

Depression and antidepressant prescribing in the elderly

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Depression in old age is common and associated with significant morbidity, yet it is frequently missed or undertreated. In this article, the authors review the specific issues that need to be taken into account when assessing and treating depression in elderly people.

Depression is the most common mental disorder in the elderly population.¹ Major depressive disorder is estimated to affect 1–4% of the elderly population living in the community. Rates as high as 35% have been reported for all clinically relevant depressive-type syndromes.¹

The elderly population is increasing. The percentage of the UK population aged over 65 years increased from 14.2% in 1976 to 18% in 2016, and is projected to reach 24.7% by 2046.² Skills in managing old age depression are therefore increasingly important for the generalist.

Though there are effective and established treatments for depression in old age, it is a diagnosis that is often either missed or not optimally treated.³ There is a danger of viewing depression in old age as an unavoidable consequence of the adjustment to the various challenges of ageing, including frailty, disability and bereavement. Expectations of wellbeing for the elderly are low and we as a society should be careful to avoid this insidious form of ageism. Chronic physical illness and low expectations of elderly functional performance can obscure diagnosis. The prevalence of depression in those living in care is higher than in the community – underdiagnosis of patients in care homes, and in particular those suffering from cognitive impairment, is a cause for concern.⁴

It is important that depression is diagnosed and treated in a timely and effective manner as it is associated with poor outcomes in the elderly population. In addition to being associated with a negative impact on quality of life, it can significantly increase disability associated with co-morbid physical conditions.⁵ Depression is also associated with increased mortality.⁶

Suicide is a major concern in old age depression. One in eight people who die by suicide are aged over 65 years and men aged over 75 years have the highest rate of completed suicide of any age/sex demographic.⁷

Old age can be a time of loss and bereavement. Death of a spouse and the progressive loss of one's friends and contem-

poraries, in addition to other adjustments and losses such as retirement, deteriorating health and reduced income, can take a cumulative toll on an individual's resilience.

Assessment and diagnosis

The diagnostic criteria for depression in the elderly are the same as in younger patients; however, there are a number of special considerations that should be taken into account when assessing an older adult. In the UK, the World Health Organization ICD-10 criteria,⁸ summarised in Box 1, tend to be the most commonly applied to diagnose depression.

The bedrock of diagnosis is undoubtedly skilled clinical interview, mental state examination and good collateral history from relatives/carers. Rating scales may be useful in determining severity and the NICE guidance on depression in adults recommends their use.⁹ Rating scales validated for use in the elderly (eg Patient Health Questionnaire 9 (PHQ-9), Geriatric Depression Scale, Hospital Anxiety and Depression Scale, Cornell Scale for Depression in Dementia) should ideally be used.

There are some important differences in the presentation of depression in old age. A meta-analysis of the phenomenology of late-life depression found that although many of the principal symptoms were similar, older people are likely to demonstrate more agitation, hypochondriasis and somatic symptoms.¹⁰ Instead of explicitly complaining of depressed mood, elderly patients may describe more non-specific symptoms such as insomnia, anorexia or fatigue.¹¹

Physical health assessment

Comprehensive physical assessment is particularly important in depression in old age, both in terms of excluding underlying organic causes and identifying potential exacerbating factors. A number of chronic health problems have been shown to be associated with depression in later life, including stroke, Parkinson's disease, cancer, heart disease, osteoarthritis, rheumatoid arthritis, COPD and endocrine disorders.¹² A substantial body of evidence suggests that depression worsens the outcome of physical disorders.¹³

Cognitive impairment/dementia

Depression in old age may often present with a degree of cognitive impairment. The term 'pseudodementia' is often used to describe the impairment associated with depression. It is generally held that the cognitive impairment is temporary and will resolve upon resolution of depressive symptoms, but there is evidence to suggest this may not be the case. Bhalla *et al.* reported that 94% of a cohort of non-demented depressed individuals who showed cognitive impairment remained impaired at 12 months, despite resolution of depression.¹⁴ However, clinical experience suggests that even if there is no objective improvement in cognitive testing, the impact of impairment is likely to be subjectively lessened by the improved mood state.

It is worth bearing in mind that late-onset depression, even in the absence of cognitive deficits, may predict later development of dementia. A systematic review and meta-analysis of community-based cohort studies showed that old-age depres-

At least 2 of the following core symptoms must be present (all 3 in severe episodes):

- Depressed mood
- Reduced energy/increased fatiguability
- Anhedonia/loss of pleasure and interest

In addition, other symptoms must be present (2 present in mild, 3–4 in moderate and >4 in severe episodes):

- a. Reduced concentration and attention
- b. Reduced self-esteem and self-confidence
- c. Ideas of guilt and unworthiness
- d. Bleak and pessimistic view of the future
- e. Ideas or acts of self-harm or suicide
- f. Disturbed sleep
- g. Diminished appetite

Symptoms must be present for at least two weeks

Diagnosis of severe depressive episode with psychotic symptoms presents with the criteria as above for severe episode, accompanied by delusions, hallucinations or depressive stupor

Box 1. Summary of the World Health Organization ICD-10 criteria for depression⁸

sion is associated with increased risk of developing dementia of all causes, including vascular and Alzheimer's type.¹⁵

Conversely, individuals who are diagnosed with dementia are at increased risk of developing depression. Up to 50% of individuals with Alzheimer's dementia experience significant depressive symptoms.¹⁶ Evidence for effective treatment of depression in Alzheimer's is scant with a recent meta-analysis of seven randomised controlled trials finding no significant difference between antidepressant treatment and placebo.¹⁷ Though high-quality evidence of benefit is lacking, we would suggest that a trial of antidepressant medication is advisable and pragmatic in suitable circumstances.

Drug treatments

Due to the common age-related changes in pharmacokinetics and pharmacodynamics, use of psychotropic medications in the elderly is not without risk. However, one should always weigh this against the risks of leaving depression untreated – poor quality of life, adverse health outcomes, functional decline, risk of suicide and increased overall mortality, as outlined above.

There is a careful balance to be struck between treating safely and treating adequately. One should always bear in mind the significant physiological heterogeneity of ageing – two individuals of the same chronological age may have quite different physiological ages, and response to medication can be difficult to predict. The old adage of 'start low and go slow' still holds true for psychotropic prescribing in the elderly.

Antidepressants

The efficacy of antidepressants in old age is well established by Cochrane review (2001).¹⁸ A further Cochrane review in 2006

found that while selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) are equally effective in the elderly, SSRIs tend to be better tolerated and associated with fewer adverse effects.¹⁹

Choice of antidepressant should take into account a number of factors, including symptom profile, medical co-morbidity, risk of interactions with other medication, frailty and susceptibility to side-effect profiles, previous treatment response, risk in overdose and patient preference.²⁰

Older adults tend to take longer to show a response to treatment. A 2008 meta-analysis of antidepressant treatment in older adults found that the odds ratio for response to treatment was significantly higher in studies with a longer trial period (10–12 weeks).²¹ While a typical trial of four weeks may be enough to see a response in a younger adult, more patience may be needed in old age.

SSRIs

In general, SSRIs tend to be the most commonly prescribed antidepressants. NICE recommends that SSRIs should normally be used as first-line treatment for depression in all age groups.⁹

Given the high rates of polypharmacy in the elderly, drug interactions are an important consideration. SSRIs such as citalopram and escitalopram (along with non-SSRIs mirtazapine and venlafaxine) have minimal effect on the cytochrome P450 system and so have a reduced risk of pharmacokinetic interactions. By contrast, fluoxetine and paroxetine are strong inhibitors of CYP2D6 while sertraline has a moderate inhibitory effect.²²

It is important to be aware of the anticholinergic side-effects of SSRIs, which include postural hypotension and sedation, though these are less common with SSRIs than with TCAs.¹⁹

Hyponatraemia is a potentially serious adverse effect associated with use of SSRIs in the elderly, and has been reported with almost all SSRIs in addition to the serotonin and noradrenaline reuptake inhibitor (SNRI) venlafaxine.²³ Particular caution should be exercised when co-prescribing with a diuretic. Other risk factors for developing hyponatraemia include increasing age, female sex and previous hyponatraemia.²³ When prescribing in at-risk groups, monitoring of urea and electrolytes can be useful, in addition to being vigilant for clinical features such as lethargy, muscle cramps, anorexia and headaches. Mild hyponatraemia can often be asymptomatic.

SSRIs are associated with a modestly increased risk of upper GI tract bleeding in older people.²⁴ Serotonin plays an important role in the maintenance of platelet function, and SSRIs may inhibit the reuptake of serotonin by platelet serotonin transporters, leading to a potential for serotonin depletion in platelets and subsequent tendency towards bleeding. NICE guidance recommend consideration should be given to co-prescribing gastroprotective medication in high-risk individuals.⁹

Although almost all psychotropics can affect the QT interval, citalopram and escitalopram are particularly associated with interval prolongation in comparison with other SSRIs.²⁵ QT inter-

- Dose reduction and retitration
- Switching to alternative antidepressant with lower propensity for causing specific side-effects
- Non-pharmacological management of side-effects, eg diet and exercise for antidepressant-associated weight gain
- Pharmacological management of side-effects, eg sildenafil for erectile dysfunction, short course of benzodiazepine for agitation/anxiety/insomnia in early treatment

Table 1. Strategies for managing severe or distressing side-effects of antidepressant treatment. Summarised from the revised British Association for Psychopharmacology (BAP) guidelines²⁰

val prolongation is potentially serious and can be associated with an increased risk of ventricular arrhythmia. Medications to treat physical disorders can also affect QT interval and so particular care should be taken in the context of polypharmacy. Medicines and Healthcare products Regulatory Agency (MHRA) guidance issued in 2011 recommends reduced maximum daily doses – 20mg citalopram or 10mg escitalopram for people aged over 65 years – in addition to considering an ECG before commencing treatment for patients with a history of cardiac disease. Sertraline, by contrast, is among the safest SSRIs in the context of cardiac disease.²⁶

Venlafaxine, mirtazapine and reboxetine

Venlafaxine can be a useful medication when an SSRI has proved ineffective²⁷ or in severe cases of depression where maximising efficacy is of overriding importance.²⁰ One should consider the risks of side-effects such as hypertension and hyponatraemia when prescribing to an older patient.

The atypical antidepressant mirtazapine can be considered as a suitable alternative in the context of failed response to an SSRI, and also has a role in augmenting treatment in combination with another antidepressant.²⁰ Again, caution should be exercised – Rush and colleagues found significant rates of adverse events with these combinations in a study of patients aged 18–75 years.²⁸ Certain common side-effects of mirtazapine such as increased appetite and sedation may be considered beneficial in patients in whom malnutrition and insomnia is a particular problem.

Risk of sexual side-effects may be an important consideration in some elderly patients. Mirtazapine and the selective noradrenaline reuptake inhibitor (NRI) reboxetine and are among the antidepressants less likely to cause sexual dysfunction.^{29,30} However, with regard to reboxetine, we would advise prescribers to be aware of certain controversies regarding publication bias and efficacy.³¹

TCAs and MAOIs

If older agents such as TCAs or monoamine oxidase inhibitors (MAOIs) are to be used in the elderly then careful consideration of side-effects and the risks vs benefits should be made, and careful monitoring and supervision may be necessary. This often necessitates referral to secondary care for advice or treatment.

Lofepramine is perhaps the best tolerated TCA, tending to be associated with fewer side-effects than other TCAs. It is much the safest in overdose and has relatively low cholinergic activity.³²

The propensity of MAOIs to cause a number of adverse effects in addition to their risk of potentially lethal pharmacodynamic interactions, including hypertensive crisis and serotonin syndrome, renders them unattractive therapeutic options except in special circumstances. Moclobemide is one of the best tolerated MAOIs, and shows comparable efficacy to both TCAs and SSRIs.³² As moclobemide is a reversible monoamine oxidase A inhibitor, the risks of dietary or drug interactions are reduced, but again its use tends to be reserved for secondary care.

Augmentation treatment

Lithium is among the most established options for augmentation in treatment-resistant or recurrent depressive disorder, and has a strong evidence base in older adults.³³ However, it is associated with a number of adverse effects that the elderly may be more vulnerable to, including lithium toxicity. One should be particularly mindful of the patient's renal status, and regular blood monitoring as per local guidelines is essential.

While antipsychotics have an established evidence base in augmentation treatment of younger adults with depression, evidence in the elderly is limited. Antipsychotic medications are known to have a number of adverse effects that can be particularly problematic in the elderly and so a careful analysis of the risk vs benefit for the individual patient is advised, in addition to regular monitoring and supervision.

Managing side-effects

Useful advice for managing persistent, severe or distressing side-effects can be found in the revised British Association for Psychopharmacology (BAP) guidelines for treating depressive disorders with antidepressants,²⁰ summarised in Table 1.

Length of treatment

The evidence base for the optimal length of treatment in older adults is uncertain. NICE guidance recommends continuing antidepressant treatment for at least six months following remission.⁹ However, NICE also recommends continuing treatment for at least two years in the case of relapse of a recurrent depressive disorder, or if there are risk factors for relapse or the consequences of relapse are likely to be severe.⁹

Non-pharmacological treatments

Psychosocial interventions are important in the elderly. Social isolation and loneliness can be particularly problematic, and referral to social services may be considered to assess for adequate care support at home. Elderly day-care centres are a vital source of social interaction and activity. NICE guidance recommends that in mild depressive episodes, supportive interventions should be considered first-line, with a stepped approach to offering psychological therapy or antidepressant medication in those that fail to respond.⁹

In view of the association between elderly depression and chronic physical illness, optimising management of these conditions is important.

Electroconvulsive therapy (ECT) is a safe and effective treatment for depression in the elderly that can achieve a good response in 70–90% of cases, though subsequent relapse remains a problem.³⁴

There is some evidence that older people may be less likely to be referred for a talking therapy.³⁵ Although the factors underlying this are not clear, there may be a perception that talking therapies are less effective in elderly people. It is important to stress that the evidence suggests this assumption is not true. There is strong evidence that psychological therapies are equally effective in old age as in younger adults.³⁶ However, there may be service barriers to accessing therapy, for example for people who are housebound or in care homes.

Prognosis

While remission rates in older people are comparable with younger adults, relapse appears to be more common in the elderly. In a study that followed up subjects for six years, almost half were depressed for more than 60% of the six-year period, with only 23% achieving sustained remission.³⁷

These statistics may seem rather bleak, but there is some evidence that thorough, persistent and sequential treatment for elderly patients who do not respond to initial treatment can achieve very good rates of remission – Kok *et al.* demonstrated 84% remission rates in patients who underwent this approach.³⁸

Referral to secondary care

Recommendations on when to refer to secondary care from the BAP guidelines on treating depressive disorders²⁰ are summarised in Table 2.

In the context of old age, complex psychosocial situations in addition to complexity arising from multimorbidity, frailty and/or cognitive impairment frequently necessitate the expertise of the old age mental health team.

Guidelines/management protocols

Comprehensive guidance on the management of depression can be obtained from the NICE guideline on depression in adults (CG90)⁹ and the British Association for Psychopharmacology evidence-based guidelines for treating depressive disorders with antidepressants.²⁰

- Significant risks of suicide/harm to others/self-neglect
- Psychotic symptoms
- History or suspicion of bipolar disorder
- Failed or insufficient response to two or more antidepressants
- Where the practitioner feels insufficiently experienced to assess or manage the condition

Table 2. Indications for referral to secondary care. Summarised from the revised British Association for Psychopharmacology (BAP) guidelines²⁰

KEY POINTS

- Depression is common in the older adult population
- Depression is commonly missed and often undertreated
- Depression can worsen the outcome of physical health problems, reduce quality of life and increase mortality
- Men aged over 75 years have the highest rate of completed suicide of any age/sex demographic
- Antidepressant medication is safe and effective in the treatment of depression in old age
- Particular consideration should be given to the physical assessment of patients with depression in old age
- Factors such as frailty and co-morbid physical conditions should be taken into account when selecting antidepressant medication
- Older patients may require more monitoring for adverse reactions and lower doses may be appropriate; full details can be found in the summary of product characteristics for each medication
- Antidepressants may take longer to show an effect in the elderly; 'start low and go slow'
- Longer periods of treatment, ie up to two years, or even maintenance treatment, may be necessary to avoid relapse in some cases
- Non-pharmacological approaches, including psychosocial interventions, are important, and psychological therapy is equally effective in older adults as younger adults
- Referral to secondary care may be required if there are significant risks, psychotic symptoms, poor response to initial treatment or significant complexity resulting from frailty or cognitive impairment

Conclusion

Depression in old age is a common and disabling disorder that has historically been under-recognised and undertreated. While careful consideration should be given to co-morbidities including frailty, treatment is safe and effective and can provide significant benefits in terms of symptoms, quality of life and overall health and wellbeing.

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Declaration of interests

None to declare.

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