspected cognitive decline, physicians in a non-specialist setting should use brief, validated cognitive tests, preferring tests that have been translated in Italian (i.e. 6-CIT, TYM) [19, 20] or are validated in the Italian population (i.e. GPCOG) [21]. They should not rule out cognitive decline based solely on normal cognitive test scores, and cognitive function should be regularly monitored. In case the suspect of cognitive decline still persists after ruling out reversible or secondary causes, physicians in a non-specialist setting should refer people to a specialist (e.g. Centres for Cognitive Disorders and Dementia, CCDDs).

Physicians in specialist settings should perform a comprehensive neuropsychological assessment as an essential part of the diagnostic process for dementia. The diagnosis of dementia subtypes should be based on internationally

validated criteria. Structural neuroimaging should be offered as a support for differential diagnosis of dementia subtypes. In case of uncertain diagnosis and a suspect of Alzheimer's dementia (AD),  $^{18}\text{F}$ FDG-PET or perfusion SPECT, if  $^{18}\text{F}$ FDG-PET is unavailable, should be considered, or cerebrospinal fluid (CSF) tests, while EEG and Apolipoprotein E  $\epsilon 4$  genotyping should not be used as part of the diagnostic process for AD. In case of uncertain diagnosis and a suspect of dementia with Lewy bodies (DLB),  $^{123}\text{I}$ -FP-CIT SPECT should be offered, or, if unavailable,  $^{123}\text{I}$ -MIBG cardiac scintigraphy or polysomnography with EEG. In case of suspect of frontotemporal dementia (FTD), either  $^{18}\text{F}$ FDG-PET or perfusion SPECT should be offered. Potential genetic causes should also be considered. In case of suspect of vascular dementia (VaD), brain MRI should be performed or, if unavailable or contraindicated, brain CT. Potential genetic causes should also be considered.

The diagnosis of MCI in specialist settings relies on clinical criteria, as no validated biomarkers are available for diagnostic purposes or for the differential diagnosis of MCI subtypes. A comprehensive neuropsychological assessment should be performed, including episodic memory tests, as part of the diagnostic process. People with a diagnosis of MCI should be offered regular neuropsychological assessments to monitor their cognitive functions over time. Based on the wide ongoing research on several biomarkers for the diagnosis and differential diagnosis of AD and MCI (e.g. plasma biomarkers, amyloid PET), the WG agreed to include three research recommendations (see [Table 6](#)).

### Drugs that may worsen cognitive decline

Anticholinergic drugs are commonly prescribed to treat various conditions. Side effects include dry mouth, drowsiness, blurred vision, urinary retention, postural hypotension and constipation. Evidence suggests that anticholinergic drugs

Table 1. Recommendations on identification, diagnosis and post-diagnostic support

| <b>Diagnosis and differential diagnosis of dementia and mild cognitive impairment</b> |   |                                    |
|---|---|------------------------------------|
| <b>Initial assessment in non-specialist settings</b>                                  |   |                                    |
| 1   | At the initial assessment take a history (including cognitive, behavioural and psychological symptoms, and the impact symptoms have on their daily life): <ul style="list-style-type: none"> <li>from the person with suspected cognitive decline and</li> <li>if possible, from someone who knows the person well (such as a family member).</li> </ul>  | <b>STRONG IN FAVOUR</b><br>Adapted |
| 2   | If cognitive decline is still suspected after initial assessment: <ul style="list-style-type: none"> <li>conduct a physical examination and</li> <li>undertake appropriate blood and urine tests to exclude reversible causes of cognitive decline and</li> <li>use cognitive testing and</li> <li>prescribe brain CT and/or MRI to exclude secondary causes of cognitive decline.</li> </ul>   | <b>STRONG IN FAVOUR</b><br>Adapted |
| 3   | When using cognitive testing to assess people with dementia or someone who knows the person well (such as a family member), use a validated brief structured cognitive instrument such as: <ul style="list-style-type: none"> <li>10-point cognitive screener (10-CS);</li> <li>6-item cognitive impairment test (6CIT)<sup>§</sup>;</li> <li>6-item screener (6-IS);</li> <li>Memory Impairment Screen (MIS);</li> <li>Mini-Cog;</li> <li>Test Your Memory (TYM)<sup>§</sup>;</li> <li>General Practitioner Assessment of Cognition (GPCOG)<sup>‡</sup>.</li> </ul>  | <b>STRONG IN FAVOUR</b><br>Adapted |
| 4   | Do not rule out cognitive decline solely because the person has a normal score on a cognitive instrument and plan a monitoring of cognitive functions in time.  | <b>STRONG AGAINST</b><br>Adapted   |
| 5   | Refer the person to a specialist dementia diagnostic service (Centre for Cognitive Disorders and Dementias) if: <ul style="list-style-type: none"> <li>reversible causes of cognitive decline (including delirium, depression, sensory impairment [such as sight or hearing loss] or cognitive impairment from medicines associated with increased anticholinergic burden) have been investigated and</li> <li>dementia is still suspected.</li> </ul>  | <b>STRONG IN FAVOUR</b><br>Adapted |
| 6   | If the person has suspected rapidly progressive dementia, refer them to a neurological service with access to tests (including cerebrospinal fluid examination) for Creutzfeldt–Jakob disease and similar conditions.   | <b>STRONG IN FAVOUR</b><br>Adapted |
| 7   | For more guidance on assessing for dementia in people with learning disabilities, see <a href="#">Table 6</a> in the Full Guideline.  | <b>STRONG IN FAVOUR</b><br>Adapted |
| <b>Diagnosis of dementia in specialist settings</b>                                   |   |                                    |
| 8   | Diagnose a dementia subtype (if possible) if initial specialist assessment (including an appropriate neurological examination and cognitive testing) confirms cognitive decline and reversible causes have been ruled out.  | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 9   | If Alzheimer’s disease is suspected, include a test of verbal episodic memory in the assessment.  | <b>STRONG IN FAVOUR</b><br>Adopted |
| 10  | Offer neuropsychological testing with validated neuropsychological tests as an essential part of the diagnostic process for dementia and dementia subtypes.   | <b>STRONG IN FAVOUR</b><br>New     |
| 11  | Use validated criteria to guide clinical judgement when diagnosing dementia subtypes, such as: <ul style="list-style-type: none"> <li>International consensus criteria for dementia with Lewy bodies;</li> <li>International FTD criteria for frontotemporal dementia (primary non-fluent aphasia and semantic dementia);</li> <li>International Frontotemporal Dementia Consortium criteria for behavioural variant frontotemporal dementia;</li> <li>NINDS-AIREN criteria for vascular dementia;</li> <li>NIA-AA criteria for Alzheimer’s disease;</li> <li>Movement Disorders Society criteria for Parkinson’s disease dementia;</li> <li>WHO and International criteria for Creutzfeldt–Jakob disease.</li> </ul> | <b>STRONG IN FAVOUR</b><br>Adopted |
| 12  | Offer structural imaging to rule out reversible causes of cognitive decline and to assist with subtype diagnosis, unless dementia is well established, and the subtype diagnosis is clear.  | <b>STRONG IN FAVOUR</b><br>Adopted |
| 13  | Only consider further diagnostic tests if: <ul style="list-style-type: none"> <li>it would help to diagnose a dementia subtype and</li> <li>knowing more about the dementia subtype would change management.</li> </ul>   | <b>WEAK IN FAVOUR</b><br>Adopted   |
| <b>Further tests for Alzheimer’s disease</b>  |   |                                    |
| 14  | If the diagnosis is uncertain (see recommendation 13) and Alzheimer’s disease is suspected, consider either: <ul style="list-style-type: none"> <li><sup>18</sup>F-FDG PET or perfusion SPECT if <sup>18</sup>F-FDG PET is unavailable or</li> <li>examining cerebrospinal fluid for: <ul style="list-style-type: none"> <li>total Tau and phosphorylated-Tau 181 and</li> <li>amyloid <math>\beta</math>1–42/amyloid <math>\beta</math>1–40 ratio or amyloid <math>\beta</math>1–42.</li> </ul> </li> </ul> <p>If a diagnosis cannot be made after one of these tests, consider using the other one.</p>   | <b>WEAK IN FAVOUR</b><br>Adapted   |
| 15  | Be aware that the older a person is, more likely they are to get a false positive with cerebrospinal fluid examination.   | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 16  | Do not rule out Alzheimer’s disease based solely on the results of CT or MRI scans.   | <b>STRONG AGAINST</b><br>Adopted   |

(Continued)

Table 1. Continued

| <b>Diagnosis and differential diagnosis of dementia and mild cognitive impairment</b> |   |                                    |
|---|---|------------------------------------|
| 17  | Do not use <i>ApoE</i> $\epsilon 4$ genotyping or electroencephalography to diagnose Alzheimer's disease.   | <b>STRONG AGAINST</b><br>Adopted   |
| 18  | Be aware that young-onset Alzheimer's disease has a genetic cause in some people.   | <b>WEAK IN FAVOUR</b><br>Adopted   |
| <b>Further tests for dementia with Lewy bodies</b>                                    |   |                                    |
| 19  | If the diagnosis is uncertain (see recommendation 13) and dementia with Lewy bodies is suspected, use $^{123}\text{I}$ -FP-CIT SPECT.   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 20  | If $^{123}\text{I}$ -FP-CIT SPECT is unavailable, consider as an alternative: <ul style="list-style-type: none"> <li><math>^{123}\text{I}</math>-MIBG cardiac scintigraphy or</li> <li>polysomnography with EEG</li> </ul>  | <b>WEAK IN FAVOUR</b><br>Adapted   |
| 21  | Do not rule out dementia with Lewy bodies based solely on normal results on $^{123}\text{I}$ -FP-CIT SPECT or $^{123}\text{I}$ -MIBG cardiac scintigraphy.  | <b>STRONG AGAINST</b><br>Adopted   |
| <b>Further tests for frontotemporal dementia</b>                                      |   |                                    |
| 22  | If the diagnosis is uncertain (see recommendation 13) and frontotemporal dementia is suspected, use, with semi-quantitative reading, either: <ul style="list-style-type: none"> <li><math>^{18}\text{F}</math>-FDG PET or</li> <li>perfusion SPECT.</li> </ul>  | <b>STRONG IN FAVOUR</b><br>Adapted |
| 23  | Do not rule out frontotemporal dementia based solely on the results of structural, perfusion or metabolic imaging tests.  | <b>STRONG AGAINST</b><br>Adopted   |
| 24  | Be aware that frontotemporal dementia has a genetic cause in some people.   | <b>WEAK IN FAVOUR</b><br>Adopted   |
| <b>Further tests for vascular dementia</b>  |   |                                    |
| 25  | If the dementia subtype is uncertain (see recommendation 13) and vascular dementia is suspected, use MRI. If MRI is unavailable or contraindicated, use CT.   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 26  | Do not diagnose vascular dementia based solely on vascular lesion burden.   | <b>STRONG AGAINST</b><br>Adopted   |
| 27  | Be aware that young-onset vascular dementia has a genetic cause in some people.   | <b>WEAK IN FAVOUR</b><br>Adopted   |
| <b>Diagnosis of mild cognitive impairment in specialist settings</b>                  |   |                                    |
| 28  | Offer a neuropsychological assessment using validated neuropsychological tests, including specific tests for episodic memory, as part of the diagnostic process for MCI and its subtypes.   | <b>STRONG IN FAVOUR</b><br>New     |
| 29  | Do not offer biomarkers for the diagnosis and differential diagnosis of MCI.  | <b>STRONG AGAINST</b><br>New       |
| 30  | Offer people with a diagnosis of MCI regular neuropsychological assessments over time to monitor possible changes in cognitive functions.   | <b>STRONG IN FAVOUR</b><br>New     |
| <b>Drugs that may worsen cognitive decline</b>  |   |                                    |
| 31  | Be aware that some commonly prescribed medicines are associated with increased anticholinergic burden, and therefore cognitive impairment.  | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 32  | Consider minimising the use of medicines associated with increased anticholinergic burden, and if possible look for alternatives: <ul style="list-style-type: none"> <li>when assessing whether to refer a person with suspected dementia for diagnosis;</li> <li>during medication reviews with people living with dementia.</li> </ul>                    | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 33  | Consider that there are validated tools for assessing anticholinergic burden (e.g. the Anticholinergic Cognitive Burden Scale).   | <b>WEAK IN FAVOUR</b><br>Adapted   |
| 34  | For guidance on carrying out medication reviews, see the indications reported in Table 7 in the Full Guideline.   | <b>STRONG IN FAVOUR</b><br>Adopted |
| <b>Distinguishing dementia from dementia with delirium or delirium alone</b>          |   |                                    |
| 35  | For people who are in hospital and have cognitive impairment with an unknown cause, consider using one of the following to find out whether they have delirium or delirium superimposed on dementia, compared with dementia alone: <ul style="list-style-type: none"> <li>the long confusion assessment method (CAM);</li> <li>4-A's Test (4AT).</li> </ul> | <b>WEAK IN FAVOUR</b><br>Adapted   |
| 36  | Do not use standardised instruments (including cognitive instruments) alone to distinguish delirium from delirium superimposed on dementia.   | <b>STRONG AGAINST</b><br>Adopted   |
| 37  | If it is not possible to tell whether a person has delirium, dementia or delirium superimposed on dementia, treat for delirium first. For guidance on the identification and treatment of delirium, see Table 6 in the Full Guideline.  | <b>STRONG IN FAVOUR</b><br>Adopted |

<sup>a</sup>Validated in the Italian population. <sup>b</sup>Translated in Italian.

Table 2. Recommendations on care models and coordination of care

| <b>Pre-, peri- and post-diagnostic counselling</b>           |  |                                    |
|--|--|------------------------------------|
| 38   | Consider offering people with dementia and their caregivers peri- and post-diagnostic counselling targeted to the specific conditions of each patient (including symptom severity).  | <b>WEAK IN FAVOUR</b><br>New       |
| 39   | For the communication of diagnosis and post-diagnostic support, see the section ‘Communication of the diagnosis of dementia’ of the document ‘Recommendations for the governance and clinical management in dementia’ <sup>21</sup> issued by the National Committee for dementia.   | <b>STRONG IN FAVOUR</b><br>New     |
| <b>Care planning, review and coordination</b>                |  |                                    |
| 40   | Provide people living with dementia with a single named health or social care professional who is responsible for their Personalized Care Plan (PAI) within an integrated care pathway. For further indications on how to organise a PAI, see: <ul style="list-style-type: none"> <li>• indication 6 from the document ‘National Guidance for the Clinical Governance of Dementia’<sup>22</sup> issued by the National Committee for Dementia;</li> <li>• the document ‘National Guidance for the Definition of Integrated Care Pathways for Dementia’<sup>23</sup> issued by the National Committee for Dementia.</li> </ul>  | <b>STRONG IN FAVOUR</b><br>Adapted |
| 41   | Named professionals should: <ul style="list-style-type: none"> <li>• arrange an initial assessment of the person’s needs, which should be face-to-face, if possible;</li> <li>• provide information about available services and how to access them;</li> <li>• involve the person’s family members or carers (as appropriate) in support and decision-making;</li> <li>• give special consideration to the views of people who do not have capacity to make decisions about their care, in line with the document ‘National Guidance for the Clinical Governance of Dementia’ issued by the National Committee for Dementia;</li> <li>• ensure that people are aware of their rights to and the availability of local advocacy services, in line with the document ‘National Guidance for the Clinical Governance of Dementia’ issued by the National Committee for Dementia;</li> <li>• develop a care and support plan, and</li> <li>• agree and review it with the involvement of the person, their family members or carers (as appropriate) and relevant professionals;</li> <li>• specify in the plan when and how often it will be reviewed;</li> <li>• evaluate and record progress towards the objectives at each review;</li> <li>• ensure it covers the management of any comorbidities;</li> <li>• provide a copy of the plan to the person and their family members or carers (as appropriate).</li> </ul> | <b>WEAK IN FAVOUR</b><br>Adapted   |
| 42   | When developing care and support plans and advance care and support plans, request consent to transfer these to different care settings as needed.   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 43   | Service providers should ensure that information (such as care and support plans and advance care and support plans) can be easily transferred between different care settings (e.g. home, inpatient, community and residential care).   | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 44   | Staff delivering care and support should maximise continuity and consistency of care. Ensure that relevant information is shared and recorded in the person’s care and support plan.   | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 45   | Service providers should design services to be accessible to as many people living with dementia as possible, including: <ul style="list-style-type: none"> <li>• people who do not have a carer or whose carer cannot support them on their own;</li> <li>• people who do not have access to affordable transport, or find transport difficult to use;</li> <li>• people who have responsibilities (such as work, children or being a carer themselves);</li> <li>• people with learning disabilities, sensory impairment (such as sight or hearing loss) or physical disabilities;</li> <li>• people who may be less likely to access health and social care services, such as people from minorities*.</li> </ul>   | <b>WEAK IN FAVOUR</b><br>Adapted   |
| <b>Post-diagnosis review for people living with dementia</b> |  |                                    |
| 46   | After a person is diagnosed with dementia or mild cognitive impairment, ensure they and their carers have access to specialist multidisciplinary dementia services (Centres for Cognitive Disorders and Dementias, CCDDs).   | <b>STRONG IN FAVOUR</b><br>Adapted |
| 47   | Specialist multidisciplinary dementia services (Centres for Cognitive Disorders and Dementias, CCDDs) should offer a choice of flexible access or prescheduled monitoring appointments.  | <b>WEAK IN FAVOUR</b><br>Adapted   |
| 48   | General practitioners, when visiting people living with dementia or mild cognitive impairment, or their carers, should assess for any emerging dementia-related needs and ask them if they need any more support.  | <b>WEAK IN FAVOUR</b><br>Adapted   |
| <b>Staff training</b>  |  |                                    |
| 49   | Care and support providers should provide all staff with appropriate training in person-centred and outcome-focused care for people living with dementia, which should include: <ul style="list-style-type: none"> <li>• understanding the signs and symptoms of dementia, and the changes to expect as the condition progresses;</li> <li>• understanding the person as an individual, and their life story;</li> <li>• respecting the person’s individual identity, sexuality and culture;</li> <li>• understanding the needs of the person and their family members or carers.</li> </ul>   | <b>WEAK IN FAVOUR</b><br>Adapted   |
| 50   | Care providers should provide additional face-to-face training and mentoring to staff who deliver care and support to people living with dementia. This should include: <ul style="list-style-type: none"> <li>• understanding the organisation’s model of dementia care and how it provides care;</li> <li>• initial training on understanding, reacting to and helping people living with dementia who experience agitation, aggression, pain or other behaviours indicating distress;</li> <li>• follow-up sessions where staff can receive additional feedback and discuss particular situations;</li> <li>• advice on interventions that reduce the need for antipsychotics and allow doses to be safely reduced;</li> <li>• promoting freedom of movement and minimising the use of restraint;</li> </ul> the specific needs of younger people living with dementia and people who are working or looking for work.  | <b>WEAK IN FAVOUR</b><br>Adapted   |

(Continued)

Table 2. Continued

| <b>Pre-, peri- and post-diagnostic counselling</b>   |   |                                    |
|--|---|------------------------------------|
| 51   | Consider giving carers and/or family members the opportunity to attend and take part in staff dementia training sessions.   | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 52   | Consider training staff to provide multi-sensory stimulation for people with moderate to severe dementia and communication difficulties.  | <b>WEAK IN FAVOUR</b><br>Adopted   |
| <b>Involving people living with dementia in decisions about care</b>   |   |                                    |
| 53   | Provide people living with dementia and their family members or carers (as appropriate) with information that is relevant to their circumstances and the stage of their condition.  | <b>STRONG IN FAVOUR</b><br>Adopted |
| 54   | Be aware of the obligation to provide accessible information. For more guidance on providing information and discussing people's preferences with them, see the document 'National Guidance for the Clinical Governance of Dementia' issued by the National Committee for Dementia.   | <b>STRONG IN FAVOUR</b><br>Adapted |
| 55   | Throughout the diagnostic process, offer the person and their family members or carers (as appropriate) oral and written information that explains: <ul style="list-style-type: none"> <li>• what their dementia subtype is and the changes to expect as the condition progresses;</li> <li>• which health and social care professionals will be involved in their care and how to contact them;</li> <li>• if appropriate, how dementia affects driving, and that they need to tell the general practitioner and healthcare staff involved in renewing their licence about their dementia diagnosis;</li> <li>• their legal rights and responsibilities, see the document 'National Guidance for the Clinical Governance of Dementia' issued by the National Committee for Dementia;</li> <li>• their right to reasonable adjustments (law 68/99<sup>4</sup> with modifications according to the Legislative Decree 151/2015<sup>5</sup>) if they are working or looking for work;</li> <li>• how the following groups can help and how to contact them: <ul style="list-style-type: none"> <li>• local support groups, online forums and national charities;</li> <li>• financial and legal advice services;</li> <li>• advocacy services.</li> </ul> </li> </ul> | <b>STRONG IN FAVOUR</b><br>Adapted |
| 56   | If it has not been documented earlier, ask the person at diagnosis: <ul style="list-style-type: none"> <li>• for their consent for services to share information;</li> <li>• which people they would like services to share information with (e.g. family members or carers);</li> <li>• what information they would like services to share.</li> </ul> Document these decisions in the person's records.   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 57   | After diagnosis, direct people and their family members or carers (as appropriate) to relevant services for information and support (see recommendations 40 and 41 on care coordination).   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 58   | For people who do not want follow-up appointments and who are not using other services, ask if they would like to be contacted again at a specified future date.  | <b>STRONG IN FAVOUR</b><br>Adopted |
| 59   | Ensure that people living with dementia and their carers know how to get more information and who from if their needs change.   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 60   | Tell people living with dementia (at all stages of the condition) about research studies they could participate in.   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 61   | Offer early and ongoing opportunities for people living with dementia and people involved in their care (see recommendation 36) to discuss: <ul style="list-style-type: none"> <li>• the benefits of planning ahead;</li> <li>• lasting power of attorney (for health and welfare decisions and property and financial affairs decisions);</li> <li>• an advance statement about their wishes, preferences, beliefs and values regarding their future care;</li> <li>• advance decisions to refuse treatment;</li> <li>• their preferences for place of care and place of death.</li> </ul>   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 62   | Explain that they will be given chances to review and change any advance statements and decisions they have made.   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 63   | At each care review, offer people the chance to review and change any advance statements and decisions they have made.  | <b>STRONG IN FAVOUR</b><br>Adopted |
| 64   | Encourage and enable people living with dementia to give their own views and opinions about their care.   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 65   | If needed, use additional or modified ways of communicating (e.g. visual aids or simplified text).  | <b>STRONG IN FAVOUR</b><br>Adopted |
| 66   | Ensure that all health and social care staff are aware of: <ul style="list-style-type: none"> <li>• the extent of their responsibility to protect confidentiality under data protection legislation and</li> <li>• any rights that family members, carers and others have to information about the person's care (see recommendation 41).</li> </ul>  | <b>STRONG IN FAVOUR</b><br>Adopted |
| 67   | Health and social care professionals advising people living with dementia (including professionals involved in diagnosis) should be trained in starting and holding difficult and emotionally challenging conversations.  | <b>WEAK IN FAVOUR</b><br>Adopted   |
| <b>Management strategies for people living with dementia/mild cognitive impairment and co-existing physical long-term conditions</b> |   |                                    |
| 68   | Ensure that people living with dementia have equivalent access to diagnosis, treatment and care services for comorbidities to people who do not have dementia. For more guidance on assessing and managing multimorbidity, see Table 6 in the Full Guideline.   | <b>STRONG IN FAVOUR</b><br>Adopted |

(Continued)



Table 2. Continued

| Pre-, peri- and post-diagnostic counselling   |   |                                    |
|---|---|------------------------------------|
| 69  | For people with dementia or mild cognitive impairment and at least one chronic physical comorbidity, when managing comorbidities (e.g. hypertension, cardiovascular diseases, type 2 diabetes, sensory deficits, urinary tract conditions) refer to the best practices for each condition, considering each person's specific clinical conditions and except in case the administration of standard care could cause more harm than benefit (see Table 6 in the Full Guideline).  | <b>STRONG IN FAVOUR</b><br>Adapted |
| Care setting transitions                      |   |                                    |
| 70  | When managing transition between care settings consider that: <ul style="list-style-type: none"> <li>• in case of hospitalisation, a comprehensive geriatric assessment should be performed on people with dementia on admission to hospital, and any care plan should be shared with the admitting team, while, at discharge, continuity of care should be ensured;</li> <li>• the NICE guideline on transition between inpatient mental health settings and community or care home settings.</li> </ul>   | <b>STRONG IN FAVOUR</b><br>Adapted |
| 71  | For guidance on medicine optimisation and reconciliation, see Table 8 in the Full Guideline. Follow the principles in these guidelines for transitions between other settings (e.g. from home to a care home or respite care).  | <b>STRONG IN FAVOUR</b><br>Adapted |
| 72  | Review the needs and wishes of people with dementia and their caregivers (including any care and support plans referring to current and future care) after every transition.  | <b>STRONG IN FAVOUR</b><br>Adapted |
| Supporting caregivers of people with dementia |   |                                    |
| 73  | Offer carers of people living with dementia a psychoeducation and skills training intervention that includes: <ul style="list-style-type: none"> <li>• education about dementia, its symptoms and the changes to expect as the condition progresses;</li> <li>• developing personalised strategies and building carer skills;</li> <li>• training to help them provide care, including how to understand and respond to changes in behaviour;</li> <li>• training to help them adapt their communication styles to improve interactions with the person living with dementia;</li> <li>• advice on how to look after their own physical and mental health, and their emotional and spiritual well-being;</li> <li>• advice on planning enjoyable and meaningful activities to do with the person they care for;</li> <li>• information about relevant services (including support services and psychological therapies for carers) and how to access them;</li> <li>• advice on planning for the future.</li> </ul> | <b>STRONG IN FAVOUR</b><br>Adopted |
| 74  | Ensure that the support offered to carers is: <ul style="list-style-type: none"> <li>• tailored to their needs and preferences and to what they want it to achieve (e.g. providing information on carer's employment rights for carers who work or want to work);</li> <li>• designed to help them support people living with dementia;</li> <li>• available at a location they can get to easily;</li> <li>• provided in a format suitable for them (e.g. individual or group sessions, or online training and support);</li> <li>• available from diagnosis and as needed after this.</li> </ul>  | <b>STRONG IN FAVOUR</b><br>Adopted |
| 75  | Advise carers about their right to the following and how to get them: <ul style="list-style-type: none"> <li>• a formal assessment of their own needs, including their physical and mental health;</li> <li>• an assessment of their need for short breaks and other respite care.</li> </ul>   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 76  | Be aware that carers of people living with dementia are at an increased risk of depression. For guidance on identifying and managing depression, see Table 6 in the Full Guideline.   | <b>WEAK IN FAVOUR</b><br>Adopted   |

\*Minorities are hereby defined as indicated by the Italian Ministry of Domestic Affairs: <https://www.interno.gov.it/it/temi/cittadinanza-e-altri-diritti-civili/minoranze> (30 August 2023, date last accessed).

may increase the risk of dementia or cognitive decline in older adults, despite the mechanisms underlying this association being still unclear [22, 23].

Additionally, the risk of cognitive decline increases with the concomitant use of anticholinergic drugs (i.e. anticholinergic burden). Therefore, the use of anticholinergic drugs should be carefully monitored in older adults and in PwD.

Two RQs were adopted from NG97. The first RQ aimed to identify commonly prescribed drugs that are associated with a higher risk of cognitive decline. This was addressed by analysing prescription data from Italian public and private pharmacies through the National Health System (NHS).

The second RQ focused on diagnostic studies assessing the accuracy of tools used to identify drugs associated with a higher risk of cognitive decline. Only cohort or cross-sectional diagnostic studies with sufficient data to

calculate accuracy measures (e.g. sensitivity, specificity) were included. Fifteen studies (eight from the literature update) were included, examining the Anticholinergic Cognitive Burden scale, the Anticholinergic Risk Scale, the Serum Anticholinergic Activity scale and the Clinician's rated Anticholinergic Scale. The WG agreed that clinicians should be aware of the risk of cognitive impairment associated with an increased anticholinergic burden and should minimise the use of anticholinergic drugs when possible, considering alternative treatments. The WG also recommended using validated tools to assess anticholinergic burden.

*Distinguishing dementia from delirium or delirium with dementia*  
PwD are known to be at a higher risk of delirium, and older adults who experienced delirium at any time are also

Table 3. Recommendations on pharmacological interventions for cognitive symptoms

| <b>Acetylcholinesterase inhibitors, memantine and new biological treatments for Alzheimer's dementia and mild cognitive impairment</b> |   |                                    |
|--|---|------------------------------------|
| 77   | The three acetylcholinesterase (AChE) inhibitors donepezil, galantamine and rivastigmine as monotherapies are recommended as options for managing mild to moderate Alzheimer's dementia under all of the conditions specified in recommendations 82 and 83.   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 78   | Offer donepezil as monotherapy for managing moderate to severe Alzheimer's dementia based on the conditions specified in recommendations 82 and 83.   | <b>WEAK IN FAVOUR</b><br>New       |
| 79   | Memantine monotherapy is recommended as an option for managing Alzheimer's dementia for people with: <ul style="list-style-type: none"> <li>• moderate Alzheimer's dementia who are intolerant of or have a contraindication to AChE inhibitors or</li> <li>• severe Alzheimer's dementia.</li> </ul> <p>Treatment should be under the conditions specified in recommendation 82.</p>   | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 80   | For people who are not taking an AChE inhibitor or memantine, prescribers should only start treatment with these on the advice of a specialist (neurologist, geriatrician, psychiatrist) who has the necessary knowledge and skills. Only specialists in Centres for Cognitive Disorders and Dementias (CCDDs) can provide refundable prescriptions for these drugs within the National Health System.  | <b>WEAK IN FAVOUR</b><br>Adapted   |
| 81   | If prescribing an AChE inhibitor, treatment should normally be started with the drug with the lowest acquisition cost (taking into account required daily dose and the price per dose once shared care has started). However, an alternative AChE inhibitor could be prescribed if it is considered appropriate when taking into account adverse event profile, expectations about adherence, medical comorbidity, possibility of drug interactions and dosing profiles.  | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 82   | When using assessment scales to determine the severity of Alzheimer's dementia, healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the results and make any adjustments they consider appropriate. Healthcare professionals should also be mindful of the need to secure equality of access to treatment for patients from different ethnic groups, in particular those from different cultural backgrounds.   | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 83   | When assessing the severity of Alzheimer's dementia and the need for treatment, healthcare professionals should not rely solely on cognition scores in circumstances in which it would be inappropriate to do so. These include: <ul style="list-style-type: none"> <li>• if the cognition score is not, or is not by itself, a clinically appropriate tool for assessing the severity of that person's dementia because of the person's learning difficulties or other disabilities (e.g. sensory impairments), linguistic or other communication difficulties or level of education or</li> <li>• if it is not possible to apply the tool in a language in which the person is sufficiently fluent for it to be appropriate for assessing the severity of dementia or</li> <li>• if there are other similar reasons why using a cognition score, or the score alone, would be inappropriate for assessing the severity of dementia.</li> </ul> <p>In such cases healthcare professionals should determine the need for initiation or continuation of treatment by using another appropriate method of assessment.</p> | <b>WEAK AGAINST</b><br>Adopted     |
| <b>Acetylcholinesterase inhibitors and memantine in people with mild cognitive impairment</b>  |   |                                    |
| 84   | Do not offer AChE inhibitors (donepezil, galantamine and rivastigmine) and memantine for the treatment of mild cognitive impairment.  | <b>STRONG AGAINST</b><br>New       |
| <b>Biological drugs in people with Alzheimer's dementia and mild cognitive impairment</b>  |   |                                    |
| 85   | Do not offer monoclonal antibodies against the different forms of amyloid $\beta$ as a treatment for Alzheimer's dementia or mild cognitive impairment.**   | <b>STRONG AGAINST</b><br>New       |
| <b>Repurposing of pharmacological interventions</b>  |   |                                    |
| 86   | Do not offer the following treatments specifically to slow the progression of Alzheimer's disease or to slow or stop the conversion from mild cognitive impairment to dementia: <ul style="list-style-type: none"> <li>• antidiabetic drugs;</li> <li>• antihypertensive drugs;</li> <li>• statins;</li> <li>• non-steroidal anti-inflammatory drugs (NSAIDs), including acetylsalicylic acid.</li> </ul>   | <b>STRONG AGAINST</b><br>Adapted   |
| <b>Co-prescription of acetylcholinesterase inhibitors and memantine in Alzheimer's dementia</b>  |   |                                    |
| 87   | For people with moderate Alzheimer's dementia who are already taking an AChE inhibitor consider memantine in addition to the AChE inhibitor.  | <b>WEAK IN FAVOUR</b><br>Adapted   |
| 88   | For people with severe Alzheimer's dementia who are already taking an AChE inhibitor offer memantine in addition to the AChE inhibitor.   | <b>STRONG IN FAVOUR</b><br>Adapted |
| <b>Discontinuation of acetylcholinesterase inhibitors and memantine in Alzheimer's dementia</b>  |   |                                    |
| 89   | Do not stop AChE inhibitors or memantine in people with Alzheimer's dementia because of disease severity alone.   | <b>STRONG AGAINST</b><br>Adopted   |
| <b>Acetylcholinesterase inhibitors and memantine for Parkinson's disease dementia</b>  |   |                                    |
| 90   | Offer AChE inhibitors <sup>6</sup> for people with mild or moderate Parkinson's disease dementia.   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 91   | Consider AChE inhibitors <sup>7</sup> for people with severe Parkinson's disease dementia.  | <b>WEAK IN FAVOUR</b><br>Adopted   |

(Continued)

Table 3. Continued

| <b>Acetylcholinesterase inhibitors, memantine and new biological treatments for Alzheimer's dementia and mild cognitive impairment</b> |  |                                    |
|--|--|------------------------------------|
| 92   | Consider memantine <sup>8</sup> for people with Parkinson's disease dementia, only if AChE inhibitors are not tolerated or are contraindicated.  | <b>WEAK IN FAVOUR</b><br>Adopted   |
| <b>Acetylcholinesterase inhibitors for dementia with Lewy bodies</b>   |  |                                    |
| 93   | Offer donepezil or rivastigmine to people with mild to moderate dementia with Lewy bodies.   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 94   | Only consider galantamine for people with mild to moderate dementia with Lewy bodies if donepezil and rivastigmine are not tolerated.  | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 95   | Consider donepezil or rivastigmine for people with severe dementia with Lewy bodies.   | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 96   | Consider memantine for people with dementia with Lewy bodies if cholinesterase inhibitors are not tolerated or are contraindicated.  | <b>WEAK IN FAVOUR</b><br>Adopted   |
| <b>Acetylcholinesterase inhibitors and memantine for types of dementia other than Alzheimer's disease</b>                              |  |                                    |
| 97   | Only consider AChE inhibitors or memantine for people with vascular dementia if they have suspected comorbid Alzheimer's disease, Parkinson's disease dementia or dementia with Lewy bodies. | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 98   | Do not offer AChE inhibitors or memantine to people with frontotemporal dementia.  | <b>STRONG AGAINST</b><br>Adopted   |
| 99   | Do not offer AChE inhibitors or memantine to people with cognitive impairment caused by multiple sclerosis.  | <b>STRONG AGAINST</b><br>Adopted   |

<sup>8</sup>Three members of the panel abstained from voting recommendation 85.

known to be at a higher risk of developing dementia [24, 25]. The onset of delirium in older people admitted to an emergency department or urgent care is usually associated with a negative prognosis in terms of length of stay [26], mortality [27], cognitive and functional decline [28], and risk of readmission at 30 days [29]. The diagnosis of delirium in an emergency setting is challenging [30], mainly due to the difficulty of establishing whether symptoms are due to an isolated episode of delirium, to delirium with underlying dementia or to dementia alone. An adequate differential diagnosis is essential, as it affects the choice of treatment strategies during the hospitalisation and after discharge.

The RQ aimed at identifying studies investigating the utility of different diagnostic tests to distinguish dementia from delirium or delirium with dementia.

Eight studies (two from the literature update) were included reporting data on nine different tools.

The WG agreed to recommend considering two instruments (the extended version of Confusion Assessment Method [31] and 4'As Test [32]) to distinguish dementia from delirium or delirium with dementia in people admitted to hospital. The WG also agreed to recommend treating delirium first when it is not possible to tell whether a person has delirium, dementia or delirium superimposed on dementia.

#### *Pre-, peri- and post-diagnostic counselling*

The diagnostic process of dementia is characterised by three main phases, one first phase immediately preceding the diagnosis, a second phase of communication of the diagnosis and a third phase immediately after diagnosis. These phases are essential steps for the definition of supportive interventions.

The literature review for this RQ aimed to identify studies investigating the effectiveness of pre-, peri- and

post-diagnostic interventions in improving outcomes for PwD and their caregivers.

Overall, seven studies (four from the literature update) were included. None of the included studies investigating interventions of post-diagnostic support reported significant results. Few studies were identified investigating interventions of pre- and peri-diagnostic counselling and support. The working group of NG97 considered available evidence as insufficient to support a recommendation. However, the WG of the present guideline agreed on the importance of supporting PwD and their caregivers in these crucial phases of the diagnostic process. Therefore, considering the relevance of care continuity when progressing from the peri-diagnostic phase to the subsequent phases of the disease, the WG agreed to include a recommendation to consider peri- and post-diagnostic counselling and support in people that received a diagnosis of dementia and their caregivers.

#### *Specific needs of people with young-onset dementia (40–65 years)*

People with young-onset dementia (YOD) may have specific needs, different from those of people who develop dementia later in life [33], that need to be addressed through targeted, structured, and accessible diagnostic and care strategies.

The RQ aimed to identify qualitative studies exploring the specific needs of people with YOD, focusing on improving outcomes for people with YOD and their caregivers.

Nine studies (two from the literature update) were included. The qualitative analysis of evidence identified three categories of themes: experiences and coping in employment, general experiences and coping, and supporting activities and services. Evidence highlighted the need for information about rights and needs in the workplace, financial and legal aspects, and access to support services. Further indications on the specific needs of people with YOD were added to the

Table 4. Recommendations on non-pharmacological interventions for cognitive symptoms

| <b>Non-pharmacological interventions for cognitive symptoms in dementia</b>                  |   |                                    |
|--|---|------------------------------------|
| 100  | Do not offer acupuncture to treat cognitive symptoms in dementia.   | <b>STRONG AGAINST</b><br>Adopted   |
| 101  | Consider aerobic physical exercise to treat cognitive symptoms in people with mild Alzheimer's dementia.  | <b>WEAK IN FAVOUR</b><br>New       |
| 102  | Consider non-aerobic physical exercise to treat cognitive symptoms in people with mild to moderate dementia.  | <b>WEAK IN FAVOUR</b><br>New       |
| 103  | Consider the combination of aerobic and non-aerobic physical exercise to treat cognitive symptoms in people with moderate dementia.   | <b>WEAK IN FAVOUR</b><br>New       |
| 104  | Do not offer specific formulas, including the combinations of supplements containing omega-3 fatty acids, phospholipids, choline, uridine monophosphate, vitamin E, vitamin C, vitamin B <sub>6</sub> , vitamin B <sub>12</sub> , folic acid and selenium to treat cognitive symptoms in people with dementia in absence of documented deficiencies.  | <b>STRONG AGAINST</b><br>New       |
| 105  | Do not offer vitamin E and folic acid supplements to treat cognitive symptoms in people with dementia in absence of documented deficiencies.  | <b>STRONG AGAINST</b><br>Adapted   |
| 106  | Do not offer ginseng, <i>ginkgo biloba</i> , huperzine A and other herbal supplements, antioxidants such as omega-3, selenium and sodium oligomannate to treat cognitive symptoms in people with dementia.  | <b>STRONG AGAINST</b><br>Adapted   |
| 107  | Do not offer ketogenic dietary interventions to treat cognitive symptoms in people with dementia.   | <b>STRONG AGAINST</b><br>New       |
| 108  | Do not offer light therapy to treat cognitive symptoms in people with moderate to severe dementia.  | <b>STRONG AGAINST</b><br>New       |
| 109  | Consider music therapy to treat cognitive symptoms in people with mild to severe dementia.  | <b>WEAK IN FAVOUR</b><br>New       |
| 110  | Do not offer psychotherapy to treat cognitive symptoms in people with mild to moderate dementia.  | <b>STRONG AGAINST</b><br>Adapted   |
| 111  | Consider reminiscence therapy to treat cognitive symptoms in people with moderate dementia.   | <b>WEAK IN FAVOUR</b><br>Adapted   |
| 112  | Do not offer therapeutic robots to treat cognitive symptoms in people with dementia.  | <b>STRONG AGAINST</b><br>New       |
| 113  | Consider occupational therapy to support functional abilities in people with mild to moderate dementia.   | <b>WEAK IN FAVOUR</b><br>Adapted   |
| 114  | Consider cognitive rehabilitation to support functional abilities in people with mild to moderate dementia.   | <b>WEAK IN FAVOUR</b><br>Adapted   |
| 115  | Offer cognitive stimulation to treat cognitive symptoms in people with mild to moderate dementia.   | <b>STRONG IN FAVOUR</b><br>Adapted |
| 116  | Consider cognitive training to treat cognitive symptoms in people with mild Alzheimer's dementia.   | <b>WEAK IN FAVOUR</b><br>New       |
| 117  | Offer a range of activities to promote well-being and autonomy that are tailored to the person's individual preferences.  | <b>STRONG IN FAVOUR</b><br>Adapted |
| <b>Non-pharmacological interventions for cognitive symptoms in mild cognitive impairment</b> |   |                                    |
| 118  | Do not consider acupuncture to treat cognitive symptoms in people with mild cognitive impairment.   | <b>WEAK AGAINST</b><br>New         |
| 119  | Do not offer aromatherapy to treat cognitive symptoms in people with mild cognitive impairment.   | <b>STRONG AGAINST</b><br>New       |
| 120  | Consider art therapy to treat cognitive symptoms and improve depressive symptoms and anxiety in people with mild cognitive impairment.  | <b>WEAK IN FAVOUR</b><br>New       |
| 121  | Consider physical exercise to treat cognitive symptoms and promote independence in people with mild cognitive impairment.   | <b>WEAK IN FAVOUR</b><br>New       |
| 122  | Consider dance to treat of cognitive symptoms and improve depressive symptoms in people with mild cognitive impairment.   | <b>WEAK IN FAVOUR</b><br>New       |
| 123  | Consider games (e.g. cards, board games) to treat cognitive symptoms and improve depressive symptoms in people with mild cognitive impairment.  | <b>WEAK IN FAVOUR</b><br>New       |
| 124  | Consider cognitive rehabilitation to treat cognitive symptoms and promote independence in people with mild cognitive impairment.  | <b>WEAK IN FAVOUR</b><br>New       |
| 125  | Offer cognitive training to treat cognitive symptoms in people with mild cognitive impairment.  | <b>STRONG IN FAVOUR</b><br>New     |
| 126  | Do not offer specific formulas, including combinations of supplements containing omega-3 fatty acids, phospholipids, choline, uridine monophosphate, vitamin E, vitamin C, vitamin B <sub>6</sub> , vitamin B <sub>12</sub> , folic acid and selenium, supplements based on combinations of fatty acids polyunsaturated, such as omega-3 and omega-6, and monounsaturated and multivitamins and/or antioxidants supplements to treat cognitive symptoms in people with mild cognitive impairment in absence of documented deficiencies. | <b>STRONG AGAINST</b><br>New       |
| 127  | Do not offer <i>ginkgo biloba</i> , ginseng, omega-3, resveratrol or other antioxidants to treat cognitive symptoms in people with mild cognitive impairment.   | <b>STRONG AGAINST</b><br>New       |
| 128  | Do not offer vitamin B and vitamin E supplements to treat cognitive symptoms in people with mild cognitive impairment in absence of documented deficiencies.  | <b>STRONG AGAINST</b><br>New       |

(Continued)

Table 4. Continued

| Non-pharmacological interventions for cognitive symptoms in dementia |  |                              |
|--|--|------------------------------|
| 129  | Do not offer ketogenic dietary interventions to treat cognitive symptoms in people with mild cognitive impairment.                       | <b>STRONG AGAINST</b><br>New |
| 130  | Do not consider transcranial stimulation interventions to treat people with mild cognitive impairment.                                   | <b>WEAK AGAINST</b><br>New   |
| 131  | Consider music therapy to treat cognitive symptoms and improve depressive symptoms and anxiety in people with mild cognitive impairment. | <b>WEAK IN FAVOUR</b><br>New |

sections on involving PwD in decisions about their care, staff training, and models of care planning and care coordination.

**Care models and care coordination**

*Care planning, review and coordination*

Disease trajectories in PwD may differ due to multiple factors [34, 35]. Appropriate, individualised care models are crucial to meet the needs and abilities of PwD. This section aimed to identify quantitative or qualitative studies on the effectiveness of models of care planning and coordination in improving outcomes for PwD or MCI and their caregivers.

A total of 28 randomised controlled trials (RCTs) (two from the literature update) and 18 qualitative studies (none from the literature update) were identified for care models for PwD. No studies were retrieved focusing on care models for people with MCI. Studies varied in terms of frequency of follow-up, contact methods and the roles of care managers. Evidence emphasised the importance of structured care and support plans from the time of diagnosis to help PwD plan for future care. Recommendations from this section were linked to those in the diagnostic process section. Identifying a single care coordinator was recommended as reported to improve the quality of life (QoL) for PwD and reduced caregiver burden and depression.

The importance of an initial assessment of the needs of PwD, preferably face-to-face, was highlighted. The WG stressed the need to provide families and caregivers with clear information on available services and how to access them. Involving family members and, when possible, PwD in decision-making and care planning was recommended to improve QoL and reduce institutionalisation. However, the active involvement of caregivers can be challenging, especially when they lack a consistent relationship with health professionals. Thus, the WG agreed to recommend further research on effective care planning models.

Additionally, the WG stressed the need for inclusive service planning to reduce barriers to access, especially for vulnerable groups, such as those living alone or in minority communities.

*Post-diagnosis review for people living with dementia*

Using strategies to monitor PwD or MCI could help preserve or improve cognitive function, abilities and QoL. Two RQs aimed to identify comparative experimental studies

(e.g. RCTs, non-randomised trials) on the effectiveness of methods, models, and settings for monitoring PwD or MCI. Eight studies involving PwD were retrieved (three from the literature update), while no studies were identified on people with MCI.

The WG confirmed that the most effective care model for CCDDs (Italian memory clinics) should be flexible, coordinated, multidisciplinary and accessible to all with cognitive decline. Since post-diagnosis reviews impact caregivers, all recommendations applied to both PwD and their caregivers, following the NG97 approach.

The WG also emphasised the importance of further investigating the role of telemedicine for remote PwD monitoring, due to its potential to reduce the stress from transferring and to optimise services. The role of interdisciplinary monitoring led by general practitioners (GPs) in collaboration with other healthcare professionals was also considered as relevant, leading to two specific research recommendations.

Although no eligible studies focused on post-diagnosis review for people with MCI, the WG extended the recommendations to include people with MCI, stressing that monitoring should be conducted by multidisciplinary specialist services offering flexible access. GPs should assess emerging needs for targeted support in both PwD and MCI.

*Staff training*

An inappropriate management of PwD can affect the progression of cognitive and non-cognitive symptoms and increase the burden on both formal and informal caregivers [36, 37].

Providing adequate training to health and social care professionals is crucial for the early identification of emerging needs and the development of appropriate intervention strategies.

This research question aimed to identify studies evaluating the effectiveness of training interventions for professionals in improving outcomes for PwD and their caregivers. A total of 27 studies (four from the literature update) were included.

Included studies were widely heterogeneous in terms of types of intervention, tools and outcomes. Therefore, the WG agreed on including general recommendations, focusing on key aspects of training rather than specific interventions. The WG recommended that training should cover general

Table 5. Recommendations on non-cognitive symptoms, intercurrent illnesses and palliative care

| <b>Management of non-cognitive symptoms in people with dementia</b>  |   |                                    |
|--|---|------------------------------------|
| 132  | Before starting non-pharmacological or pharmacological treatment for distress in people living with dementia, conduct a structured assessment to: <ul style="list-style-type: none"> <li>• explore possible reasons for the person's distress and</li> <li>• check for and address clinical or environmental causes (e.g. pain, delirium or inappropriate care).</li> </ul>   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 133  | As initial and ongoing management, offer psychosocial and environmental interventions to reduce distress in people living with dementia.  | <b>STRONG IN FAVOUR</b><br>Adapted |
| 134  | Ensure that people living with dementia can continue to access psychosocial and environmental interventions for distress while they are taking antipsychotics and after they have stopped taking them.  | <b>STRONG IN FAVOUR</b><br>Adopted |
| 135  | For people living with dementia who experience agitation or aggression, offer personalised activities to promote engagement, pleasure and interest.   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 136  | Consider interventions aimed at specifically training staff for the management of non-cognitive symptoms in people living with dementia.  | <b>WEAK IN FAVOUR</b><br>New       |
| 137  | Consider providing access to therapeutic gardens for the management of non-cognitive symptoms in people living with dementia who experience BPSDs.  | <b>WEAK IN FAVOUR</b><br>New       |
| 138  | Consider interventions of active and/or receptive music therapy for the management of non-cognitive symptoms in people living with dementia who experience BPSDs.   | <b>WEAK IN FAVOUR</b><br>New       |
| 139  | Consider psychological treatments in people with mild to moderate dementia who experience mild to moderate depressive symptoms and/or anxiety.  | <b>WEAK IN FAVOUR</b><br>New       |
| 140  | Consider the use of therapeutic robots in people with dementia who experience depressive symptoms, anxiety and/or agitation.  | <b>WEAK IN FAVOUR</b><br>New       |
| 141  | For people living with dementia who have sleep problems, consider a personalised multicomponent sleep management approach that includes sleep hygiene education, exposure to daylight, exercise and personalised activities.  | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 142  | Before starting antipsychotics, discuss the benefits and harms with the person and their family members or caregivers (as appropriate). Consider using a decision aid to support this discussion.   | <b>STRONG IN FAVOUR</b><br>Adopted |
| 143  | When using antipsychotics: <ul style="list-style-type: none"> <li>• use the lowest effective dose and use them for the shortest possible time;</li> <li>• reassess the person at least every 4 weeks, to check whether they still need medication.</li> </ul>   | <b>STRONG IN FAVOUR</b><br>Adapted |
| 144  | Only offer antipsychotics for people living with dementia who are either: <ul style="list-style-type: none"> <li>• at risk of harming themselves or others or</li> <li>• experiencing agitation, hallucinations or delusions that are causing them severe distress.</li> </ul>  | <b>STRONG IN FAVOUR</b><br>Adopted |
| 145  | Stop treatment with antipsychotics: <ul style="list-style-type: none"> <li>• if the person is not getting a clear ongoing benefit from taking them and</li> <li>• after discussion with the person taking them and their family members or caregivers (as appropriate).</li> </ul>  | <b>STRONG IN FAVOUR</b><br>Adopted |
| 146  | Do not offer valproate to manage agitation or aggression in people living with dementia, unless it is indicated for another condition.  | <b>STRONG AGAINST</b><br>Adopted   |
| 147  | Do not routinely offer antidepressants to manage mild to moderate depression in people living with mild to moderate dementia, unless they are indicated for a pre-existing severe mental health condition.  | <b>STRONG AGAINST</b><br>Adopted   |
| 148  | Do not offer bupropion to manage depressive symptoms in people living with dementia.  | <b>STRONG AGAINST</b><br>New       |
| 149  | Be aware that for people with dementia with Lewy bodies or Parkinson's disease dementia, antipsychotics can worsen the motor features of the condition, and in some cases cause severe antipsychotic sensitivity reactions. For more guidance, see the advice on managing delusions and hallucinations in Table 6 in the Full Guideline. Be aware that interventions may need to be modified for people living with dementia. | <b>WEAK IN FAVOUR</b><br>Adopted   |
| <b>Assessing intercurrent illness in people living with dementia</b> |   |                                    |
| 150  | Consider using a structured observational pain assessment tool: <ul style="list-style-type: none"> <li>• alongside self-reported pain and standard clinical assessment for people living with moderate to severe dementia;</li> <li>• alongside standard clinical assessment for people living with dementia who are unable to self-report pain.</li> </ul>   | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 151  | For people living with dementia who are in pain, consider using a stepwise treatment protocol that balances pain management and potential adverse events.   | <b>WEAK IN FAVOUR</b><br>Adopted   |
| 152  | Repeat pain assessments for people living with dementia: <ul style="list-style-type: none"> <li>• who seem to be in pain;</li> <li>• who show signs of behavioural changes that may be caused by pain;</li> <li>• after any pain management intervention.</li> </ul>  | <b>STRONG IN FAVOUR</b><br>Adopted |

(Continued)

Table 5. Continued

**Management of non-cognitive symptoms in people with dementia**

**Treating intercurrent illness in people living with dementia**

- 153 For managing the risk of falling for people living with dementia refer to the standard treatment for the prevention of falls (see Table 6 in the Full Guideline).  
When using this guidance:
- take account of the additional support people living with dementia may need to participate effectively;
  - be aware that multifactorial falls interventions may not be suitable for a person living with severe dementia.

**STRONG IN FAVOUR**  
Adopted

**Caring for people living with dementia who are admitted to hospital**

- 154 Be aware of the increased risk of delirium in people living with dementia who are admitted to hospital. See Table 6 in the Full Guideline for interventions to identify and treat delirium.
- 155 In case of people with dementia admitted to hospital, ensure the availability of a multidimensional assessment, the monitoring and review of all pharmacological treatments, and the reconciliation of pharmacological treatment plans, and any possible issues related to safety, considering the involvement of a pharmacist or pharmacologist. For further indications on the optimisation and reconciliation of pharmacological treatments, see Table 7 in the Full Guideline and the recommendation on the reconciliation of pharmacological treatments provided by the Ministry of Health.<sup>9</sup>
- 156 Consider the involvement of a multidisciplinary team in case of people with dementia admitted to hospital to ensure personalised interventions based on a multidimensional assessment of their overall health, including their nutritional status.

**WEAK IN FAVOUR**  
Adopted

**STRONG IN FAVOUR**  
New

**WEAK IN FAVOUR**  
New

**Palliative care**

- 157 From diagnosis, offer people living with dementia flexible, needs-based palliative care that takes into account how unpredictable dementia progression can be.
- 158 Encourage and support people living with dementia to eat and drink, taking into account their nutritional needs.
- 159 Consider involving a speech and language therapist if there are concerns about a person's safety when eating and drinking.
- 160 Do not routinely use enteral feeding in people living with severe dementia, unless indicated for a potentially reversible comorbidity.
- 161 When thinking about admission to hospital for a person living with severe dementia, carry out an assessment that balances their current medical needs with the additional harms they may face in hospital, e.g.:
- disorientation;
  - a longer length of stay;
  - increased mortality;
  - increased morbidity on discharge;
  - delirium;
  - the effects of being in an impersonal or institutional environment.
- 162 For people living with dementia who are approaching the end of life, use an anticipatory healthcare planning process (see recommendation 41 on advance care planning). Involve the person and their family members or carers (as appropriate) as far as possible, and use the principles of best-interest decision-making if the person cannot make decisions about their own care.
- 163 For standards and measures on palliative care, see Table 10 in the Full Guideline.
- 164 For guidance on care for people in the last days of life, see Table 11 in the Full Guideline.
- 165 For guidance, on best-interest decision-making, see Table 12 in the Full Guideline.
- 166 When thinking about admission to hospital for a person living with dementia, take into account:
- any advance care and support plans;
  - the value of keeping them in a familiar environment.
- 167 Consider using a structured tool to assess the likes and dislikes, routines and personal history of a person living with dementia.

**STRONG IN FAVOUR**  
Adopted

**STRONG IN FAVOUR**  
Adopted

**WEAK IN FAVOUR**  
Adopted

**STRONG AGAINST**  
Adopted

**STRONG IN FAVOUR**  
Adopted

**STRONG IN FAVOUR**  
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**STRONG IN FAVOUR**  
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**STRONG IN FAVOUR**  
Adopted

**STRONG IN FAVOUR**  
Adopted

**WEAK IN FAVOUR**  
Adopted

**WEAK IN FAVOUR**  
Adopted

dementia knowledge, symptoms assessment and management of non-cognitive symptoms, i.e. agitation, aggressive behaviour and pain.

Training interventions aimed at managing agitation and aggressive behaviour often focused on reducing antipsychotic prescriptions and the use of physical restraints. Some

interventions successfully reduced antipsychotic use and physical restraints without increasing behavioural symptoms. Thus, the WG recommended including these elements in staff training, with a strong emphasis on minimising the use of physical and pharmacological restraints, limiting them to cases where they are necessary

Table 6. Research recommendations approved by the panel of experts

| <b>Case-finding for people at high risk of dementia</b>                                       |  |         |
|---|--|---------|
| 1R  | What is the effectiveness of structured case-finding (including a subsequent intervention for people identified as having dementia) in people at high risk of dementia, following up both people identified as having or not having dementia?  | Adopted |
| <b>Diagnosis and differential diagnosis of dementia and mild cognitive impairment</b>         |  |         |
| 2R  | What is the utility and cost-effectiveness of amyloid PET imaging as an additional test to support the diagnosis of Alzheimer's disease and other dementias when compared with standard diagnostic procedures and other imaging or biomarker tests?  | Adapted |
| 3R  | What is the utility of plasma biomarkers as additional tests to support the diagnosis of Alzheimer's disease and other dementias when compared with standard diagnostic procedures and other imaging or biomarker tests?   | New     |
| 4R  | What is the utility of biomarkers within the diagnostic process, and for the differential diagnosis and prognosis of MCI?  | New     |
| <b>Drugs that may worsen cognitive decline</b>  |  |         |
| 5R  | Does actively reducing anticholinergic burden in people living with dementia or mild cognitive impairment improve cognitive outcomes compared with usual care?   | Adopted |
| <b>Distinguishing dementia from dementia with delirium or delirium alone</b>                  |  |         |
| 6R  | In people with treated delirium who no longer meet the DSM-5 criteria for delirium, but who have persistent cognitive deficits, when is the most appropriate time to carry out an assessment for dementia?   | Adopted |
| 7R  | What is the accuracy of 4-A's Test (4AT) and Confusion Assessment Method (CAM) in distinguishing people with delirium or delirium superimposed on dementia from dementia alone in a primary care setting or in a residential care setting?   | New     |
| <b>Care planning, review and coordination</b>   |  |         |
| 8R  | What is the effectiveness and cost-effectiveness of high-intensity case management compared with usual care on quality of life (for the person living with dementia and for their carer) and the timing of entry to long-term care?  | Adopted |
| 9R  | What are the most effective methods of care planning for people in residential care settings?  | Adopted |
| 10R   | What are the most effective methods of care planning for people who do not have regular contact with an informal carer?  | Adopted |
| <b>Post-diagnosis review for people living with dementia</b>                                  |  |         |
| 11R   | What is the effectiveness of telemedicine interventions for the post-diagnosis review of people with dementia?   | New     |
| 12R   | What is the effectiveness of an interdisciplinary review from general practitioners in collaboration with other healthcare professionals in assessing for interventions for any emerging dementia-related needs?   | New     |
| <b>Staff training</b>   |  |         |
| 13R   | What is the cost-effectiveness of implementing a dementia-specific addition to training for community staff, including dementia-specific elements on managing anxiety, communication, nutritional status, personal care and environment adaptation?  | Adapted |
| 14R   | What is the effectiveness of training acute hospital staff in managing behaviours that challenge in people living with dementia on improving outcomes for people and their carers?   | Adopted |
| <b>Managing mental health conditions alongside dementia/mild cognitive impairment</b>         |  |         |
| 15R   | What are the optimal management strategies for people with enduring mental health problems (including schizophrenia and other psychotic disorders) who subsequently develop dementia or mild cognitive impairment?   | Adapted |
| <b>Supporting caregivers of people with dementia</b>  |  |         |
| 16R   | What is the effectiveness and cost-effectiveness of group-based cognitive-behavioural therapy for carers of people living with dementia who are at high risk of developing depression?   | Adopted |
| <b>Acetylcholinesterase inhibitors and memantine in people with mild cognitive impairment</b> |  |         |
| 17R   | What is the efficacy of AChE inhibitors and memantine for the treatment of the different subtypes of mild cognitive impairment?  | New     |
| <b>Biological drugs in people with Alzheimer's dementia and mild cognitive impairment</b>     |  |         |
| 18R   | What is the safety and efficacy of monoclonal antibodies targeted to the different forms of amyloid $\beta$ for the treatment of Alzheimer's dementia or mild cognitive impairment in terms of: <ul style="list-style-type: none"> <li>• long-term safety and efficacy (e.g. ARIA events),</li> <li>• generalisability of results (e.g. interactions with other treatments for comorbidities),</li> <li>• choice of outcomes proving the clinical relevance of treatment effects?</li> </ul> | New     |
| <b>Acetylcholinesterase inhibitors for the treatment of DLB</b>                               |  |         |
| 19R   | What is the effectiveness of combination treatment with a cholinesterase inhibitor and memantine for people with dementia with Lewy bodies if treatment with a cholinesterase inhibitor alone is not effective or no longer effective?   | Adopted |
| <b>Non-pharmacological interventions for cognitive symptoms in dementia</b>                   |  |         |
| 20R   | What is the effectiveness of art therapy for improving cognition in people with dementia?  | New     |
| 21R   | What is the effectiveness of dance for improving cognition in people with dementia?  | New     |
| 22R   | What is the effectiveness of pet therapy for improving cognition in people with dementia?  | New     |
| 23R   | What is the effectiveness of cognitive training for improving cognition in people with moderate Alzheimer's dementia or other types of dementia?   | New     |
| 24R   | What is the effectiveness of interventions targeted at promoting cognitive, communication and linguistic abilities in people with dementia?  | New     |
| <b>Non-pharmacological interventions for cognitive symptoms in mild cognitive impairment</b>  |  |         |
| 25R   | What is the effectiveness of specific memory interventions for the treatment of people with mild cognitive impairment?   | New     |
| 26R   | What is the effectiveness of transcranial stimulation for the treatment of people with mild cognitive impairment?  | New     |

(Continued)



Table 6. Continued

| <b>Case-finding for people at high risk of dementia</b>        |  |         |
|--|--|---------|
| 27R  | What is the effectiveness of psychosocial interventions for the treatment of people with mild cognitive impairment?  | New     |
| 28R  | What is the effectiveness of rehabilitative interventions based on serious games or virtual reality for improving cognition in people with mild cognitive impairment?                | New     |
| 29R  | What is the effectiveness of interventions targeted at promoting cognitive, communication and linguistic abilities in people with mild cognitive impairment?                         | New     |
| <b>Treating non-cognitive symptoms in people with dementia</b> |  |         |
| 30R  | What is the effectiveness and safety of citalopram for managing depressive symptoms in people living with dementia?  | New     |
| 31R  | What is the effectiveness and safety of vortioxetine for managing depressive symptoms in people living with dementia?  | New     |
| 32R  | What is the effectiveness of pharmacological treatments for managing sleep disorders in people living with dementia?   | Adapted |
| 33R  | What is the effectiveness and cost-effectiveness of dextromethorphan-quinidine for managing agitation in people living with dementia?  | Adopted |
| 34R  | What is the effectiveness and cost-effectiveness of choline alphoscerate for managing apathy in people living with dementia?   | Adopted |
| 35R  | What is the effectiveness of aromatherapy in people living with dementia experiencing agitation or aggression?   | New     |
| 36R  | What is the utility of physical exercise in people living with dementia experiencing depressive symptoms, agitation or apathy?   | New     |
| 37R  | What are the most effective psychological treatments for managing depression or anxiety in people living with dementia at each stage of the condition?                               | Adopted |
| <b>Palliative care</b>   |  |         |
| 38R  | What are the most effective models of general and specialist palliative care support to meet the needs of people with advanced dementia?   | Adopted |
| 39R  | What are the most effective interventions to support staff to recognise advanced dementia and develop appropriate escalation/end of life plans to facilitate care to remain at home? | Adapted |

and after proper consultation with PwD and/or their caregivers.

*Involving people living with dementia in decisions about care*

A person-centred approach focused on people and their needs and wishes can allow for effective and ethical care [38]. However, health and social care professionals may find this approach challenging, as it requires them to be aware of the emotional and psychological impact of the disease on PwD and their caregivers [39].

The RQs aimed to identify qualitative evidence exploring the potential barriers and facilitators to the involvement of PwD in decisions about their present and future care, and to their access to advance care planning.

The systematic literature review identified 20 studies (11 from the literature update). Overall, the analysis of the evidence allowed to identify two categories of themes: barriers and facilitators to the involvement of PwD in decisions about their care. In line with the NG97, the WG agreed that PwD should be offered tailored support and information, and should be provided the opportunity to discuss it regularly.

Based on available evidence, the WG agreed to recommend offering PwD and their caregivers information that is relevant to their circumstances and the stage of the condition, including adequate explanations of dementia subtypes and their expected prognosis, professionals involved in their care and how to contact them, legal rights and responsibilities, and available groups providing support. The WG, in line with NG97, also underlined the importance of discussing advance statements and advanced directives with PwD as

long as they have the capacity to be involved in decision-making and of offering PwD regular opportunities to make changes to their decisions.

*Management strategies for people living with dementia or MCI and co-existing physical long-term conditions*

PwD often show complex clinical pictures, with either comorbidities or multimorbidity, which can affect the progression of dementia or worsen its symptoms [40]. Therefore, planning and implementing an appropriate management of comorbid health conditions can directly affect the well-being and QoL of PwD [41].

The RQs aimed to identify studies investigating the effectiveness of interventions and strategies aimed at slowing the progression of comorbidities, specifically considering the following: incontinence, recurrent falls, hypertension, diabetes, risk of cardiovascular diseases and sensory impairments.

Ten studies enrolling PwD (one from the literature update) and four studies enrolling people with MCI were included in the literature review.

The WG, considering the complexity of managing comorbidities in PwD, confirmed the recommendation to ensure that PwD have equivalent access to diagnosis, treatment and care services for comorbidities to people who do not have dementia.

Included studies reported no indication to specific treatments for comorbidities in people with cognitive deficits. Therefore, the WG agreed to include a recommendation to refer, when managing comorbidities in PwD or MCI and at least one chronic physical comorbidity, to the best practices for each condition, considering each person’s specific clinical

conditions and except in case the administration of standard care could cause more harm than benefit.

#### *Managing mental health conditions alongside dementia or MCI*

The relationship between dementia and mental disorders is extremely complex. Mental disorders are reported to be a risk factor for dementia, and mental disorders with onset in young adulthood are associated with a higher risk of developing dementia at an earlier age [42].

The two RQs aimed to identify studies investigating the effectiveness of interventions and strategies aimed at managing pre-existing psychiatric disorders in PwD or MCI. However, no studies were included for both RQs.

The WG discussed how the management of people with pre-existing mental disorders is more complex due to the two-way interaction between the two conditions. The presence of pre-existing mental disorders can make dementia more difficult to identify and manage, while the onset and progression of dementia can make managing the underlying mental disorders more difficult.

The WG agreed not to make any recommendations for clinical practice. However, considering the lack of studies on this topic, the WG confirmed the research recommendation from NG97 to support further studies on the best strategies to manage people with a pre-existing mental disorder receiving a diagnosis of dementia or MCI.

#### *Care setting transitions*

PwD and their caregivers interact with various professionals across different care settings (e.g. home, residential facilities, hospitals), especially during transitions. Ensuring continuity of care is crucial for optimising medications, communication between professionals, and managing the effects of these changes on the well-being of PwD and their caregivers', as their health affects the person with dementia.

The research question aimed to identify RCTs comparing methods of managing transitions between care settings. The NG97 review identified four studies, none from the literature update. Three studies focused on social support or psychosocial interventions for caregivers, while one investigated spatial orientation interventions for PwD transitioning to new environments.

The WG highlighted some key challenges, including poor communication between healthcare professionals and the lack of shared care plans. Inadequate treatment reconciliation can lead to errors, potentially affecting the safety of PwD and the quality of care during transitions between or within care settings, especially as disease progresses. Interventions emphasised providing caregivers with information about accessing care and involving them in care processes, as well as assessing the needs of PwD and the environment of the receiving facility. Strategies for monitoring, reconciling, and optimising pharmacological and non-pharmacological treatments were also addressed. The WG agreed that the needs and wishes of PwD should be reviewed after every care setting transitions.

The WG agreed that comprehensive geriatric assessments should be performed on PwD admitted to hospitals, and care plans should be shared with the admitting team, while continuity of care should be ensured at discharge, considering differences in local services. The WG also agreed that PwD admitted to mental health services should be granted social and legal protections and monitoring by territorial services throughout the course of the disease.

Although no specific model emerged as the most effective, the WG agreed on supporting the principles of person-centred planning, communication, collaboration and support during transitions, ensuring that all parties are aware of the necessary support and resources available.

#### *Supporting caregivers of people with dementia*

Caregivers are essential resources for both people requiring care and healthcare professionals. However, the burden of caring for and supporting PwD can lead them to an increased risk of developing some pathological conditions. Therefore, preventing negative physical, psychological and social outcomes in caregivers is extremely relevant.

The two RQs aimed to identify quantitative comparative studies investigating the utility of different methods for assessing the needs of caregivers, and RCTs investigating the effectiveness of interventions and services for supporting informal caregivers of PwD.

For the first RQ, neither the NG97 nor LG DEM included any study. For the second RQ, the NG97 identified 93 studies while 29 new studies were included after updating the literature. Studies were classified according to the type of considered intervention and the way they were delivered (e.g. group, individual, etc.).

Nine types of interventions were identified (i.e. psychoeducational interventions, skill-training interventions, psychoeducational and skill-training interventions, supportive interventions, cognitive-behavioural therapy, case management, physical exercise interventions, multicomponent interventions, meditation/mindfulness interventions).

Based on gathered evidence, the WG agreed to recommend offering psychoeducation and skill-training interventions including education about dementia, development of personalised strategies and building carer skills, specific training to provide care and adapt communication styles, advice on their own physical and mental health, advice on planning enjoyable and meaningful activities to do with the person they care for, information about relevant services and advice on planning for the future. The WG also agreed to recommend offering carers support tailored to their needs and preferences, available at a location they can get to easily, provided in a format suitable for them, and available from the diagnosis. Included studies suggested that group cognitive-behavioural therapy could be useful, especially for depressive symptoms. Therefore, the WG agreed to include a research recommendation encouraging further studies investigating the effectiveness of these interventions in a more specific group of people at risk of depressive disorders.

### Pharmacological treatments for cognitive symptoms

#### *Acetylcholinesterase inhibitors, memantine, and new biological treatments for Alzheimer's disease and MCI*

In Italy, acetylcholinesterase inhibitors (AChEIs)—donepezil, galantamine, rivastigmine—and the NMDA receptor antagonist memantine are the only approved drugs with an indication for the treatment of cognitive symptoms in people with Alzheimer's dementia (AD). Their use is regulated, and, despite limited evidence and uncertain safety profile, they are sometimes prescribed off-label in people with MCI. New molecules, such as monoclonal antibodies (mAbs) targeted against amyloid-beta ( $A\beta$ ), are under investigation due to their potential disease-modifying mechanism (e.g. aducanumab, lecanemab, donanemab). However, none of them has yet received marketing authorisation in Europe.

The guideline included three RQs addressing the pharmacological treatment for cognitive symptoms in people with AD or MCI. Two RQs focused on the safety and efficacy of AChEIs and memantine in people with AD or MCI, while one explored the safety and efficacy of active and passive immunotherapies in people with mild to moderate AD or MCI.

Fifty-five studies on AChEIs and memantine in people with AD and six on AChEIs in people with MCI were reviewed, while no studies on memantine in people with MCI were retrieved. The WG agreed on offering AChEIs and memantine for treating cognitive symptoms in people with AD, despite their mild effects and limited evidence on long-term outcomes. The WG agreed on recommending these drugs in people with AD after a careful assessment of disease severity, tolerability and the potential for drug interactions. However, evidence did not support their use in people with MCI, and the WG recommended not offering AChEIs and memantine in this population, underlining the risk for adverse events, particularly gastrointestinal and cardiovascular.

As for immunotherapies, 43 studies were included. Two mAbs, lecanemab and donanemab, were reported as having statistically significant but modest effects on cognitive symptoms, while significantly increasing the risk of amyloid-related imaging abnormalities (ARIA). ARIA were usually reported as being asymptomatic, but moderate to severe, and in some cases even life threatening. The WG emphasised the need for more research on the long-term safety and efficacy of these drugs, the generalisability of results and the actual clinical relevance of their effects. The WG also underlined that mAbs could cause a substantial financial burden on the healthcare system. Furthermore, only a small number of CCDDs in Italy are currently equipped to administer them, which could cause inequalities in access to these treatments. Therefore, the WG recommended not offering anti- $A\beta$  mAbs to people with MCI due to AD or AD, and recommended further research. Available evidence on anti-Tau mAbs and active immunotherapies was limited and still

preliminary; therefore, the WG agreed not to make any recommendation.

#### *Repurposing of pharmacological interventions*

Drug repositioning involves evaluating existing therapies for new indications based on pre-clinical or clinical data [43]. In dementia research, this approach focuses on the attempt to modify specific risk factors including diabetes, hypertension and dyslipidaemia to delay the onset of the disease or to slow its progression. Two RQs investigated the repurposing of drugs targeting specific risk factors in PwD or MCI who did not have the condition the drug is indicated to treat (e.g. PwD or MCI without diabetes).

The systematic literature review identified 21 studies that examined the safety and efficacy of interventions addressing 12 known modifiable risk factors [44]. Of these, 10 studies enrolled PwD: 2 on antidiabetic drugs, 4 on antihypertensive drugs, 4 on statins and 10 on non-steroidal anti-inflammatory drugs (NSAIDs). Additionally, four studies involved people with MCI: one on metformin, two on NSAIDs and one on candesartan.

Evidence did not support the use of antidiabetic drugs, antihypertensive drugs, statins or NSAIDs to slow the progression of AD nor to slow or prevent the conversion from MCI to dementia, leading the WG to recommend against their use.

The WG underlined that these recommendations only apply to cases where the drugs are prescribed specifically to slow the progression of dementia or to slow or prevent the conversion from MCI to dementia. PwD or MCI needing these treatments for the conditions they are meant to treat should continue receiving them as indicated by available valid and reliable guidelines.

#### *Acetylcholinesterase inhibitors and memantine for AD dementia: co-prescription and withdrawal*

Treatment for AD typically involves the use of one of the three AChEIs in its mild to moderate stage, and of memantine in its moderate to severe stage. Evidence suggests that adding memantine to an ongoing treatment with one AChEI can be more effective than maintaining the treatment with one AChEI alone in people with moderate to severe AD, improving functional abilities, global functions and behavioural symptoms.

Two RQs examined the co-prescription of AChEIs and memantine and the impact of discontinuing these treatments in people with AD. Ten studies (including two from the literature update) assessed the efficacy of the combined treatment with AChEIs and memantine, while four studies (including one from literature update) analysed the effects of treatment withdrawal [45].

The WG recommended considering memantine in addition to the AChEI in people in moderate AD already receiving an AChEI, and offering memantine in addition to the AChEI in people with severe AD who are already taking an

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AChEI. The WG also recommended against discontinuing AChEIs or memantine solely due to disease severity.

### *Acetylcholinesterase inhibitors and memantine for Parkinson's disease dementia or dementia with Lewy bodies*

Two RQs explored the comparative effectiveness of AChEIs and memantine in Parkinson's disease dementia (PDD) and DLB. Overall, six studies focused on PDD (four on AChEIs and two on memantine), while four studies focused on DLB (three on AChEIs and one on memantine). Based on available evidence, the WG agreed to recommend offering AChEI in people with mild or moderate PDD and considering AChEIs in people with severe PDD. In case AChEIs are not tolerated or contraindicated, the use of memantine can be considered as an alternative.

The WG agreed to recommend offering donepezil or rivastigmine to people with mild to moderate DLB, and considering galantamine if donepezil and rivastigmine are not tolerated. The use of donepezil or rivastigmine, or memantine if AChEIs are not tolerated or are contraindicated, can be considered in people with severe DLB.

### *Acetylcholinesterase inhibitors and memantine for types of dementia other than Alzheimer's disease*

The objective of the systematic review for this RQ was to identify all RCTs investigating the comparative efficacy of donepezil, galantamine, rivastigmine and memantine for cognitive enhancement in dementia types other than AD [8].

Overall, 16 RCTs and one open-label study were included in the literature review. Nine studies enrolled people with VaD, three studies enrolled people with FTD, three studies enrolled people with cognitive impairment caused by multiple sclerosis and one study enrolled people with Huntington disease. Based on available evidence, the WG agreed to recommend only considering AChEIs or memantine in people with VaD if they have suspected comorbid AD, PDD or DLB, and not to offer them in people with FTD or cognitive impairment caused by multiple sclerosis.

### **Non-pharmacological treatments for cognitive symptoms in dementia or MCI**

Non-pharmacological interventions are an essential therapeutic approach for PwD or MCI, helping maintain cognitive functions and independence, and manage behavioural symptoms. A wide variety of non-pharmacological interventions are available, and treatment options can vary based on the specific needs due to disease severity or to personal preferences or expectations. With the progression of the disease, tailored interventions can help in maintaining independence and managing everyday functions. Group activities can also offer the opportunity for social interaction and peer support, as well as facilitate engagement. Creative and leisure activities can help maintain well-being in PwD at every stage of the disease.

Four RQs focused on the effectiveness of these interventions for cognitive functions, functional abilities, well-being and independence—three in PwD and one in MCI.

The review included 168 studies on PwD (58 from the literature update) and 68 on people with MCI (see [Supplementary Table S5](#)). Based on available evidence, the WG recommended offering cognitive stimulation to treat cognitive symptoms in people with mild to moderate dementia and considering reminiscence therapy to treat cognitive symptoms in people with moderate dementia. Cognitive training was recommended only in mild AD dementia due to the lack of evidence in other dementia subtypes. Therefore, further research was recommended on its potential effectiveness in people with moderate AD dementia or other dementia subtypes. Cognitive rehabilitation was effective in improving daily activities but not cognitive functions or quality of life in people with mild to moderate dementia.

The WG agreed considering physical activity to improve cognitive symptoms in PwD, and occupational therapy and cognitive rehabilitation to support functional activities in people with mild to moderate dementia. Evidence did not support the use of supplements or nutritional interventions, psychotherapy, acupuncture, light therapy or therapeutic robots to treat cognitive symptoms. Available evidence on art therapy, dance and pet therapy was inconclusive but suggestive of a potential benefit, thus further research was recommended. The WG agreed considering music therapy to treat cognitive symptoms in PwD.

The WG agreed to offer cognitive training and consider art therapy, physical exercise, dance, games, cognitive rehabilitation and music therapy in managing cognitive symptoms for the same outcome in people with MCI. Based on available evidence, the WG agreed not offering supplements, nutritional interventions, acupuncture, aromatherapy or transcranial stimulation to treat cognitive symptoms in people with MCI. Further research was recommended on the effect of serious games, virtual reality, and interventions for cognitive and linguistic abilities.

### **Non-cognitive symptoms, intercurrent illnesses and palliative care**

#### *Interventions for treating non-cognitive symptoms in people with dementia*

Behavioural and Psychological Symptoms of Dementia (BPSD) are linked to negative outcomes such as faster cognitive decline, greater dependency, and higher risks of institutionalisation and mortality [46, 47]. BPSD also affects the well-being and QoL of PwD and their caregivers [48], making management challenging for healthcare professionals, who require specific training. Clinical assessment should aim to identify medical, psychological and environmental triggers. Non-pharmacological treatments are widely considered as a first-line intervention for non-cognitive symptoms, though psychotropic agents are often used despite their being off-label and their uncertain risk–benefit profile [49, 50].

Two RQs focused on RCTs assessing the safety and efficacy of pharmacological and non-pharmacological treatments for non-cognitive symptoms in PwD. Overall, 143 studies were included in the literature review, of which 72 on pharmacological interventions (16 from the literature update) and 71 on non-pharmacological interventions (34 from the literature update). Evidence summaries and therapeutic indications for pharmacological interventions are provided in [Supplementary Tables S6 and S7](#).

The WG underlined that psychotropic agents should be prescribed with caution in PwD, carefully considering the balance between potential benefits and the risk for adverse event. Available evidence did not support the use of antidepressants for the treatment of mild to moderate depressive disorders in people with mild to moderate dementia. Therefore, the WG agreed to recommend not offering antidepressants in people with mild to moderate dementia, if not indicated for a pre-existing severe mental health condition. A specific recommendation against offering bupropion was included due to its risk–benefit profile.

When considering antipsychotics, based on their risk–benefit profile, the WG agreed to recommend limiting their use in people at risk of harm themselves or experiencing agitation, hallucinations or delusions causing them severe distress. When needed, antipsychotics should be used at the lowest effective dose for the shortest possible time, reassessing people every 4 weeks. The option of discontinuing treatment should be considered in case the person is not getting a clear ongoing benefit and should be discussed with PwD and their caregivers. Antipsychotics may worsen motor symptoms in PDD and DLB, potentially causing severe sensitivity reactions.

The WG agreed to recommend starting non-pharmacological or pharmacological treatment, and conducting structured assessment to explore possible causes of distress. Psychosocial and environmental interventions should be offered as an initial and ongoing approach to reduce distress in PwD. Healthcare professionals should receive appropriate training for the management of BPSDs. PwD experiencing agitation or aggression should be offered personalised activities promoting engagement and pleasure. The WG also recommended considering interventions based on therapeutic gardens, music therapy, the use of interactive companion robots and integrated approaches for sleep hygiene. Evidence on the impact of physical activity on agitation, depression or apathy was promising though insufficient to support a recommendation, thus further research was recommended on this topic.

### *Assessing and treating intercurrent illness in people living with dementia*

Managing comorbidities in PwD is highly complex [51, 52], with multimorbidity and frailty associated with greater disability, mortality and reduced QoL [53]. Comorbidities complicate care and demand better coordination in managing the different conditions. Frail individuals are at higher

risk of acute conditions including pain, falls, delirium and urinary tract infections, which can affect their global health and QoL, and increase caregiver burden [54, 55]. These conditions, whose onset is unrelated to the presence of dementia, were defined as intercurrent illnesses and were the object of two specific RQs investigating available methods for assessing and treating intercurrent illnesses in PwD.

Overall, 36 studies were included, 9 (2 from the literature update) on the utility of specific assessment tools and 27 (four from the literature update) on specific interventions for the management of intercurrent illnesses in PwD.

Due to the nature of dementia, pain is often underdiagnosed in PwD. The WG agreed considering the use of structured tools for pain assessment and repeating assessments in PwD who appear to be in pain or show behavioural changes that may be pain related, and after pain management interventions.

For the management of the risk of falling, the WG agreed to recommend referring to standard intervention for the prevention of falls (NICE CG161), while taking into account that PwD may require additional support, and that multifactorial falls interventions may not be suitable for people with severe dementia.

### *Caring for people living with dementia who are admitted to hospital*

PwD may experience acute conditions that require hospitalisation. This RQ aimed to identify all comparative quantitative studies investigating the utility and effectiveness of different care models for PwD admitted to hospital.

Eight studies were included (three from the literature update). Studies investigated the effectiveness of care models for PwD admitted to hospital reporting information on the type of ward, its organisation and environment, the need for additional support from hospital staff and/or other professionals, the need for individual assessments, considerations on time to discharge, and the use of multidimensional assessments and protocols for medicine reconciliation and optimisation.

The WG agreed to recommend always considering the higher risk of delirium in PwD who are admitted to hospital. The WG also agreed to recommend ensuring hospitalised PwD are offered multidimensional assessment, monitoring and review of all pharmacological treatments, and reconciliation of pharmacological treatment plans, and any possible issues related to safety, considering the involvement of a pharmacist or pharmacologist. The WG also agreed to recommend considering the involvement of a multidisciplinary team to ensure personalised interventions based on a multidimensional assessment of overall health, including nutritional status.

### *Palliative care*

Dementia is a life-limiting condition often co-existing with chronic diseases, requiring structured palliative care. However, international guidelines often lack detailed guidance for

PwD. Managing PwD can be extremely challenging due to difficulties in assessing pain and distress, the impossibility of predicting the moment of death, and the difficulty in establishing whether and when PwD have the ability to decide for themselves on palliative and end-of-life care [56]. Establishing when to begin palliative care is crucial, yet dementia's unpredictable trajectory complicates defining an end-of-life phase, leading to inconsistencies in the quality of care and in the access to palliative care.

The literature review included 12 quantitative studies (9 from the literature update) and 9 qualitative studies (one from the literature update). The WG agree to recommend offering flexible, needs-based palliative care from diagnosis, considering individual preferences, personal identity and involving caregivers in decision-making by providing appropriate support.

The WG agree to recommend, when considering hospitalisation for people with severe dementia, performing an assessment balancing their current medical needs with the potential additional harms that could come with being in hospital (e.g. disorientation, delirium, increased mortality). The WG also agree to recommend encouraging and supporting PwD to eat and drink accounting for their nutritional needs, and considering involving a speech therapist in case of concerns about a person's safety when eating and drinking. They also recommended not routinely using enteral feeding in people with severe dementia, unless indicated for a potentially reversible comorbidity.

The WG agreed recommending using anticipatory healthcare planning for PwD approaching the end of life, involving family and caregivers as far as possible, and using the principles of best-interest decision-making when PwD cannot make decisions on their own. A research recommendation was included to investigate the effectiveness of general and specialist palliative care models for advanced dementia and support interventions for healthcare professionals.

## **Commentary**

This is the first Italian guideline developed by a National public entity providing evidence-based recommendations on the diagnosis and treatment of dementia and mild cognitive impairment that are adapted to the context of the Italian National Healthcare System.

Based on the methodology adopted by the SNLG, the guideline WG included several stakeholders (e.g. clinicians, methodologists, researchers and caregivers). Despite being a challenging process, the coordination was constantly aimed at ensuring the active involvement of all participants, as well as the harmonisation and consideration of all different perspectives.

Based on a preliminary scoping review, the WG agreed to adapt and adopt the NG97. The NG97 was developed as part of the 2020 Prime Minister's Challenge on Dementia, aimed at improving care and research on dementia, and setting out the steps to enhance the quality of care for PwD and their

caregivers [57]. The experience leading to the development of NG97 was therefore similar to the IFAD in Italy. The MoH, in fact, approved a first public health response to dementia in 2014 by establishing the first National Dementia Plan [58]. In 2018, the Strategic Committee of the SNLG identified dementia as a priority topic for the development of a guideline, which subsequently became one of the IFAD's strategic objectives [59].

The WG agreed to adapt and adopt the entire content of the NG97. After extensive discussion, they also agreed to include the diagnosis and management of MCI within the scope of the guideline. A recent surveillance conducted by NICE assessed the potential inclusion of MCI in the NG97, but concluded that, due to the complexity and heterogeneity of MCI, existing evidence was not strong enough to support evidence-based recommendations [60]. However, the WG, considering the variability in the management of people with MCI in Italy, agreed to include 10 RQs on the diagnosis and management of MCI.

The WG further discussed the inclusion of a RQ addressing the efficacy and safety of biological drugs for the treatment of people with AD. The NG97 did not include this topic, as NICE is currently conducting two health technology assessments on donanemab and lecanemab [61]. The WG, based on the potential impact that the approval of these medications by regulatory agencies could have on PwD, their families and the healthcare system, agreed to include this topic as within the scope of the guideline.

This guideline, in line with NG97, considered both qualitative and quantitative evidence as a basis for the definition of clinical practice recommendations. In case of topics where evidence was limited but suggestive of potentially promising results, the same approach used in the NG97 was adopted, and specific research recommendations were issued. Based on the GRADE approach, recommendations were graded as strong or weak.

When considering the diagnostic process, the WG agreed on underlining the role of primary care physicians in appropriately referring people with a suspect of dementia to specialist services. The decision to refer individuals with a suspect of dementia to a specialist should be based on a comprehensive evaluation, which should include cognitive tests that are both accurate and require a short amount of time to be administered. The initial assessment in primary care should also be aimed at ruling out potentially reversible causes of cognitive decline based on a complete examination including the prescription of blood and urine tests and neuroimaging (i.e. brain CT and/or MRI). Compared to the NG97, which did not include neuroimaging among the initial evaluation in primary care, the WG agreed to include these tests as they could help in the timely identification of specific conditions (e.g. vascular disorders, neoplasms) which may cause cognitive disorders and require timely intervention by a specialist team in a secondary care setting.

As for the diagnostic process of dementia and MCI in the specialist setting, the WG agreed to underline that the diagnosis is primarily clinical, while the use of biomarkers

is either considered to support the differential diagnosis of dementia subtypes or for research purposes. Research on the use of biomarkers in the diagnostic process of dementia and its subtypes is extremely wide. The WG agreed to include most biomarkers within the scope of the review. However, despite the promising results, they agreed not to include blood-based markers (BBMs). BBMs are currently being extensively investigated as, being inexpensive and minimally invasive, they have the potential for being widely implemented in clinical practice [62, 63]. Using a routine blood test has the potential to accelerate the diagnostic process, facilitating access to new treatment options, enrolment in clinical trials and access to advanced care planning. However, evidence is still preliminary and their use of BBMs remains limited to research purposes [64] to understand whether they can replace more invasive and expensive examinations (i.e. CSF, PET) in identifying people with an uncertain diagnosis who need further evaluation [63, 64].

The process of diagnosing dementia should be considered as also including the phase immediately preceding diagnosis, the communication of the diagnosis and the phase immediately after diagnosis. These phases are crucial to define adequate supportive interventions. In line with NG97, results from the literature review reported no significant results for any of the considered post-diagnostic interventions (i.e. psychosocial support or self-management). Despite the lack of evidence, the WG emphasised the importance of supporting PwD and their carers throughout the entire diagnostic process. As a result, the WG agreed to include a recommendation to consider peri- and post-diagnostic counselling for people who receive a diagnosis of dementia and their caregivers, based on the relevance of ensuring continuity of care when progressing from the peri-diagnostic phase to the subsequent phases, which may require more general supportive services.

When considering caregivers, the WG agreed to highlight their essential role throughout all the phases of the disease. The amount of time they dedicate to caregiving allows them to acquire an intimate knowledge of people they care for, and to be able to provide useful information to facilitate treatment or choosing aids. The relevant burden of caring and supporting people needing assistance can lead caregivers to being exposed to different conditions that could trigger the onset of some pathological conditions. Therefore, preventing negative physical, psychological and social outcomes in caregivers is extremely relevant. Caregivers' burden and quality of life are extremely relevant factors, which should be monitored to allow timely interventions to reduce burden and ensure to maintain the best quality of life, thus facilitating preventing actions.

The burden of care can be a relevant issue also for health and social care professionals involved in caring for PwD, especially when considering the management of BPSDs. This could be managed by adequately training staff in all aspects that could reduce challenging aspects of the care process and the resulting burden. Available evidence on staff training mostly focused on interventions for nursing home staff on

the management of BPSDs or challenging behaviours of people with moderate to severe dementia. This specificity could lead to underestimate the effect of this type of interventions in a more general population. Further research should encompass personnel, from a wider variety of care settings, working with people with different stages of dementia to provide a more comprehensive understanding of the impact of staff training interventions.

An extensive chapter of the guideline is dedicated to the pharmacological management of dementia, including the new biological drugs that are still under investigation. AChEIs and memantine are currently the only approved drugs for the treatment of cognitive symptoms in people with AD. The WG underlined that the prescription and management of pharmacological treatments in people with AD should be part of a structured care plan that begins at the time of diagnosis and considers all pre-existing conditions and intercurrent illnesses throughout the disease. This section of the guideline updated the HTA developed by NICE [65] in and referenced in the NG97, and adapted the resulting recommendations on the use of cognitive enhancing medications (i.e. AChEIs and memantine) to the Italian regulations that require anti-dementia drugs to be prescribed by experts within a specialist setting. When considering MCI, evidence did not support the use of AChEIs and memantine in this population, and further research was recommended.

Research on new medications and potentially disease-modifying treatments for dementia is constantly evolving. When considering biological drugs, available evidence on this class of drugs led to variable regulatory decision worldwide. The recommendation included in the LG DEM not to offer monoclonal antibodies against the different forms of amyloid- $\beta$  as a treatment for AD or MCI is in line with the recent refusal of marketing authorisation of lecanemab by the European Medicine Agency [66] and NICE pronouncement to rule out the drug being available on the UK NHS [67]. However, some other countries (e.g. Japan, USA) agreed on licencing these drugs [68, 69]. On this basis and based on the growing research on these drugs and other new molecules, the WG agreed that in case of new breakthrough evidence the LG DEM will be updated.

In line with the NG97, an extensive section of the LG was dedicated to non-pharmacological approaches for PwD and people with MCI. Available evidence on this type of interventions was significantly heterogeneous in terms of type of intervention, setting, way of implementation, and in the application of techniques and strategies. The effectiveness of these interventions can also be affected by the unique training and expertise of the individual professional administering it, and by the individual needs and goals of PwD, resulting in different interpretations of intervention protocols. These differences, along with the heterogeneity of settings, the use of different definitions to describe similar interventions and the differences in the professional figures involved in administering them, affect the reliability, generalisability and reproducibility of results. Adequately considering the organisational models where these interventions

are meant to be implemented is crucial, as the inclusion or exclusion of specific professions from the interdisciplinary teams can affect the treatment outcomes.

Non-pharmacological approaches are not only essential when managing cognitive symptoms, but are also recommended as the first-line approach to manage non-cognitive symptoms including BPSDs and challenging behaviours. In line with the NG97, the WG agreed that the initial strategy to manage non-cognitive symptoms should start from conducting a structured assessment to explore possible reasons for distress and check for and address its causes. The WG also underlined the importance of ensuring PwD have access to a variety of non-pharmacological interventions irrespective of their need to undergo, even for a limited time, pharmacological treatment for specific non-cognitive symptoms and the need to provide staff with adequate training to manage BPSDs.

Due to the nature of dementia, ensuring the participation and adequate involvement of PwD in making decisions about their present and future care can be extremely difficult. This guideline, in line with NG97, extensively addressed the potential barriers and facilitators to involving PwD and their carers in decision-making, discussing access to advance care planning and palliative care. Most PwD and their carers would prefer to receive information in advance, preferably immediately after diagnosis. As dementia is a complex disease and its progression can vary from person to person, information provided by healthcare professionals should be tailored to each individual circumstance and to each subgroup of PwD, including younger people with YOD. Considering the progressive nature of dementia and its impact on the capacity of the person to be involved in decision-making, healthcare professionals should discuss immediately both advance statements and advance directives with PwD and their caregivers. They should also offer people the chance to review and change any advance statements and decisions they have made, to ensure they do not feel discouraged from planning their future care, due to concerns about being unable to change their decisions in the future. As mentioned, due to the nature of dementia, PwD and their caregivers should be offered the opportunity to discuss palliative care starting from diagnosis. Palliative care for PwD should be person centred, accounting for all individual aspects, including all physical, psychological, social and spiritual aspects of each person's life. Informal caregivers, due to their crucial role, should be involved in decision-making throughout the entire course of the disease, and should be provided adequate support, especially in extremely delicate phases such as transferring PwD between different care settings or in case of PwD approaching the end of life. Health and social care professionals that are involved in managing palliative and end-of-life care should be adequately trained and provided with appropriate tools and the knowledge required to implement them. The whole care process for people with dementia, including the end of life, should be based on appropriate and adequate care models that should ensure, throughout all of their stages, preserving people's dignity as a substantial and inalienable value.

## Conclusions

The effectiveness of any guideline in improving the quality of care relies on the dissemination and implementation of its recommendations. The Dementia Observatory of the ISS, within the 2024–2026 IFAD, will develop a structured strategy for implementing and disseminating the Italian guideline on dementia and MCI. This activity will be based on a significant organisational strategy and on the collaboration between the ISS and several local entities. The implementation strategy will be based on the approach adopted by NICE (67). A toolkit will be created comprising some structured tools that are under development, and some already available tools, including an interactive care pathway available in both Italian and English, offering guidance on dementia care, and leaflet dedicated to family members and caregivers of PwD. At the end of the process, a handbook will be developed reporting the methodology for the definition of strategies for the implementation and dissemination of national guidelines. The handbook will include the final version of toolkit to allow for a standardised data collection, management and analysis.

The guideline will be updated by January 2027. In case of significant advancements in the diagnosis and management of dementia or MCI, earlier updates will be implemented to guarantee the inclusion of the latest available evidence.

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