

Management of depression in later life

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Abstract Both antidepressants and psychological treatments are effective in the management of late-life depression. Nevertheless, there remains a considerable challenge to improve the prognosis for depression in older people. Endlessly increasing the range of antidepressants does not seem to be the answer, so attention is turning to new combinations of treatments and new ways of delivering care and improving treatment uptake. Collaboration between specialist and primary care, case management and multifaceted interventions are currently the most exciting prospects. There is good evidence for the role of both medication and psychological treatment in keeping the patient well after recovery.

Depressive disorder is the most frequent psychiatric illness of older people (Beekman *et al*, 1999). It has a negative impact on quality of life, adds significantly to disability from physical disorder (Penninx *et al*, 2000) and is the leading cause of suicide in older people. It is also an independent predictor of mortality (Cuijpers & Smit, 2002). Although effective treatment exists, depression is not well recognised and often not optimally managed (Baldwin *et al*, 2002). This article updates an earlier review of the subject (Katona, 1996).

Box 1 Factors to take into account when diagnosing late-life depression

Altered symptoms in late-life depression

- Reduced complaint of sadness
- Hypochondriasis and somatic concern instead of sadness
- Poor subjective memory or a dementia-like picture
- Late-onset neurotic symptoms (marked anxiety, obsessive–compulsive or hysterical symptoms)
- Apathy and poor motivation

Symptoms that may be hard to interpret because of comorbid physical disorder¹

- Anorexia
- Weight loss
- Reduced energy

1. For a discussion, see Koenig *et al* (1997).

Prevalence in older people

In a meta-analysis the prevalence of clinically significant depression among older people living in the community was 13.5% (Beekman *et al*, 1999). Important determinants of prevalence are disability and handicap so, unsurprisingly, rates are at least doubled among patients in hospital or nursing homes. There are possible neurobiological links between depression and stroke, Parkinson's disease and the dementias (vascular dementia having the highest rate of comorbid depression), but also a high rate of depressive symptoms in a range of chronic medical disorders, including heart disease (Ariyo *et al*, 2000) and chronic obstructive pulmonary disease (Yohannes *et al*, 1998).

Assessing depression in later life

Special factors to take into account when assessing depression in older people are listed in Box 1. The skills of history-taking, conducting a mental state examination, physical evaluation and organisation of relevant investigations are no less important than in other branches of psychiatry. Given the increased likelihood of finding an organic condition contributing to depression with advancing age, these skills are arguably more important. Boxes 2 and 3 list the more important causes of organic depressive episodes.

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Box 2 Medications that may cause organic depression*Antihypertensives*

Beta-blockers

Methyldopa

Calcium-channel blockers (e.g. nifedipine)

Digoxin

Corticosteroids

Prednisolone

Analgesics

Codeine

Opioids

COX-2 inhibitors (e.g. celecoxib, rofecoxib)

Anti-Parkinsonian drugs

Levo-dopa

Amantadine

Tetrabenazine

Psychotropics (may cause clinical picture resembling depression)

Antipsychotics

Benzodiazepines

Screening

The most widely validated screening instrument is the Geriatric Depression Scale, introduced in 1983 (Yesavage *et al*, 1983). Short and long versions and translations of the scale are available at <http://www.stanford.edu/~yesavage/GDS.html>. The 15-item version (with its 4- and 5-item derivatives) is shown in Box 4. The 5-item version has recently been validated in a sample comprising individuals living in the community, hospitalised patients and nursing-home residents (Rinaldi *et al*, 2003).

Types of depression in older people**Minor and major depression**

Although 13.5% of older people are significantly depressed, the prevalence of depressive episode (major depression) is much lower, at around 2% (Beekman *et al*, 1999). Minor depression is one term used to describe the less severe depression affecting the remaining group. Recent evidence suggests that minor and major depression in older people share similar risk factors and that in population terms the adverse consequences of minor depression lie midway between major depression and not having depression at all (Cuijpers & Smit, 2002). Minor depression is perhaps characterised by more cognitive symptoms of depression and fewer

somatic ones. There is a striking lack of data about effective treatment. In one study, paroxetine was moderately effective for both persistent minor depression and dysthymia in patients with functional impairment, but problem-solving treatment was not (Williams *et al*, 2000). However, there was marked site variation in the quality of the problem-solving treatment. In another study (Mossey *et al*, 1996) a treatment similar to the problem-solving treatment was effective in patients with sub-threshold depression with medical comorbidity.

Vascular depression

The clinical features of this proposed new subtype include apathy, psychomotor retardation, poor executive function on cognitive testing, less depressive thinking (such as guilt or unworthiness) and a late age at onset. The basis is thought to be ischaemically induced white matter changes (Baldwin & O'Brien, 2002). This subtype is probably less responsive to antidepressant drugs (Simpson *et al*, 1998), but patients may recover with electroconvulsive therapy (ECT), although with an increased risk of post-treatment delirium.

Prognosis

Cole & Bellavance (1997a) reported that after an index episode about 60% of secondary care patients either

Box 3 Physical disorders that may cause organic depression*Endocrine/metabolic*

Hypo- and hyperthyroidism

Cushing's syndrome

Hypercalcaemia (primary hyperparathyroidism or carcinoma)

Pernicious anaemia

Folic acid deficiency

Organic brain disease

Cerebrovascular disease/stroke

Tumours of the central nervous system

Parkinson's disease

Alzheimer's disease

Systemic lupus erythematosus

Occult carcinoma

Pancreas

Lung

Chronic infections

Neurosyphilis

Brucellosis

Herpes zoster

Box 4 The 15-item Geriatric Depression Scale, also showing questions for the 4- and 5-item scales

Instructions: Choose the best answer for how you have felt over the past week.

| | | | |
|----|--|--------|-------|
| 1 | Are you basically satisfied with your life? | Yes/No | (No) |
| 2 | Have you dropped many of your activities and interests? | Yes/No | (Yes) |
| 3 | Do you feel your life is empty? | Yes/No | (Yes) |
| 4 | Do you often get bored? | Yes/No | (Yes) |
| 5 | Are you in good spirits most of the time? | Yes/No | (No) |
| 6 | Are you afraid something bad is going to happen to you? | Yes/No | (Yes) |
| 7 | Do you feel happy most of the time? | Yes/No | (No) |
| 8 | Do you often feel helpless? | Yes/No | (Yes) |
| 9 | Do you prefer to stay at home, rather than going out and doing new things? | Yes/No | (Yes) |
| 10 | Do you feel you have more problems with your memory than most? | Yes/No | (Yes) |
| 11 | Do you think it is wonderful to be alive now? | Yes/No | (No) |
| 12 | Do you feel pretty worthless the way you are? | Yes/No | (Yes) |
| 13 | Do you feel full of energy? | Yes/No | (No) |
| 14 | Do you feel that your situation is hopeless? | Yes/No | (Yes) |
| 15 | Do you think most people are better off (in their lives) than you are? | Yes/No | (Yes) |

Questions 1, 2, 6 and 7 make up the 4-item version.

Questions 1, 4, 8, 9 and 12 make up the 5-item version.

The answers shown in parentheses indicate possible depression.

Possible cut-offs: ≥ 5 for the 15-item version; ≥ 2 for the 4-item and 5-item versions.

remained well or had treatable relapses. About 1 in 5 developed chronic symptoms. Outcome for individuals living in the community was worse. In another meta-analysis of depressed patients in acute medical and surgical care, only about 1 in 5 recovered (Cole & Bellavance, 1997b). Low rates of detection and undertreatment may partly explain these poor results (Baldwin, 2000).

Katona's statement in an earlier review (Katona, 1996) still holds true: depression in old age is associated with chronicity and a high risk of relapse after recovery. However, this is just as true for younger adults, prompting current interest in managing depressive disorder within a chronic disease model (Rost *et al*, 2002).

Mortality is high in older patients with depression, largely because of concurrent physical disorder (Tuma, 2000).

Principles of management

The management of depressive disorder in older people should be multimodal (involving physical and psychological modalities along with social interventions) and multidisciplinary (with help from specialists such as nurses, social workers and occupational therapists, and help as needed from dieticians, speech and language therapists and podiatrists). Some broad goals of treatment and ways of achieving them are shown in Table 1 (Baldwin *et*

al, 2002). Handicap, the social disadvantage caused by illness, is closely associated with depression in old age. Thus, social factors such as the availability of transport and crime reduction may have very positive effects on reducing rates of depression.

Treatments that work are the same as for younger adults: antidepressants, psychosocial and psychological interventions, or combinations of these (Anderson *et al*, 2000), and ECT.

Drug treatment

Pharmacodynamics and pharmacokinetics alter with ageing and are also affected by concomitant medication and physical illness. Older people exhibit marked inter-individual variation in how medication is metabolised. This can lead to difficulty in predicting the target dose. The adage 'start low, go slow' then applies. This is less of a problem with the newer antidepressants, for which the starting dose and the therapeutic dose are identical. However, therapeutic trials often exclude the very old and the very frail, so that our knowledge is incomplete. Although many newer antidepressants require no dose adjustments for older patients, impaired renal or hepatic function necessitates caution with all antidepressants. Table 2 lists the main antidepressants, starting doses and average dosages for older patients by consensus (Alexopoulos *et al*, 2001; Baldwin *et al*, 2002), along with side-effect profiles.

Table 1 Management principles

| Goal | Ways to achieve goals |
|--|--|
| Reduction of risk of suicide or self-neglect | Carry out risk assessment and monitor risk (review regularly) Ensure prompt referral of urgent cases (in primary care and on medical wards) to a specialist |
| Remission of all depressive symptoms (residual symptoms increase the risk of chronicity) | Provide appropriate treatment (antidepressants, psychological treatment or electroconvulsive treatment) Give the patient and supporters/carers timely education about depression (e.g. <i>Depression in Older Adults</i> leaflet, free at http://www.rcpsych.ac.uk/info/help/doa/index.htm) |
| Optimise function | Treat comorbid physical health problems Attend to sensory deficits Review medication Enable practical support Facilitate access to appropriate helping agencies ('sign-posting') |
| Prevention of relapse and recurrence | Encourage the patient to stay on medication when recovered Continue treatment for 12 months after recovery (see text) Give maintenance treatment when indicated (see text) |

Older patients take longer to recover. Whereas 4 weeks may be a sufficient time in which to see a response in younger adults, 6–8 weeks or longer may be more typical for older patients. Nearly 20 antidepressant drugs are currently available for use in the UK. With such a wide variety of antidepressants it is best to tailor the drug to the patient, the choice being determined by symptom profile, tolerance and the likelihood of drug interactions or side-effects.

Efficacy

A recent Cochrane systematic review (Wilson *et al*, 2001) has demonstrated that antidepressants are an effective treatment for elderly patients with major depression and it revealed no important differences between classes of antidepressants. However, only 17 trials met inclusion criteria and there were few placebo-controlled studies of newer antidepressant drugs. Most recent trials have been head-to-head comparisons of older and newer drugs. These show a trend for selective serotonin reuptake inhibitors (SSRIs) and venlafaxine to be preferred because of a favourable adverse effects profile (Katona & Livingston, 2002). Lastly, there is some evidence from trials involving patients of mixed ages (Anderson *et al*, 2000) that SSRIs may be less effective than tricyclics in in-patients with melancholic depression. Wilson *et al* (2001) concluded that there was insufficient evidence to recommend low-dosage antidepressant treatment in depressive episode in primary care. More research is needed.

Comorbidity

Patients with psychotic depression usually require a combined approach with the addition of anti-psychotics or ECT. Physical comorbidity is common in older patients. A meta-analysis of antidepressant therapy *v.* placebo, although not exclusively in older patients, showed a number-needed-to-treat (NNT) of 4 for patients with depression and a range of physical disorders (Gill & Hatcher, 1999). A similar figure is reported in the reviews of Wilson *et al* (2001) and Katona & Livingston (2002) in older depressed patients without comorbidity. MacHale has outlined practical therapeutic strategies for patients with physical comorbidity in an earlier article in *APT* (MacHale, 2002).

Tolerability and side-effects

An important principle when treating older people is to remember that they have less physiological reserve and are more likely to lose homeostasis rapidly. For example, severe depression in an older person may quickly lead to dehydration, weight loss and even pressure sores. Likewise, older people are more susceptible to medication side-effects.

Anticholinergic side-effects of tricyclics, such as constipation, blurred vision and dry mouth, can be very troublesome for elderly patients, and postural hypotension, cardiac arrhythmia or overdose can be very dangerous. Delirium can occur, but is more likely in patients who are also acutely medically unwell. Lofepamine is a second generation tricyclic which is less likely to cause these adverse effects.

Table 2 Average dosages and side-effect profiles of antidepressants (after Baldwin *et al*, 2002)

| | Anticholinergic | Antihistaminic | α_1 -adrenergic blocking | Starting dose (mg) | Average daily dose (mg) |
|-----------------------|-----------------|----------------|---------------------------------|--------------------|--------------------------|
| Amitriptyline | ++++ | ++++ | ++++ | 25–50 | 75–100 |
| Imipramine | +++ | ++ | +++ | 25 | 75–100 |
| Nortriptyline | +++ | ++ | ++ | 10–30 | 75–100 |
| Dosulepin (dothiepin) | +++ | ++ | ++ | 50–75 | 75–150 |
| Lofepramine | + | + | + | 70–140 | 70–210 |
| Trazodone | 0 | +++ | + | 100 | 300 |
| Fluvoxamine | 0/+ | 0/+ | 0 | 25–100 | 100–200 |
| Sertraline | 0/+ | 0 | 0 | 25–50 | 50–100 |
| Fluoxetine | 0/+ | 0 | 0 | 10 | 20 |
| Paroxetine | 0/+ | 0 | 0 | 10–20 | 20–30 |
| Citalopram | 0/+ | 0 | 0 | 10–20 | 20–30 |
| Escitalopram | 0 | 0 | 0 | 5–10 | 20 |
| Phenelzine | 0/+ | 0 | ++ | 15 | 30–45 (divided doses) |
| Moclobemide | 0/+ | 0 | 0 | 300 | 300–400 |
| Venlafaxine | 0/+ | 0 | 0/+ | 25–75 | 75–150 |
| Mirtazapine | 0 | ++ | 0 | 7.5–15 | 15–30 |

Magnitude of effect: from small (+) to marked (++++).

It is more expensive than the older tricyclics, but no more expensive than SSRIs. The latter drugs are not cardiotoxic and are not usually lethal in overdose, but they have other undesirable side-effects. Gastrointestinal symptoms are well recognised, but there is growing concern about gastrointestinal haemorrhage, particularly in elderly patients (van Walraven *et al*, 2001). Caution should be exercised in patients treated with non-steroidal anti-inflammatory drugs or aspirin. Sertraline and citalopram have the least potential for drug interactions. Epilepsy is a caution for the use of antidepressants.

Discontinuation symptoms may occur with all classes of antidepressants after 8 or more weeks of treatment. They are more common and severe with antidepressants that have a short half-life. Inappropriate antidiuretic hormone (ADH) secretion is often linked to SSRIs, but may occur as a side-effect of all classes of antidepressants. There is a paucity of systematic data, but increased age, female gender and drugs that lower sodium levels are all risk factors (Kirby & Ames, 2001). Symptoms often (but not invariably) occur when the blood serum level falls below 130 mmol/l. Symptoms of ADH, which include lethargy, fatigue and sleep disturbance as well as muscle cramps and headaches, overlap with those of depression. A high level of suspicion is needed.

Moclobemide is well tolerated by older people. Although a special diet is not required, patients should be aware of the drug interactions with painkillers and other antidepressants. Venlafaxine is an effective drug in this age group and is generally well

tolerated, particularly if the dose is increased slowly. The main side-effects of nausea and gastrointestinal disturbance tend to be transitory. Venlafaxine does have an effect on blood pressure, but studies have found that elderly people (at least, those that are fit) are no more susceptible to this problem than younger patients. There is some evidence to support the use of venlafaxine in patients who have not responded to SSRIs, although not specifically in older patients (Poirier & Boyer, 1999).

The SSRIs have minimal impact on cognitive function in older patients with depression and there is also evidence that SSRIs and lofepramine cause less impairment than the older tricyclics in cognitive skills relevant to driving.

Psychological interventions

Older patients with depression are rarely offered a psychological intervention. Changing attitudes and increased awareness are likely to alter this. In a large primary-care-based study in which a treatment choice was offered to older patients with depression, 50% expressed a preference for a psychological approach over drugs (Unützer *et al*, 2002). Additionally, there is emerging evidence that for older adults with mild-to-moderate depressive episodes a psychological intervention is as effective as medication (McCusker *et al*, 1998; Piquart & Sorensen, 2001). Whether services are adequately configured to meet the need is more questionable. Nevertheless, in England, the National Health Service Executive's strategic review of psychotherapy services has

endorsed the need for accessibility and equity across patient groups (National Health Service Executive, 1996). General areas of importance when working psychodynamically with older people have been addressed in a previous *APT* article (Garner, 2002).

Cognitive-behavioural therapy (CBT) is the best-established treatment in depression and good evidence exists for its effectiveness in older adults (Thompson *et al*, 2001). However, most studies have looked at its use in cognitively intact and medically stable patients and so its effectiveness outside this patient group is not fully established. Small studies and case reports have indicated that CBT can be adapted for use with physically frail patients and those with mild cognitive impairment, but further research is needed. Interpersonal therapy is also effective in relapse prevention (Reynolds *et al*, 1999a,b). There is a smaller but developing evidence base for problem-solving treatment (Areal *et al*, 1993; Unützer *et al*, 2002). In major depression, a combination of antidepressants with psychotherapy is more effective than either of these treatments alone, especially in relapse prevention (Reynolds *et al*, 1999b; Thompson *et al*, 2001). Psychoeducational techniques have also been used in this age group with good effect. For example, in one recent study a group course on coping with depression and anxiety was effective in reducing scores on the Geriatric Depression Scale (Schimmel-Spreeuw *et al*, 2000).

Lastly, family therapy has been successfully adapted for use with older adults, including those with depression (Benbow *et al*, 1990), but no controlled data have been published regarding efficacy.

Electroconvulsive therapy

Electroconvulsive therapy remains the most effective treatment available for severe depression, with a recovery rate in the region of 80%. It is well tolerated, even by very elderly people (Tew *et al*, 1999). Its use is generally reserved for when there is a threat to life due to insufficient dietary intake or suicidal behaviour, or if treatment with antidepressants has been ineffective. There is evidence that it is particularly effective in psychotic depression (Baldwin *et al*, 2002). There are no absolute contraindications, but a review of medical risk by a senior anaesthetist is advisable. Wherever possible hypertension and cardiac failure should be treated optimally before ECT. It should be avoided in the first 3 months following a myocardial infarction or stroke. Elderly patients are more likely to suffer post-ECT confusion and cognitive impairment and therefore this should be carefully monitored during

treatment. Memory impairment is often worse with bilateral electrode placement although the response to bilateral treatment may be more rapid.

Other treatments

Rapid transcranial magnetic stimulation (rTMS) is a promising new treatment for depression. The early evidence suggests that it may be less effective in older adults, especially in the presence of even mild frontal atrophy (Manes *et al*, 2001). St John's Wort, a herbal remedy, is popular but lacks a satisfactory evidence base. Epidemiological data support a link between depressive symptoms and lack of exercise in older people (Baldwin *et al*, 2002), but data have not been published on the use of exercise as a treatment for late-life depression.

In an important study designed to replicate models of enhanced care (also known as 'stepped care') developed for use with younger patients in primary care, Unützer *et al* (2002) showed that a multifaceted intervention for depression was more effective than usual care for older adults. The model chosen emphasised case management, the use of antidepressants and/or problem-solving treatment, and improved links between primary and specialist care.

Treatment-resistant depression

Although definitions of treatment resistance vary, at least 30% of elderly patients with depression do not respond to first-line treatment with an antidepressant (McCusker *et al*, 1998). The initial steps are to ensure that a medical cause for depression has not been overlooked, that the patient tolerates and takes the medication and that the dosage is optimal.

New data suggest that if the patient has shown little or no response (in objective terms less than a quarter improvement on an appropriate rating scale) within the first 4 weeks at therapeutic dosage, recovery is unlikely (Mottram *et al*, 2002). The best course is to change to an antidepressant of a different class. If, however, there has been a partial response, the clinician is faced with a choice. Other things being equal, because older patients take longer to recover (Anderson *et al*, 2000), waiting and supporting the patient may be a reasonable course of action. Otherwise, the advantages and disadvantages of augmentation and substitution, the two main strategies open to the clinician, are outlined in Box 5 (augmentation refers to adding another treatment to the original medication).

Clinicians in the UK tend to be 'swappers' – from one class of antidepressant to another. The use of

Box 5 Factors favouring augmentation or substitution regimens (after Mulsant *et al*, 2001)*Augmentation*

- Maintains improvement already achieved in partial responders
- Prevents delays associated with withdrawal of existing drug
- May have synergistic effects on two neurotransmitter systems
- Allows current partially successful agent to be continued for longer

Substitution

- Avoids potential drug–drug interactions
- Simpler regimen
- Lower costs
- Easier to attribute side-effects and understand tolerance

non-reversible monoamine oxidase inhibitors as an option has gone out of favour, although there was an early evidence base for their efficacy. Another approach, of combining a tricyclic with an SSRI, has given way to the newer dual-acting antidepressants such as venlafaxine or combinations such as SSRIs with mirtazapine. Both have some evidence to support their use in resistant depression (Anderson, 2003), although not specifically in older people. The high doses of venlafaxine sometimes recommended are not always tolerated by older patients. Likewise, augmentation with lithium has a reasonable evidence base, but tolerability can be a significant problem in older patients. Serum monitoring is required.

Maintenance treatment

How long to continue with maintenance therapy is not yet clear. A recent expert consensus statement suggests that after a first episode of major depression a majority of clinicians opt to keep the patient on continuation treatment for at least 1 year. For two episodes there was less agreement, but for patients with three or more relapses or recurrences most clinicians recommended long-term treatment (Alexopoulos *et al*, 2001). As with other age groups, it is important to maintain the patient on the same medication regimen that led to remission.

Surprisingly, one would be hard pressed to find any evidence to show that the new range of antidepressants developed over the past 20 years has led to an improved prognosis for late-life depression. However, there is more optimism with

respect to prevention. Once a patient has recovered, there is good evidence that ongoing treatment with a tricyclic (Old Age Depression Interest Group, 1993), the SSRI citalopram (Klysner *et al*, 2002) or a combination of medication with a psychological treatment (Reynolds *et al*, 1999b) are effective. In a recent trial, sertraline at conventional therapeutic dosage was not effective in preventing relapse in older community-dwelling patients over a period of 2 years (Wilson *et al*, 2003). Therefore, it cannot be assumed that all antidepressants are equally effective in prophylaxis.

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Multiple choice questions

1 Depressive disorder in older people:

- is prevalent in 1 in 100
- strongly predicts later dementia
- affects almost half of patients with Parkinson's disease
- is more common in vascular than in Alzheimer's dementia
- often presents with hypochondriasis.

2 Management principles include:

- symptom improvement as the main goal
- dietary advice
- assessment of self-neglect
- a serum ferritin level
- detailed neuropsychological examination.

3 Treatment:

- always starts with an SSRI
- should be changed if there has been a 25–50% response at 4 weeks
- with cognitive-behavioural therapy is an effective alternative to antidepressants for moderate depression
- of mild cases with a combination of medication and a psychological intervention is more effective than either alone
- with ECT is hardly ever effective in the 'old-old'.

4 Prevention:

- a of relapse requires treatment for about 6 months at most
- b of recurrence has been demonstrated only for tricyclic antidepressants
- c of recurrence after a third episode is an indication for long-term antidepressant treatment
- d of recurrence in moderate-to-severe depression is best achieved by combining an antidepressant with interpersonal therapy
- e of depression should include attending to handicap.

MCQ answers

| | | | |
|-----|-----|-----|-----|
| 1 | 2 | 3 | 4 |
| a F | a F | a F | a F |
| b F | b T | b F | b F |
| c T | c T | c T | c T |
| d T | d F | d F | d T |
| e T | e F | e F | e T |

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