

Diagnosing and managing mild cognitive impairment

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What are the common underlying causes?

How should patients be assessed?

Which patients should be referred?



THERE HAS BEEN A RAPID RISE IN THE NUMBER OF PEOPLE DIAGNOSED WITH DEMENTIA IN ENGLAND

from 232,000 in 2008 to 850,000 in 2014.¹ The ageing population and improved public awareness of dementia are likely to be contributing factors to this increase.

A historical lack of consensus on diagnostic criteria for mild cognitive impairment has made estimates of prevalence and trends in diagnosis difficult to estimate. Currently it is estimated that the prevalence of mild cognitive impairment in adults aged 65 and over is 10-20%.² It is likely that this figure will increase in line with the trends in dementia diagnosis.

PRESENTATION

The National Dementia Strategy, published in 2009,³ sparked research into public understanding of dementia and campaigns to raise awareness of the importance of early diagnosis, such as the Alzheimer's Society campaign 'Worried about your memory?'⁴

Many of those who present with memory problems in primary care may be the worried well but, given the limitations of thorough cognitive

examination in short appointments, there should be a low threshold for referral to a memory clinic for those with subjective cognitive impairment. Relatives may suspect a person has cognitive impairment and encourage them to see their GP, or a GP may suspect a patient has cognitive impairment during a review for an unrelated complaint.

This may be a difficult consultation for the GP. A survey in 2005 found that 71% of GPs across Europe felt uncomfortable discussing the possibility of dementia with a patient for the first time.⁵

At present, routine screening for mild cognitive impairment by cognitive assessment is not justified as screening instruments suitable for use in a primary care setting are not adequately validated and predictive values are not known.⁶

COMMON UNDERLYING CAUSES

In some cases, mild cognitive impairment may be a prodrome for dementia (see below), and may be caused by any of the dementia pathology subtypes e.g. Alzheimer's disease, vascular dementia, dementia with Lewy bodies/Parkinson's disease dementia and frontotemporal lobe dementia.

The relationship between depression in the elderly and mild cognitive impairment is difficult to tease out as they are frequently comorbid conditions and both have been found to be independent risk factors for subsequent dementia.⁷

Other causes of mild cognitive impairment may be reversible and are thus important to consider. Physical comorbidities such as deranged thyroid function, and B12/folate deficiency can contribute to a picture of cognitive impairment and can be easily treated.

Similarly, concerns about a patient's cognitive function should trigger a medication review with the benefits and potential risks of each medication reviewed. In particular, medications with anticholinergic effects, sedative medication and some hormone replacement therapies are associated with cognitive impairment.²

Also, overzealous treatment of hypertension and hyperglycaemia leading to hypotension and hypoglycaemia respectively have been correlated with cognitive decline.²

A diagnosis of mild cognitive impairment may be an opportunity to optimise cardiovascular risk factors. There is an increased incidence of mild

cognitive impairment in those with raised vascular risk factors⁸ and controlling the risk factors may reduce the risk of further vascular damage to the brain, and hence slow the rate of cognitive decline.

‘There is an increased incidence of mild cognitive impairment in those with raised vascular risk factors ...

The relationship between delirium and mild cognitive impairment is similarly complex. A chronic delirium may present with mild cognitive impairment, but it is likely that other features would be evident, such as a relatively sudden onset and fluctuating course, clouded consciousness, affective symptoms, and an underlying causative disease process. However, it is possible that an episode of delirium may also expose an underlying cognitive impairment and that the patient does not recover full cognitive function even when the delirium has fully resolved.⁹

DEMENTIA RISK

People with mild cognitive impairment are at higher risk of developing dementia: about 10% convert to dementia each year, compared with 1-2% of the general elderly population.¹⁰

There are different types of mild cognitive impairment, defined by the number of affected cognitive domains (single domain vs multidomain) and the presence or absence of memory impairment (amnesic vs non-amnesic).^{10,11} Amnesic mild cognitive impairment is associated with progression to Alzheimer’s disease, while patients with non-amnesic mild cognitive impairment more often develop dementias that are not related to Alzheimer’s disease such as vascular, frontotemporal or dementia with Lewy bodies.¹⁰

A recent study of 357 patients in primary care found that patients were at higher risk of progressing from mild cognitive impairment to dementia if they had symptoms of depression, impairment in more than one cognitive domain, more severe cognitive impairment, or were older.¹²

The result on a test of episodic memory

was the best predictor for differentiating between remittent and progressive mild cognitive impairment.¹²

Other studies have identified additional risk factors such as the presence of the ApoE4 allele, lower educational level, vascular risk factors (e.g. diabetes and hypertension), vitamin D deficiency, sleep disorders and prior critical illness.²

Biomarkers have been used to predict progression, but only in research studies; they are not recommended for routine clinical use.¹¹ Biomarkers for Alzheimer’s disease include certain neuroimaging features and CSF markers, see table 1, below.¹¹ Further research is needed before these biomarkers can be used in routine practice, but the aim is that eventually they will guide clinical care for patients with mild cognitive impairment.¹³

... and controlling the risk factors may reduce the risk of further vascular damage to the brain, and hence slow the rate of cognitive decline’

ASSESSMENT

NICE recommends that all patients with suspected cognitive impairment should undergo a comprehensive assessment, including history, cognitive examination, mental state, physical (including neurological) examination, medication review and laboratory testing.¹⁴ The aim is to identify potentially reversible causes of

cognitive impairment such as depression, B12 deficiency or medication side effects.

Structural neuroimaging to exclude other cerebral pathologies and to help establish the diagnosis subtype is also recommended, with magnetic resonance imaging (MRI) being the preferred modality because of its higher sensitivity.¹⁴

Cognitive function

First, it is important to obtain a history of cognitive changes over time, as well as information about the onset and nature of cognitive symptoms, confirmed by a reliable informant, if available, see table 2, opposite. The history also provides information that can help to infer the likely primary aetiology.

A progressive memory decline is suggestive of Alzheimer’s type pathology, multiple vascular risk factors point towards a vascular aetiology, while a fluctuating course, visual hallucinations, parkinsonism and REM-sleep behaviour disorder are associated with Lewy body pathology.

To confirm the diagnosis objective evidence of cognitive impairment is required. However, there are no specific neuropsychological tests for patients with mild cognitive impairment.

The neuropsychological test used should assess all cognitive domains, including executive function, visuospatial skills, attention, language, and memory. In some cases, serial testing to detect decline in an individual is required.¹⁴ On neuropsychological tests, individuals with mild cognitive impairment typically score 1-1.5 SD below the mean for their age and education, although these ranges are guidelines and not cut-off scores.¹¹ When interpreting cognitive test scores, factors that affect performance, such as

Table 1

Biomarkers for Alzheimer’s disease (adapted from Albert et al, 2011¹¹)

Biomarkers of amyloid-beta protein (Aβ) deposition

- Decreased CSF Aβ 42
- Increased cortical binding on PET amyloid imaging

Biomarkers of neuronal injury

- Increased CSF tau/phosphorylated-tau
- Hippocampal or medial temporal lobe atrophy by volumetric measures or visual rating on structural imaging
- Accelerated rate of brain atrophy
- Temporoparietal hypometabolism on FDG-PET imaging
- Temporoparietal hypoperfusion on HMPAO-SPECT imaging

PET = positron emission tomography; FDG = fluorodeoxyglucose;

HMPAO = hexamethylpropyleneamine oxime; SPECT= single photon emission tomography

Table 2

Criteria for diagnosis of mild cognitive impairment (adapted from Albert et al ¹¹)

- Self- or informant-reported cognitive decline/observed evidence of cognitive decline by clinician
- Objective cognitive impairment
- Preserved general functional abilities
- No dementia

education, prior level of functioning or psychiatric illness, should be considered.¹⁴ There are no brief screening tests available to detect mild cognitive impairment in primary care; completion time for more detailed testing excludes their routine use in primary care. Screening tests such as the Mini-Cog, the GPCOG or the AMTS are only recommended for use in primary care if dementia is suspected. (See Useful information box, p20.) Although these tests can detect dementia, they are not suitable for detecting mild cognitive impairment because of their lower sensitivity.

‘It is important to obtain a history of cognitive changes over time, as well as information about the onset and nature of cognitive symptoms’

A systematic review of the performance of screening tools for mild cognitive impairment demonstrated that only three out of eleven non-comprehensive tests (DemTect, M@T, ABCS) had sensitivities > 80%. In contrast all four comprehensive screening tests (ACE-R, MoCA, CAMCOG, CERAD) had sensitivities > 80% for detecting mild cognitive impairment among healthy volunteers.⁶ The comprehensive screening tests, however, take 15-20 minutes to complete which is unlikely to be feasible in primary care.

Activities of daily living

Standardised instruments, such as the Bristol Activities of Daily Living Scale, are available for assessment of everyday functioning. Although significant impairment in activities of daily living is not consistent with a diagnosis of mild cognitive impairment, individuals with

mild cognitive impairment often have some difficulty with complex tasks, such as the ability to deal with financial affairs.¹⁵

REFERRAL

The assessment of mild cognitive impairment is generally a task for specialists. GPs should consider referring people who show signs of mild cognitive impairment for assessment by specialist memory assessment services to aid early identification of dementia, because more than 50% of people with mild cognitive impairment later develop dementia.¹⁴ With the advent of increased targets for diagnosis of cognitive impairment,¹⁶ GPs should have a relatively low threshold for referral to secondary care memory clinics for comprehensive assessment and management.

Although the results of cognitive screening tests may be a steer towards a referral, if the patient, their family or the GP has significant concerns about cognition, then a referral is indicated. This is particularly important for people with high premorbid function, where screening tests are unlikely to detect subtle changes in cognition effectively, and the subjective experience of individuals is particularly important.

Prior to making a referral GPs should screen for depression and anxiety. Standardised rating scales (such as the PHQ9 or GAD7) may aid diagnosis, but should not be relied upon given the overlap of depression and mild cognitive impairment symptoms. If clinical assessment indicates the presence of significant symptoms, these should be treated according to the NICE guidelines prior to making a referral.

Patients with focal neurological symptoms may require referral to a neurology clinic specialising in cognitive disorders. Referral to a generic memory service may not be appropriate for all patients with cognitive concerns: people with learning disability, alcohol or substance misuse or significant head injury may need referral to specialist services.

Finally, patients must consent to referral for specialist assessment for

mild cognitive impairment. There are a number of reasons why patients may not consent to referral (or their doctors may not recommend it), for example fear of causing unnecessary anxiety in those who do not progress to dementia, and lack of effective clinical interventions for mild cognitive impairment. On the other hand, the prospect of novel therapies targeting those with minimal symptoms to prevent the development of dementia may, in future, radically change referral pathways and patterns.

MANAGEMENT

There is no specific treatment or medication for mild cognitive impairment.² Systematic reviews show that cholinesterase inhibitors are not effective in those with mild cognitive impairment, and do not reduce the risk of conversion to Alzheimer’s disease.¹⁷ There are no studies of memantine in mild cognitive impairment.

‘Patients with focal neurological symptoms may require referral to a neurology clinic specialising in cognitive disorders’

Treatment should aim at secondary prevention i.e. to reduce the risk of conversion to dementia. Evidence to support effective secondary prevention strategies is limited, but primarily includes reducing cardiovascular risk factors (particularly hypertension and diabetes) and prevention of stroke.² To optimise cognition, depression should be proactively treated and medication should be reviewed with a view to reducing or stopping medication with a high cholinergic burden.

Encouraging patients to take exercise, engage in mentally stimulating activity and social activities may also help decrease the risk of further cognitive decline.² A diagnosis of mild cognitive impairment should also prompt a discussion on longer term planning including appointing a power of attorney and addressing financial affairs. Clinicians should consider whether there are risks relating to driving or home safety, and address these where necessary.

NICE recommends that memory assessment services should offer follow-up to people with mild cognitive »

key points

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There has been a rapid rise in the number of people diagnosed with dementia in England from 232,000 in 2008 to 850,000 in 2014. Currently, it is estimated that the prevalence of mild cognitive impairment in adults aged 65 and over is 10-20%. It is likely that this figure will increase in line with trends in dementia diagnosis.

In some cases, mild cognitive impairment may be a prodrome for dementia, and may be caused by any of the dementia pathology subtypes. The relationship between depression in the elderly and mild cognitive impairment is difficult to tease out as they are frequently comorbid conditions and both have been found to be independent risk factors for subsequent dementia.

People with mild cognitive impairment are at higher risk of developing dementia: about 10% convert to dementia each year, compared with 1-2% of the general elderly population. Amnesic mild cognitive impairment is associated with progression to Alzheimer's disease, while patients with non-amnesic mild cognitive impairment more often develop dementias that are not related to Alzheimer's disease such as vascular, frontotemporal or dementia with Lewy bodies.

It is important to obtain a history of cognitive changes over time, as well as information about the onset and nature of cognitive symptoms, confirmed by a reliable informant, if available. A progressive memory decline is suggestive of Alzheimer's type pathology, multiple vascular risk factors point towards a vascular aetiology, while a fluctuating course, visual hallucinations, parkinsonism and REM-sleep behaviour disorder are associated with Lewy body pathology.

To confirm the diagnosis objective evidence of cognitive impairment is required. However, there are no specific neuropsychological tests for patients with mild cognitive impairment. On neuropsychological tests, individuals with mild cognitive impairment typically score 1-1.5 SD below the mean for their age and education, although these ranges are guidelines and not cut-off scores.

GPs should consider referring people who show signs of mild cognitive impairment for assessment by specialist memory assessment services to aid early identification of dementia, because more than 50% of people with mild cognitive impairment later develop dementia. Prior to making a referral GPs should screen for depression and anxiety. If this indicates the presence of significant symptoms, these should be treated according to the NICE guidelines prior to making a referral. There is no specific treatment for mild cognitive impairment. Treatment should aim at secondary prevention i.e. to reduce the risk of conversion to dementia. Evidence to support effective secondary prevention strategies is limited, but primarily includes reducing cardiovascular risk factors and prevention of stroke.

impairment to monitor cognitive decline and other signs of possible dementia, in order to plan care at an early stage.¹⁷ In practice, with increased service demands this may not always be possible. Indeed, given the relative lack of effective management options, regular follow-up may not change treatment approaches significantly (although it would help early detection of dementia). Where services are not able to follow up patients with mild cognitive impairment routinely, there is an additional responsibility for patients, families and GPs to consider whether there has been a decline in cognition, and whether re-referral is necessary.

GPs should have a system to ensure that patients with mild cognitive impairment are not lost to follow-up, for example through entering mild cognitive impairment Read Codes and setting up an electronic reminder to call patients for annual review. At annual review any change to symptoms or function should be assessed through a history (including collateral history), rather than relying on brief cognitive screening tests. Depression case finding is also important as one in three patients with mild cognitive impairment will be depressed.¹⁸

At diagnosis patients should be given clear information about the possibility of conversion to dementia, and should be alerted to new signs and symptoms that should prompt them to seek further assessment, such as: decline in more than one cognitive domain, change in physical function (e.g. gait change, decline in mobility and falls), or behavioural change (reduced range of activity, reduced level of function).

CONCLUSION

The prevalence of mild cognitive impairment is likely to increase over time and because of pressures on secondary care services, once a diagnosis has been established it is likely that many will be discharged to primary care unless, or until, the patient develops dementia.

It is possible that in the future improved biomarkers will facilitate identification of those at risk of developing dementia and this subgroup may be more rigorously followed up in secondary care. Although no specific treatment is indicated, a diagnosis of mild cognitive impairment may be a good impetus to optimise the patient's health from both a physical and mental health perspective and will also act as a trigger for conversations about long-term planning for financial and legal affairs.

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Useful information

Alzheimer's Society

Assessing cognition in older people: a practical toolkit for health professionals. 2015

www.alzheimers.org.uk/download/downloads/id/3475/alzheimers_society_cognitive_assessment_toolkit.pdf

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