# Depression and dementia

peression and dementia are common syndromes in older people and are usually managed by general practitioners. Comorbidity compounds the impact on patients, carers and health services.<sup>1-3</sup> Yet, the relationship between the two is complex — features overlap and each seems to be a possible risk factor, symptom or consequence of the other. Thus, identification and effective management of depression in people with dementia remains a challenging task in clinical practice.

This article provides a clinically oriented selective review of current knowledge about depression in dementia, specifically aimed at primary care practitioners. Practice pearls are provided (Box 1). Although the literature overwhelmingly focuses on Alzheimer disease, here we also discuss mild cognitive impairment and other types of dementia. Mild cognitive impairment refers to a clinical status where a patient performs below norms on cognitive tests but does not have dementia. Either the patient or someone who knows him or her well should have noticed a change from premorbid cognitive function. Statistically, people with mild cognitive impairment are at increased risk of developing dementia over time, although the individual risk can vary significantly.<sup>4</sup>

## Epidemiology

Reported rates of depression in dementia vary substantially, depending on the population sampled, means of assessment and definition of caseness. Overall, most well conducted population-based studies report prevalences between 8% and 30%.<sup>1,5,6</sup> In hospitalised patients and nursing home residents, the prevalence may be over 40%.<sup>1,5</sup> Variance in prevalence estimates is greater in studies of mild cognitive impairment.<sup>6</sup> A recent review of depression in mild cognitive impairment found median proportions of 44% in samples of hospital-based patients and 16% in community-based samples.<sup>1</sup> The limited studies investigating depression in people with vascular dementia, Lewy body dementia or dementia associated with Parkinson disease suggest that depression may be more common in these syndromes than in Alzheimer disease.<sup>1</sup>

Reported risk factors include female sex, earlier age at dementia onset,<sup>7</sup> a past history of depression or emotional problems,<sup>7,8</sup> and recent losses.<sup>8</sup> There is some

#### 1 Practice pearls

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- Consider early dementia in older people who present with new-onset depression
- Regularly assess patients with dementia for depression (eg, 6-monthly), especially if they
  are in residential care
- Consider any difficult-to-explain change in mood or behaviour as possible depression
- Exclude physical illness or medications as a cause for depressed mood
- Antidepressants may be helpful in moderate to severe depression: start low and go slow, monitor for therapeutic effect, and monitor for side effects
- Incorporate psychological and social interventions as usual practice, tailored to the cognitive abilities of the patient
- Involve and consider carers in both assessment and management, including issues of carer burden

## Summary

- Depression in people with dementia is a common presentation in primary care, but it is often missed or mismanaged.
- This problem has substantial public health implications and adversely affects the quality of life and physical health of patients and carers.
- Many aspects of diagnosis and management remain controversial.
- A high degree of suspicion and repeated assessment is essential for diagnosis.
- Medication use should be considered. Psychological and social strategies should be incorporated into most management plans.

evidence that, contrary to conventional wisdom, stage of dementia and insight into the diagnosis have little impact on depression rates.<sup>1,9</sup>

The consequences of depression in people with dementia include increased burden on patients and caregivers,<sup>10</sup> increased caregiver depression,<sup>10</sup> exacerbation of cognitive and functional decline,<sup>3,11,12</sup> more dementia-related behavioural disturbance,<sup>13</sup> poor outcomes from other medical or surgical interventions,<sup>3,14</sup> earlier admission to nursing homes, and increased mortality.<sup>12,15-17</sup>

## Relationship between dementia and depression

There is substantial academic interest in the relationship between depression and dementia, particularly regarding the direction of causality and possible disease mechanisms. There is now reasonable evidence that a history of depression is a risk factor for developing dementia, particularly when the depression occurs early in life or is severe.<sup>18</sup> Conversely, incident depression occurring temporally close to the onset of cognitive impairment may represent very early or prodromal symptoms of dementia itself.<sup>1,19-21</sup>

A neuropathological mechanism common to both conditions, such as cerebrovascular disease or hippocampal atrophy, has been suggested.<sup>22-26</sup> However, as with most psychiatric illness, the literature does not consistently support any "neat" pathophysiological hypothesis. It is likely that a complex intertwining of multiple factors is variably involved in different individuals.

## Assessment

Depression in people with dementia remains underdiagnosed, particularly in residential care settings.<sup>27,28</sup> Disease, patient, clinician, family and system-level factors may all hinder accurate assessment.

Depression may present differently in people with comorbid dementia, particularly when the dementia is advanced. Although typical major depressive disorder

2 Summary of Cornell Scale for Depression in Dementia<sup>32</sup>

## Symptom domain\*

## Mood-related

Anxiety Sadness Lack of response to pleasant events Irritability

#### Behavioural disturbance

Agitation

Slowed movement Physical complaints Reduced activities

#### Physical signs

Appetite loss

Weight loss

Fatigue

# Cyclic functions

Mood worse in morning Problems falling asleep Waking during night

Waking earlier than usual

#### Disturbed thinking

Suicidality Poor self-esteem Pessimism

Delusions

\* Score up to four symptoms per domain, for a total score per domain of 0–8. Scoring system: A = unable to evaluate; 0 = absent; 1 = mild or intermittent; 2 = severe. A total score of over 10 is suggestive of depression and an indication for further investigation.

(MDD) is seen, the clinical picture often lacks prominent sadness, hopelessness and guilt and is, overall, less severe.<sup>29</sup> Anxiety, psychomotor retardation, loss of energy or appetite, anhedonia, irritability, delusions and hallucinations may all be more common (and prominent) than in people without dementia. These symptoms can also be part of the dementia itself or suggest delirium.<sup>3,24,30</sup> Unexpected or rapid change in mood, cognitive deterioration, or increased behavioural and psychological symptoms of dementia (eg, disinhibition, agitation, anxiety or aggression) may be the only indicators of superimposed depression.<sup>13</sup>

Conventional techniques and instruments for assessing depression may not be reliable or practicable in people with dementia. When obtaining a patient history, patients may underreport, and their carers overreport, symptoms of depression.<sup>10</sup> As dementia advances, cognitive and communication difficulties may also hamper assessment of the intrapsychic symptoms of depression, including subjective mood states, thoughts about oneself or others, and general outlook for the future. The use of standardised questionnaires is helpful only if they are validated in this population, which is not the case for many of the common depression rating scales.<sup>31</sup>

A useful scale is the Cornell Scale for Depression in Dementia (CSDD; Box 2).<sup>32</sup> There are also modified *Diagnostic and statistical manual of mental disorders, 4th edition* (DSM-IV) criteria for MDD that include the diagnosis of Alzheimer disease.<sup>33</sup> In Australia, the CSDD is incorporated into the Aged Care Funding Instrument, which is used to determine the funding allocated to aged care facilities for individual residents. However, due to limited time and staff in such facilities, attention to completing the CSDD is often cursory, and the results rarely alter management for individual residents. Moreover, serial evaluations are uncommon.<sup>28</sup> Regularly combining use of rating scales with a thorough history would improve detection rates.

Obtaining as much history as possible regarding mood and behavioural symptoms from the patient and carers, such as family or residential care staff, is essential, particularly when communication difficulties are evident. This should be repeated at regular intervals (eg, 6-monthly) or if there is any evidence of a significant change in behaviour.<sup>28,34,35</sup> It is important to enquire about a past history of depression and past treatments for depression, as well as family history, medical history, and drug and alcohol history. Physical illnesses, prescription medications, functional disability, social isolation, life stressors, bereavement and other losses are also important, as they may increase vulnerability to depression.<sup>1,29</sup>

Where there is clinical suspicion of depression (eg, change in mood or any difficult-to-explain change in behaviour), definitive treatment is usually worthwhile, especially when communication difficulties due to dementia act as a barrier to obtaining a detailed history.

#### Management

Management of a patient with depression and dementia should encompass biological, psychological, social, cultural and spiritual factors, particularly those that may have precipitated or may be perpetuating the depression. investigations are essential to exclude any treatable medical cause for low mood. Such causes are more likely to be present in older people and may include physical illness and prescription medications. Common medical causes of depressed mood are listed in Box 3, and important screening investigations for an organic cause are listed in Box 4. Patients also frequently present with physical illness and depressed mood where there is a known association, but it is neither causal nor reversible (eg, depression and ischaemic heart disease). Overall physical health should be reviewed and optimised, and the depression should be specifically treated. Addressing vascular risk factors is particularly important.

A focused physical examination and

Risks associated with depression in people with dementia must be considered throughout, as they may determine the type, location and urgency of treatment. Every patient with depression should be asked directly but sensitively about suicidal thoughts, plans and intent (Box 5). Suicide risk also depends on available protective supports, supervision and the patient's access to means. Other risks include harm to others or to relationships due to agitation, aggression or irritability; loss of accommodation or a move to institutional care; and medical

compromise. Generally, most depression in people with dementia can be managed in the community.

#### Pharmacotherapy

Recent studies, including a large, double-blind, randomised, placebo-controlled trial of the selective serotonin reuptake inhibitor (SSRI) sertraline and the noradrenaline–serotonin specific antidepressant (NaSSA) mirtazapine in people with Alzheimer disease,<sup>16</sup> and a meta-analysis of seven placebo-controlled trials of antidepressants,<sup>17</sup> have failed to demonstrate effectiveness of antidepressant medication for depression in the context of dementia. However, these studies may have had significant limitations, including significant heterogeneity between studies in the meta-analysis, that affected their conclusions.<sup>36</sup> Earlier trials found

## 3 Common organic causes for low mood

Physical	Medication
Hypothyroidism	ß-blockers
Congestive cardiac failure	Calcium channel blockers
Cerebrovascular disease and stroke	Digoxin
Other intracerebral lesion	Steroids
Delirium	Alcohol withdrawal $\blacklozenge$

antidepressants beneficial.<sup>37</sup> Pharmacological therapy, particularly SSRIs, may exert some degree of protection against the negative effects of depression on cognition when people are also taking cholinesterase inhibitors.<sup>38</sup> Cholinesterase inhibitors themselves may slow the rate of cognitive impairment and progression to Alzheimer disease in patients with depression and mild cognitive impairment,<sup>39</sup> although this finding is preliminary and not without controversy.

Thus, the effectiveness of antidepressant medications in this population is currently in question. Studies that included patients with mild depressive symptoms,<sup>16,40</sup> thought to respond poorly to medication, may have diluted any response seen in those with more severe illness. A small trial of patients with dementia and DSM-IV-diagnosed MDD (ie, with relatively more "severe" symptoms) did find sertraline effective on measures of global response, as rated by two psychiatrists, and on changes on standardised rating scales.<sup>37</sup> Conversely, a sensitivity analysis in another study, including only patients with higher CSDD scores, failed to show any effect of antidepressants.<sup>16</sup> It remains too early to draw definitive conclusions about the treatment role of antidepressants for this patient group.

One study group considered possible indicators for early antidepressant treatment, such as past history of antidepressant response, present or past suicide risk, and high distress levels.<sup>36</sup> This seems a reasonable approach in clinical practice. A risk–benefit approach, tailored to the individual patient, should be employed. Antidepressant medication may also be considered in patients taking cholinesterase inhibitors for cognitive enhancement,<sup>38</sup> or where depression is associated with a deterioration in cognition or development of behavioural and psychological symptoms of dementia. In patients with mild depression, non-pharmacological strategies should be attempted first.

Cautious prescribing is paramount in older people, as they are more susceptible to medication side effects, often have multiple comorbid physical illnesses, and may be taking medications that can interact with antidepressants. There must be a clear plan to monitor efficacy and adverse effects. Data regarding the rate of adverse events are conflicting, but such events may be significantly increased.<sup>16,17</sup> Hyponatraemia is of particular concern and should be screened for. The adage "start low and go slow" (a low starting dose, with small and slow dose titrations) should be followed to avoid potential side effects. However, many older patients may still require similar doses of antidepressants to younger adults.

There is little evidence that any class of antidepressants is superior.<sup>17</sup> Newer antidepressants such as SSRIs, NaSSAs or serotonin–noradrenaline reuptake inhibitors

- 4 Screening investigations for patients presenting with low mood
- Full blood examination
- Electrolyte screen
- Renal function
- Liver function
- Thyroid function
- Consider cerebral imaging

(venlafaxine, desvenlafaxine and duloxetine) are thought to be associated with fewer side effects and drug interactions, and to carry less risk in overdose, compared with tricyclic antidepressants, although this assumption has been challenged.<sup>41</sup> The decision to commence any antidepressant medication should include consideration of the adverse effects associated with the particular drug and the vulnerabilities of the individual patient.

There is no research regarding management of difficult-to-treat depression in dementia. A systematic review of difficult-to-treat depression in older people (including studies that did not exclude people with cognitive impairment) identified only three randomised drug trials, including one placebo-controlled trial.<sup>42</sup> The authors concluded that lithium augmentation was the only treatment for which there was consistent evidence.

Failure to respond to antidepressant medication should prompt review of the diagnosis, patient adherence to medication, and the dose and duration of treatment. Following this, difficult-to-treat depression in people with dementia is an indication for referral to specialist services.

#### Non-pharmacological management

Patients with cognitive impairment may benefit from many types of psychotherapy. Any specific causes of psychological distress should be addressed. In older patients with dementia, these are often manifold and may include boredom, loneliness, restricted access to meaningful activities, and overstimulation.

Music and recreation therapy have demonstrated moderate effect sizes for depression in dementia, including in severe dementia.<sup>24,43</sup> Planning recreational activities that the person used to enjoy in the company of someone he or she appreciates may enhance response. Regular physical activity has been shown to improve mood, including in people with dementia.<sup>43</sup>

For people with mild dementia, empathic education may aid adjustment to their diagnosis. Formal, structured therapies, including cognitive and interpersonal therapies, may also have some role.<sup>44</sup> Validation therapy, using empathic activities such as handholding and singing, has also demonstrated effectiveness over that achieved through general "social contact".<sup>43</sup>

Cognitive impairment has conventionally been viewed as a relative contraindication to electroconvulsive therapy (ECT), largely due to the potential for cognitive side effects. However, a recent review of ECT in people with depression and dementia suggested that it can be effective and that cognitive side effects are not universal.<sup>45</sup> Any decision to commence ECT needs to be thoroughly considered by a specialist psychogeriatrician.

Familial or institutional carers should be involved throughout the process of assessment and management. They are often best placed to notice a change in

#### 5 Ways of asking about suicidality

- Has it seemed that life is not worth living?
- Do you wish that you were dead?
- Have you any thoughts of ending your life?
- Have you planned what to do?
- Do you intend to carry it through?
- Is there anything or anyone that would stop you ending your life?

behaviour that may indicate depression and can be enlisted to provide some of the non-pharmacological treatment approaches. Education about the diagnoses will likely improve carers' abilities in both regards. They also face a significant burden in caring for a person with dementia and depression. Due consideration should be given to this burden and the impact on the mental health and quality of life of the carers themselves.

## Conclusions

Depression is common in people with dementia, and the relationship between mood and cognitive symptoms is complex. The nature of this relationship, disease stage, and environmental and clinician factors all contribute to underdiagnosis and undertreatment. Although evidence regarding antidepressant treatment is limited and equivocal, there is no cause for therapeutic nihilism. Organic causes of depressed mood should be excluded, physical health optimised, and medications, where possible, rationalised. Best management includes individually tailored psychosocial strategies and, in moderate to severe depression, judicious use of antidepressant medication with a "start low, go slow" approach. Regular review and effective engagement of carers are both essential and may have significant positive impacts for patients and carers. Difficult-to-treat or complex depression is an indication for specialist referral.

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