Diagnostic criteria for dementia

This sheet provides information about the diagnostic criteria for dementia and related conditions, and the use of biomarkers for earlier and more accurate diagnosis.

What are the diagnostic criteria?

Diagnostic criteria for dementia incorporate the scientific knowledge and technological advances gained in recent times and reflect the contemporary state of understanding regarding the detection and diagnosis of dementia and related disorders characterised by cognitive impairment.

In 2011, the National Institute on Aging and the Alzheimer's Association (NIA/AA) in the United States published new diagnostic guidelines for Alzheimer's disease. The original guidelines had not been updated for 27 years. The aim of the new guidelines was to improve current diagnosis, and establish research priorities for the future.

In 2013, the American Psychiatric Association published the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Dementia was renamed 'major neurocognitive disorder' in the DSM-5, which also recognises earlier stages of cognitive decline as 'mild neurocognitive disorder'. The aims of this reclassification include reducing stigma associated with dementia and bringing the diagnostic guidelines into line with current clinical practice.

The newer NIA/AA guidelines and the DSM-5 revisions have many similarities; however, the NIA/AA guidelines have a primary focus on future research directions, while the DSM-5 focuses exclusively on clinical diagnosis. Further, the NIA/AA guidelines are for diagnosis of Alzheimer's disease only, while the DSM-5 includes diagnostic criteria for various causes of cognitive impairment, or forms of dementia.

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Another major diagnostic guideline is the International Classification of Diseases (ICD) published by the World Health Organisation. ICD-11 was released in June 2018. ICD-11 adopted the terminology 'neurodevelopmental disorders' and very similar diagnostic criteria to those of the DSM-5.

The introduction of 'neurocognitive disorders' in these documents does not mean that 'dementia' is not an appropriate term to use. In fact, the DSM-5 includes 'or dementia' in parentheses when referring to major neurocognitive disorder, in recognition of dementia's history and familiarity.

Diagnostic and Statistical Manual of Mental Disorders – fifth edition

Dementia was named major neurocognitive disorder (NCD) in the DSM-5. However, the term dementia may still be used as an acceptable alternative. The two terms are essentially different labels for the same condition; major NCD is equivalent to dementia. The DSM-5 also recognises a less severe level of cognitive impairment, mild NCD, which now provides a diagnosis for less disabling syndromes that may nonetheless be causing concern and could benefit from treatment. Mild NCD is equivalent to mild cognitive impairment (MCI) and to prodromal dementia, again different labels for the same condition. DSM-5 provides diagnostic criteria for both major NCD and mild NCD, followed by diagnostic criteria for the different subtypes or causes of NCD. Although the threshold between mild NCD and major NCD is inherently arbitrary, the two levels of impairment are considered separately for consistency with other fields of medicine and to capture the care needs of people living with NCD.

NCDs are characterised by cognitive impairment as the most prominent and defining feature of the condition. The term 'cognitive' broadly refers to thinking and related processes, and the term 'neurocognitive' was applied to these disorders to emphasise that brain disease and disrupted brain function lead to symptoms, and that, in most cases, such disruption can be reliably measured. NCDs are also characterised by acquired deficits, which represent a decline from previous functioning, rather than neurodevelopmental deficits present from birth or early life.

A listing of cognitive domains is also provided in DSM-5, to guide clinicians in establishing the presence of NCD, distinguishing between the major and mild levels of impairment, and differentiating among subtypes. The DSM-5 details six cognitive domains which may be affected in both mild and major NCD:

- **Complex attention**, which includes sustained attention, divided attention, selective attention and information processing speed

- **Executive function**, which includes planning, decision making, working memory, responding to feedback, inhibition and mental flexibility

- **Learning and memory**, which includes free recall, cued recall, recognition memory, semantic and autobiographical long term memory, and implicit learning

- **Language**, which includes object naming, word finding, fluency, grammar and syntax, and receptive language

- **Perceptual-motor function**, which includes visual perception, visuoconstructional reasoning and perceptual-motor coordination

- **Social cognition**, which includes recognition of emotions, theory of mind and insight

Mild neurocognitive disorder

Mild NCD is a diagnostic category in the DSM-5, added to recognise the substantial clinical needs of individuals living with this disorder, which might also be termed mild cognitive impairment (MCI) or prodromal dementia. Diagnosis of MCI has become increasingly common in clinical practice, partly because people with cognitive decline are seeking assessment and treatment earlier, before a diagnosis of dementia is justified. The move to diagnose NCDs as early as possible also emerged from the recognition of a long predementia stage in neurodegenerative diseases such as Alzheimer's, improvements in early diagnosis, and the increasing emphasis on early intervention to prevent or postpone dementia. Importantly, mild NCD is not always a precursor of major NCD, and the diagnosis does not require further decline. There may be continued decline, as in neurodegenerative diseases, or the impairment may be static or even improve, as in traumatic brain injury.

Diagnosis of mild NCD requires evidence of modest cognitive decline from a previous level of performance in one or more of the cognitive domains outlined above. These cognitive deficits must be insufficient to interfere with independence in daily activities, although greater effort and compensatory strategies may be required to maintain the level of independence. Further, the cognitive deficits must not be due to another mental disorder (such as depression).

Major neurocognitive disorder

Diagnosis of major NCD requires evidence of significant cognitive decline from a previous level of performance in one or more of the cognitive domains outlined above. Additionally, the cognitive deficits must be sufficient to interfere with independence in activities of daily living. The cognitive deficits must not be attributable to another mental disorder. The criterion of maintenance or loss of independent functioning represents the key distinction between mild and major NCD.

The introduction of major NCD as an alternative term for dementia was prompted by a desire to address the limitations of and the stigma associated with the term 'dementia'. Dementia is most commonly used to refer to older people, has become synonymous with Alzheimer's disease and memory loss, and has negative connotations in part due to its literal meaning 'without mind'. It is hoped that major NCD more accurately captures the many different causes and manifestations of significant cognitive impairment that can affect people at any age.

Subtypes of neurocognitive disorders

Diagnosing mild or major NCD should be followed by an examination of potential causes so that a subtype can be assigned. In many people with NCDs, there is evidence of a causative disorder, such as Huntington's disease or HIV infection. In others, the cognitive symptoms emerge first and progression provides evidence of a causative disorder such as Alzheimer's disease or Lewy body disease. In many cases, especially for older people, there are multiple causative factors, and the diagnosis should recognise this. Subtypes of minor and major NCD in the DSM-5 include:

- Major or Mild Neurocognitive Disorder Due to Alzheimer's Disease

- Major or Mild Frontotemporal Neurocognitive Disorder

- Major or Mild Neurocognitive Disorder With Lewy Bodies

- Major or Mild Vascular Neurocognitive Disorder

- Major or Mild Neurocognitive Disorder Due to Traumatic Brain Injury

- Substance/Medication-Induced Major or Mild Neurocognitive Disorder

- Major or Mild Neurocognitive Disorder Due to HIV Infection

- Major or Mild Neurocognitive Disorder Due to Prion Disease

- Major or Mild Neurocognitive Disorder Due to Parkinson's Disease

- Major or Mild Neurocognitive Disorder Due to Huntington's Disease

- Major or Mild Neurocognitive Disorder Due to Another Medical Condition

- Major or Mild Neurocognitive Disorder Due to Multiple Etiologies

- Unspecified Neurocognitive Disorder

One key element of all sub-types is the removal of the requirement for memory impairment as a criterion for all dementias.

There is an increasing understanding that other cognitive domains, such as language or attention, may be impaired first, or exclusively, in other NCDs, depending on which parts of the brain are affected by the underlying disease.

The National Institute on Aging/Alzheimer's Association diagnostic guidelines for Alzheimer's disease

The NIA/AA diagnostic guidelines for Alzheimer's disease (AD) were designed to reflect research which indicates that AD begins affecting the brain many years before problems in memory, thinking and learning are noticeable. This means that if we can develop ways to detect and treat the disease in the pre-symptomatic stage, we can prevent symptoms occurring, i.e. prevent dementia.

Three phases of AD progression are outlined – preclinical AD (where the disease is present in the brain but there are no symptoms), mild cognitive impairment due to AD (also called prodromal AD), and dementia caused by AD.

The guidelines include tests that measure biological changes in the brain associated with AD (known as biomarkers). Two biomarker categories are highlighted; biomarkers which indicate the level of beta-amyloid accumulation in the brain, and biomarkers which indicate injured or degenerating nerve cells in the brain.

Dementia caused by Alzheimer's disease

Dementia caused by AD involves memory, thinking and behavioural symptoms that impair a person's ability to function in daily life.

Dementia caused by AD can be further classified as:

1. **Probable Alzheimer's disease dementia**, to be diagnosed when the person meets all the core clinical criteria

2. **Possible Alzheimer's disease dementia**, to be diagnosed when there is an atypical or mixed presentation

3. **Probable or possible Alzheimer's disease dementia with evidence of the Alzheimer's disease pathological process**, to be diagnosed when there is biomarker evidence to increase the certainty that the dementia is due to Alzheimer's disease

Mild cognitive impairment due to Alzheimer's disease

MCI due to AD involves mild changes in memory or thinking abilities, which are noticeable to the person and/or to others, but are not severe enough to significantly compromise activities of daily living.

MCI can be further classified as:

1. **MCI – core clinical criteria**, to be diagnosed when the person meets all the core clinical criteria

2. **MCI due to Alzheimer's disease – intermediate likelihood**, to be diagnosed when the person meets all the core clinical criteria in addition to some biomarker evidence in one of the two biomarker categories (beta-amyloid accumulation or neurodegeneration)

3. **MCI due to Alzheimer's disease – high likelihood**, to be diagnosed when the person meets all the core clinical criteria in addition to biomarker evidence in both of the categories

4. **MCI – unlikely due to Alzheimer's disease**, to be diagnosed when biomarker tests indicate that there is the lowest likelihood of underlying AD pathology

Preclinical Alzheimer's disease

Preclinical AD involves the detection of changes in biomarkers that indicate the very earliest signs of AD in the brain, before any cognitive or behavioural symptoms are noticeable.

A three stage framework for preclinical AD includes:

Stage 1 – when there is biomarker evidence of beta-amyloid accumulation in the brain, but no biomarker evidence of degenerating nerve cells in the brain and no cognitive or behavioural symptoms

Stage 2 – when there is biomarker evidence of both beta-amyloid accumulation in the brain and degeneration of nerve cells in the brain, but no cognitive or behavioural symptoms

Stage 3 – when there is biomarker evidence of both beta-amyloid accumulation in the brain and degeneration of nerve cells in the brain, and evidence of subtle cognitive decline

Using biomarkers for earlier diagnosis

Biological markers (biomarkers) are naturally occurring, measurable substances or conditions in the body that act as reliable predictors and indicators of a disease process. For example, blood glucose levels are a biomarker of diabetes. Experts believe that biomarkers may help to discover an easy and accurate way to detect AD and other forms of dementia before the onset of cognitive or behavioural symptoms. This is vital, as if treatments can be found that stop the disease before symptoms arise, we can effectively cure dementia.

Several promising areas of research are working toward establishing biomarkers for dementia, especially AD. These include brain imaging, cerebrospinal fluid proteins and substances in blood. While recent research has provided knowledge about the average progression of AD and the subsequent changes in biomarkers, more work is needed to define how this knowledge can be applied to individuals for clinical diagnosis.

Brain imaging

Neuroimaging is among the most promising areas of research focused on earlier diagnosis of AD. It is used in current clinical practice to rule out other causes of cognitive impairment (such as a brain tumour) and sometimes to identify characteristic changes that suggest AD or vascular disease or another cause of dementia.

Structural brain imaging provides information about the shape, position or volume of brain tissue. Structural techniques include magnetic resonance imaging (MRI) and computerised tomography (CT). MRI provides much better resolution than CT, to see the brain structure in more detail, and is likely to be more widely used. Structural imaging studies have shown that the brains of people with AD shrink significantly as the disease progresses. Research has also shown that shrinkage in specific brain regions such as the hippocampus may be an early sign of AD. Patterns of shrinkage in other brain regions may help identify other forms of dementia. For example, frontotemporal dementia is often associated with reduced volume in the frontal and/or temporal lobes. However, more work is needed to standardise values for brain volume that would establish the significance of a specific amount of shrinkage for any individual person at a single point in time.

Functional brain imaging reveals how well cells in various brain regions are working by showing how actively the cells use sugar or oxygen. Functional techniques include positron emission tomography (PET) and functional MRI (fMRI). The technique currently most commonly used in dementia is fluorodeoxyglucose (FDG)-PET, which measures the use of glucose by the brain. FDG-PET studies indicate that AD is often associated with reduced use of glucose in brain areas important for memory, learning and problem solving. Other forms of dementia may be associated with patterns of reduced glucose metabolism in other brain regions. As with the shrinkage detected by structural imaging, more work is needed to establish firm criteria for using these general patterns of reduced activity for diagnosis in an individual.

Molecular brain imaging uses highly targeted radiotracers to detect cellular or chemical changes linked to specific diseases. Molecular imaging technologies include PET, fMRI and single photon emission computed tomography (SPECT).

Molecular imaging technologies are among the most active areas of research aimed at finding new approaches to diagnose AD in its earliest stages. These strategies may detect biological clues indicating AD is under way before the disease changes the brain's structure or function, or takes an irreversible toll on memory, thinking and reasoning. Molecular imaging also may offer a new strategy to assess the effectiveness of next generation, disease modifying treatments.

Radiotracers that bind to beta-amyloid in the brain have been developed for use with PET scans, so that for the first time the presence of AD pathology can be detected in the living brain. Pittsburgh compound B (PIB) was the first radiotracer capable of highlighting deposits of beta-amyloid (one pathological hallmark of AD) during a PET scan. It has been used widely in research and been instrumental in recent gains in knowledge about the development and progression of AD. However, its short half-life makes it impractical for widespread use. Other similar radiotracers have been developed that remain stable significantly longer than PIB, potentially increasing their usefulness outside research settings. Three such compounds have been approved by the Food and Drug Administration in the United States for evaluating the presence or absence of beta-amyloid plaques in people being clinically assessed for AD. In Australia, amyloid imaging is currently only available as part of a research study, but it will likely become more widely used in the clinical setting in the future.

Other radiotracers that bind to different chemicals in the brain may be used to assist in the diagnosis of other types of dementia. For example, PET scans that detect receptors for dopamine may be used to show the reductions in this chemical in Lewy body disease.

Cerebrospinal fluid proteins
Cerebrospinal fluid (CSF) is a clear fluid that bathes and cushions the brain and spinal cord. Adults have about half a litre (one pint) of CSF, which doctors can sample through a procedure called a lumbar puncture, or spinal tap.

Research suggests that AD causes changes in CSF levels of tau and beta-amyloid, two proteins that form abnormal brain deposits in this disease. In the early stages of AD, beta-amyloid levels in the CSF fall, as less of the protein is cleared from the brain and instead gets stuck in the plaques that characterise AD. Levels of phosphorylated tau in the CSF rise, as more of this form of tau is produced in the brain and forms the tangles that are another characteristic of AD.

More work is needed to standardise values for CSF protein levels that would establish the significance of specific levels for any individual person at a single point in time. Nonetheless, this technique can detect early changes indicating AD is under way before any symptoms are noticeable, and is less expensive than amyloid brain imaging.

Ongoing research is also investigating whether other CSF biomarkers or combinations may be useful for the diagnosis of AD and other neurocognitive disorders. Molecules associated with brain cell degeneration and inflammation in the brain are being investigated for characteristic changes in the CSF in different types of dementia. Tau is also implicated in other neurocognitive disorders including frontotemporal dementia, and research is investigating whether CSF biomarkers can help detect the earliest signs of this condition.

Blood biomarkers

Researchers are also investigating whether preclinical AD causes consistent, measurable changes in urine or blood levels of tau, beta-amyloid or other protein biomarkers. Levels of the candidate proteins tend to be less stable in blood than they are in CSF, so developing a blood test for AD is proving difficult. Other substances in the blood that might change with progression of AD are also being investigated, with some promising early results. Research is ongoing, as there are many obvious advantages to being able to provide a simple blood test for diagnosis.

Further Information

Much of the information provided in this help sheet is taken from the following sources. More detailed information about changes to diagnostic criteria and using biomarkers for earlier diagnosis is also available at the websites.

American Psychiatric Association. DSM-5 Development. **http://www.dsm5.org/**

American Psychiatric Association. DSM-5. **http://www.psychiatry.org/dsm5**

Perminder S. Sachdev et al. Classifying neurocognitive disorders: the DSM 5 approach. **Nature Reviews Neurology** (2014), 10:634-642. doi:10.1038/nrneurol.2014.181

Alzheimer's Association. **New diagnostic criteria and guidelines for Alzheimer's disease. http://www.alz. org/research/diagnostic_criteria/**

Alzheimer's Association. **Alzheimer's and dementia testing for earlier diagnosis. http://www.alz.org/ research/science/earlier_alzheimers_diagnosis.asp**

Articles detailing the National Institute on Aging/Alzheimer's Association diagnostic guidelines for Alzheimer's disease were published in **Alzheimer's and Dementia**, Volume 7, Issue 3, May 2011, and can be downloaded using the links below.

Clifford R. Jack Jr. et al. 'Introduction to the recommendations from the National Institute on Aging – Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease.' **Alzheimer's & Dementia** (2011), 7(3):257-262.

Guy M. McKhann et al. 'The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging – Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease.' **Alzheimer's & Dementia** (2011), 7(3):263-269.

Marilyn S. Albert et al. 'The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging – Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease.' **Alzheimer's & Dementia** (2011), 7(3):270-279.

Reisa A. Sperling et al. 'Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging – Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease.' **Alzheimer's & Dementia** (2011), 7(3):280-292.

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Further Information

Dementia Australia offers support, information, education and counselling. Contact the National Dementia Helpline on **1800 100 500**, or visit our website at **dementia.org.au**

For language assistance phone the Translating and Interpreting Service on **131 450**