ARTICLE

Review of treatment for late-life depression

Charlotte L. Allan & Klaus P. Ebmeier

Charlotte Allan is a specialist trainee in old age psychiatry and a Clinical Research Fellow in the Department of Psychiatry, Warneford Hospital, University of Oxford. She graduated from Leeds Medical School in 2006, then completed an Academic Foundation Programme in Leeds and an Academic Clinical Fellowship in Psychiatry in Oxford. She has a special interest in late-life mood disorder. **Klaus Ebmeier** is Professor of Old Age Psychiatry, also at Warneford Hospital. He studied medicine in Bonn and psychiatry in Aberdeen, and worked as a clinical scientist with the Medical Research Council before being appointed to one of the two Edinburgh Chairs of Psychiatry. He moved to Oxford in 2006, where he works on neurobiology of ageing, and on causes and treatment of cognitive impairment and depression.
Correspondence Dr Charlotte Allan, Department of Psychiatry, University of Oxford, Warneford Hospital, Oxford OX3 7JX, UK. Email: charlotte.allan@psych.ox.ac.uk

SUMMARY

Depressive disorder in those over the age of 60 has many clinical similarities to depression in younger adults, but biological changes related to ageing may necessitate a different approach to treatment. We present an evidence-based review of treatment for late-life depression, focusing on pharmacological approaches, including monotherapy, combination and augmentation strategies. Selective serotonin reuptake inhibitors such as sertraline and citalopram are well tolerated, have the advantage of a favourable side-effect profile, and are good options for first-line treatment. Second-line treatment options include combination therapy with a second antidepressant, or treatment augmentation with an antipsychotic or lithium. We also consider evidence for non-pharmacological treatment strategies, including psychological therapy and neurostimulation. Finally, we summarise evidence for treatment of depression in patients in dementia.

Late-life depressive disorder, occurring in those over the age of 60 years, is common, affecting over 9% of people living in the community (Beekman 1999; McDougall 2007) and 25% of those living in institutions (McDougall 2007). It is associated with reduced quality of life and high morbidity (Alexopoulos 2009a; Volicer 2012). It has a detrimental impact on recovery from physical illness (patients with moderate to severe depression have been shown to have delayed recovery following hip fracture (Morghen 2011)) and leads to increased mortality through suicide and self-neglect (Djernes 2011).

Diagnosis and aetiology

Diagnosis is based on standard ICD-10 or DSM-IV criteria (World Health Organization 1992; American Psychiatric Association 1994). However, there may be subtle differences in clinical presentation, with higher rates of somatic symptoms, anxiety and psychomotor retardation, reduced interest in activities and poorer executive dysfunction compared with younger age groups. These symptoms are not sufficiently different or reliable to classify this as a distinct disorder (Alexopoulos 2009a).
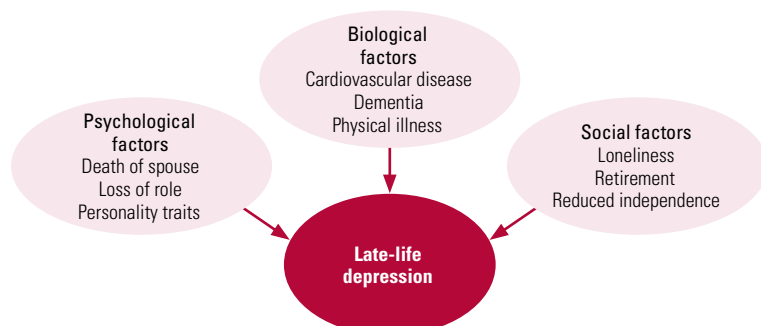
The aetiology of late-life depression is multifactorial (Fig. 1) and includes biological (Alexopoulos 1997), psychological (Kivela 1998; Steunenberg 2007) and social factors (Steptoe 2003; Schwarzbach 2013).

These risk factors can lead to relapse of depressive symptoms in those with an existing vulnerability, or first onset of the disorder in later life. Since many of the aetiological factors are age related, there has been (and continues to be) a misconception that depression in older people is inevitable given the frequency of physical ill health, bereavement and loss of role in this age group. This prejudice may affect help-seeking by patients and treatment offered by health professionals, and could be one reason why late-life depression remains an underrecognised and undertreated disorder, particularly among those living in nursing homes (Brown 2002). Given the significant adverse impact on patients, their families and carers, late-life depression warrants greater efforts at recognition and effective, evidence-based treatment.
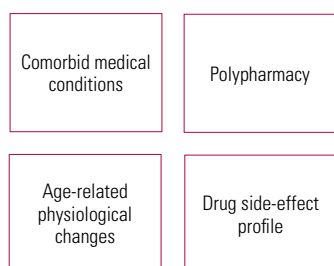
Prescribing for older adults

Pharmacotherapy can be used effectively for late-life depression (Cipriani 2009), but

FIG 1 Aetiology of late-life depression.

FIG 2 Considerations before prescribing for older adults.

treatment requires a distinct approach because of age-related physiological changes, which alter pharmacokinetics and pharmacodynamics. Drug distribution within the body changes as a result of increased body fat and reduced volume of water. Hydrophobic compounds (e.g. antidepressants and antipsychotics) are therefore more readily distributed, whereas there is reduced distribution of hydrophilic compounds. Renal excretion is reduced, so there may be increased concentrations of active compounds that are renally excreted (Turnheim 2003). These changes mean that lower doses, slow titration and careful monitoring are needed (Roose & Schatzberg 2005; Nelson 2008). The increased prevalence of comorbid medical conditions in this age group means that patients are more vulnerable to medication side-effects. Polypharmacy is a risk, and care is needed to minimise the effects of drug interactions (Mark 2011). These considerations should not discourage the use of pharmacological treatment of late-life depression, but they do necessitate a careful review of medical history before drug regimens are changed (Fig. 2).

The evidence base

This article gives an overview of treatments for late-life depression (pharmacological, psychological and neurostimulation) based on a search of four databases (MEDLINE, Embase, PsycINFO and PubMed) for the terms [treatment or therapy] and [depression or depressive] and [old age or older or late-life or geriatric]. We have aimed to summarise important and recent research findings in a format that is clinically relevant.

Pharmacological treatment

Monotherapy

SSRIs: sertraline and citalopram

Selective serotonin reuptake inhibitors (SSRIs) are the most common first-line treatment for late-life depression, as is the case for younger patients. Sertraline has the best evidence for efficacy and tolerability, although there is also good evidence

for escitalopram and citalopram in those over 65 (Alexopoulos 2009b; Cipriani 2009). All three have the advantage of a favourable side-effect profile and can be taken by people with a history of cognitive impairment and stroke (Apler 2011).

Although citalopram was previously recommended for use in those with cardiovascular disease, recent data have highlighted the risk of prolonged QT interval with the drug, and the maximum recommended dose for older adults has now been reduced (Waring 2010; Fayssoil 2011; Howland 2011). Citalopram should not be prescribed in conjunction with other agents that prolong the QT interval, such as antipsychotics and certain antibiotics (e.g. erythromycin). It is not yet clear whether the effect on the QT interval is specific to citalopram, or whether it represents a side-effect across SSRIs more generally. Until more data are obtained to support or refute this, sertraline could be considered the best first-line SSRI option for the treatment of late-life depression on the basis of efficacy and tolerability (Cipriani 2010).

It should be noted that some studies have cast doubt on the efficacy of SSRIs in late-life depression. For example, in two randomised, double-blind trials escitalopram did not show superior efficacy over placebo in treating depression in patients over 60 years of age (Kasper 2005; Bose 2008). A meta-analysis failed to find a significant difference between citalopram and other antidepressants (e.g. tricyclics or alternative SSRIs) in terms of depression remission (Seitz 2010). There may also be clinical reasons to avoid use of SSRIs, for example in those with a history of gastrointestinal bleeding or on other medications that may precipitate this.

Mirtazapine

Where SSRIs are contraindicated, or poorly tolerated, other classes of antidepressant can be used as first-line treatment (Fig. 3). Mirtazapine is one alternative for first-line treatment in older adults (Cipriani 2009; Watanabe 2011). It has few cardiac side-effects and a weaker association with hyponatraemia (Jung 2011); in patients with insomnia and anorexia, its side-effects may be
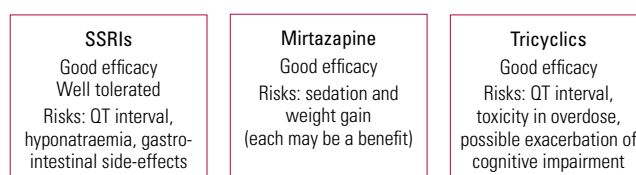
FIG 3 Monotherapy in late-life depression.

exploited for therapeutic benefit. It appears to have a faster onset of action than SSRIs, with beneficial effects found at 2 weeks (Watanabe 2011). It is worth noting that these studies supporting use of mirtazapine in older adults were not specific for this age group, but older patients were included in the analysis.

Tricyclics: nortriptyline

Tricyclic antidepressants are also effective treatments in older age groups. Nortriptyline shows efficacy and tolerability comparable to those of sertraline, with a response rate of 61% (95% CI 49%–73%) for patients on nortriptyline, compared with 72% (95% CI 61%–82%) for patients on sertraline (Bondareff 2000). Adverse effects were similar in both groups, although those prescribed nortriptyline had a significant increase in specific symptoms, including dry mouth and constipation (Bondareff 2000). Tricyclic antidepressants should be used with caution because of the risk of cardiac side-effects (e.g. prolongation of QT interval with amitriptyline) and toxicity in overdose, and because their antimuscarinic effects are more likely to exacerbate cognitive impairment.

Side-effects from all antidepressants are more common in older adults. A population-based study showed that rates of adverse effects were highest in the first 28 days after starting a prescription; SSRIs were associated with the highest risk of falls and hyponatraemia (Coupland 2011). Although Coupland *et al* did not find an increased risk of adverse events from tricyclic antidepressants (which would traditionally be associated with increased cardiovascular morbidity), given that their study was based on information from a prescribing register, it is likely that certain antidepressants would not have been prescribed to at-risk groups in clinical practice. This would have given rise to an important source of selection bias (Coupland 2011). For example, dosulepin and reboxetine are not recommended for use in older adults (National Collaborating Centre for Mental Health 2009a,b).

Second-line agents: venlafaxine

Response to antidepressants can take at least 6 weeks. If there is only a modest improvement at this stage, the antidepressant should be continued for a further 4 weeks or, if tolerated, the dose should be increased (Rush 2007). Using this strategy, a large proportion of patients would be expected to respond or remit by 12 weeks (Rush 2007). Where first-line monotherapy has been ineffective, switching to a second-line agent (in the same or a different class) is a useful strategy, particularly for those who received minimal benefit or could not tolerate the first-choice antidepressant (Rush 2007).

Venlafaxine has been proposed as a useful second-line antidepressant (Rush 2006; Lenox-Smith 2008; Cipriani 2009). An open-label study demonstrated the efficacy of venlafaxine in older patients with an atypical subtype of depression, with symptoms of mood reactivity, hypersomnia and increased appetite (Roose 2004). Venlafaxine may, however, exacerbate hypertension and therefore close monitoring of this is needed at treatment initiation.

Combination and augmentation therapy

In practical terms, stopping one antidepressant and replacing it with an alternative can be difficult in someone who is severely ill. In such cases, the use of combination (two antidepressants) or augmentation (antidepressant plus another agent) strategies may be preferable (Fig. 4). Antidepressants with separate mechanisms of action can be combined for individuals with treatment-resistant depression (Dodd 2005). Combining an SSRI with venlafaxine provides more effective treatment compared with augmentation by psychological therapy (Thase 2007). Combining mirtazapine with venlafaxine may be associated with increased side-effects, without significant therapeutic benefit (Rush 2011).

There is evidence of the beneficial effects of augmentation strategies in depression, yet despite this, those who require augmentation show lower recovery rates and recover more slowly; comorbid medical conditions and symptoms of anxiety are associated with a poorer prognosis (Dew 2007). As in younger populations, lithium can be used as an effective augmenting agent (Dew 2007). For older adults, this should be accompanied by careful monitoring of renal function, using lower doses than in younger patients. Sodium valproate is not recommended as an augmenting agent in older adults (National Collaborating Centre for Mental Health 2009a,b).
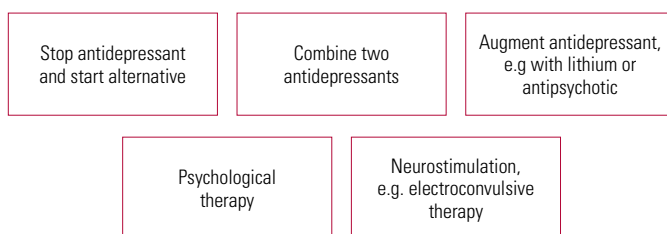
FIG 4 Strategies for treating resistant depression.

Antidepressants and antipsychotics

Augmentation of antidepressant treatment with antipsychotic medication is useful for those with severe depression, particularly where there are psychotic symptoms, providing there has been careful consideration of the risks and benefits (Alexopoulos 2011). For psychotic depression in older adults, treatment with olanzapine and sertraline has shown significantly higher remission rates than treatment with olanzapine alone (Meyers 2009). Olanzapine is associated with increased cholesterol and triglyceride concentrations, although the associated weight gain may be less significant in older people than in younger adults (Meyers 2009). In a randomised placebo-controlled study of older people with resistant depression, augmentation of citalopram with risperidone led to symptom resolution in a substantial number of participants, and a delay in time to relapse (56% in the risperidone group and 65% in the placebo group relapsed) (Alexopoulos 2008). Although these results were non-significant, they add to evidence that suggests antipsychotics may be a clinically useful strategy, particularly for subgroups of patients with severe depression and psychotic symptoms.

In older adults, especially in those with a history of cardiovascular disease, antipsychotics should be used cautiously and with careful monitoring to minimise side-effects. Antipsychotics should be avoided if there are concerns that the individual has cognitive impairment, because of the increased risk of stroke associated with their use in that context (Sacchetti 2008).

Cognitive impairment is a core feature of late-life depression, and this has resulted in the hypothesis that treating the cognitive symptoms could improve outcomes for the depression. One randomised double-blind trial compared antidepressant plus donepezil with antidepressant plus placebo in patients with late-life depression (Reynolds 2011). The addition of donepezil resulted in no clear benefit in either preventing recurrence of depression or preventing the development of mild cognitive impairment or dementia.

Relapse prevention

There is good evidence that maintenance therapy in patients over 60 who have achieved remission is effective in preventing relapses and recurrences. Tricyclic antidepressants have comparable efficacy and both show good tolerability (Kok 2011). In patients over 70, depression was less likely to recur if they maintained antidepressant treatment with paroxetine for 2 years; monthly maintenance psychotherapy (interpersonal psychotherapy) did not prevent recurrence (Reynolds 2006). Given the high risk of relapse in older patients (Beekman 2002), pharmacotherapy should be continued for at least 2 years.

Psychological therapies

Informal psychotherapeutic approaches can increase the effectiveness of pharmacological therapy. One 'treatment intervention programme' (a brief, early intervention that provided psycho-education and support) in addition to pharmaco-therapy led to improved outcomes for older adults, compared with pharmacotherapy alone (Sirey 2005). In another study, the outcome of depression among older people living in residential homes was improved by better training of care staff and by providing residents with activity programmes and education about depression (Llewellyn-Jones 1999). A package of supportive care may be particularly useful for people with mild depression or dysthymia (Ciechanowski 2004).

The evidence for use of formal psychological approaches to treat late-life depression is weak. A review of group psychotherapy for older adults with depression showed that interventions based on cognitive–behavioural therapy (CBT) had modest efficacy over waiting-list controls, and that these benefits were maintained at follow-up (Krishna 2011). A Cochrane review of psychological therapies for older people with depression found that CBT was superior to active control interventions. However, as the studies were few and heterogeneous, the evidence overall is weak. There were no trials comparing psychodynamic psychotherapy with control conditions (Wilson 2008).

An early meta-analysis of 17 studies found that a range of psychosocial treatments for depression in older adults were reliably more effective than no treatment on self- and clinician-rated depression measures (Scogin 1994). Although the evidence is weak, these may still represent an important treatment modality.

Modifications to psychotherapeutic techniques such as consideration of the context, the patients' generational group, their maturity and additional factors (e.g. physical illness and cognitive impairment) may help to improve efficacy when used with older adults (Knight 2009). Although there is limited evidence, psychological approaches to treatment on an individual level may be very useful for patients, and should therefore be considered when treating older patients with late-life depression.

There is limited evidence regarding the addition of psychological therapies to prevent relapse in older adults. In older patients with recurrent major depression, maintenance treatment with nortriptyline plus interpersonal therapy was superior to interpersonal therapy plus placebo in terms of relapse prevention, and showed a trend towards superior efficacy over nortriptyline monotherapy (Reynolds 1999). On the contrary, in older patients who showed a partial response to escitalopram, there was no additional benefit from augmenting treatment with interpersonal therapy compared with depression care management (Reynolds 2010).

Neurostimulation

Electroconvulsive therapy

Electroconvulsive therapy (ECT) is an effective and well-tolerated treatment for depression in older people (Tew 1999). It is an option for patients who have not responded to pharmacological therapy, or for patients with depressive disorder who need rapid treatment owing to the risk of self-neglect or suicide (Allan 2011a).

The main risks of ECT are related to use of a general anaesthetic, so careful assessment of medical and anaesthetic risk is needed, with clinical examination and relevant physical investigations (e.g. electrocardiogram, venepuncture and chest X-ray) prior to first ECT, repeated at regular intervals as necessary. Another important consideration is the risk of cognitive side-effects, and cognition needs to be carefully monitored before and during ECT (Kennedy 2009).

Bilateral electrode placement acts more rapidly and is more effective than unilateral, but it is associated with greater cognitive side-effects (Carney 2003). Therefore, in older patients who are at risk of cognitive impairment, unilateral placement is preferred initially, unless there are urgent clinical reasons which necessitate use of bilateral ECT. The efficacy of ECT is substantially increased by the addition of an antidepressant medication (Sackeim 2009).

Electroconvulsive therapy can be administered on an out-patient basis, provided that the patients are effectively supervised, particularly in the 24 hours following treatment. This is a useful treatment option for patients with severe depression who prefer to avoid hospital admission. Continuation ECT (where the interval between treatments is gradually increased) can reduce the number of admissions and shorten their duration for older people with severe depressive disorder (O'Connor 2010).

Alternatives to ECT

Alternative neurostimulation therapies that do not require an anaesthetic may be beneficial for patients with a range of comorbid medical conditions, although there is little research specifically on older adults. Transcranial magnetic stimulation (TMS), though not widely used in clinical practice at present, shows promise as a treatment of depression (Allan 2011b, 2012). Transcranial direct-current stimulation (tDCS) also appears to have good antidepressant efficacy (Allan 2012; Kalu 2012; Loo 2012). Both treatments have the benefit of fewer side-effects and no significant effects on cognition. They will require further evaluation, including trials in older patients, before routine use becomes widespread.

Depression and dementia

Depression is found in up to 20% of people with dementia (Nelson 2011), and is underdiagnosed and undertreated in nursing home residents with cognitive impairment (Volicer 2012). Diagnosing depression in those with cognitive impairment can be challenging, as presenting symptoms may be subtle behavioural change, sleep disturbance and reduced appetite.

Unfortunately, there is limited evidence for use of antidepressants in this patient group (Bains 2002). A meta-analysis of antidepressant treatment of people with depression and dementia showed limited efficacy; there was significant heterogeneity between studies and many were underpowered to detect differences, leading to inconclusive findings (Nelson 2011).

One of the first large studies of sertraline for the treatment of moderate depressive disorder in people with cognitive impairment showed a favourable effect (Weintraub 2010), yet follow-up studies have failed to replicate this (Rosenberg 2010). One of the largest studies in this field included over 300 patients with Alzheimer's dementia and depression, who were randomised to receive placebo, mirtazapine or sertraline; there were no significant differences between groups in terms of depression scores following treatment (Banerjee 2011). This was an important clinical finding, suggesting that antidepressants may not be a good first-line treatment for patients with depression who also have dementia. However, this study did not include patients with suicidal thoughts, and it may be that those with severe depression and suicidal ideation would have a different pattern of response to antidepressant medication.

The lack of efficacy of antidepressants in those with dementia raises the interesting question of

whether the pathophysiological mechanisms for developing depression differ in people with and without dementia. If this is the case, it could explain why antidepressants show reduced efficacy.

Although the formal evidence for efficacy of antidepressants in people with dementia is weak, it might be worthwhile trying them on individual patients in clinical practice even if there is coexisting cognitive impairment. In addition, clinicians should also focus on non-pharmacological treatments of depression such as CBT, problem-solving therapy and reminiscence therapy, which can be used to target mood as well as cognitive symptoms (Wilkins 2010). The use of behavioural treatments, including exercise, shows beneficial outcomes for depressed patients and their carers (Teri 1997, 2003).

Finally, it is important to note that depressive presentations can mimic cognitive impairment, so care must be taken to avoid diagnosing dementia in someone who has a treatable depressive illness. Clinicians should also be alert to the difficulties of differentiating subcortical vascular disease from depression; a history of treatment-resistant depression should prompt the use of neuroimaging to investigate vascular pathology such as lacunar infarcts. Magnetic resonance imaging is the preferred option for this, but vascular changes may also be visible on computed tomography (National Collaborating Centre for Mental Health 2006). Treatment approaches for subcortical vascular disease involve use of a strict behavioural approach and a highly structured daily routine.

Conclusions

Late-life depression is a common disorder, which is underrecognised and undertreated (Box 1). It is associated with high morbidity and mortality and therefore needs to be correctly diagnosed and appropriately treated. Selective serotonin reuptake inhibitors are a good first-line strategy, with particularly strong evidence for sertraline in terms of efficacy and tolerability (Cipriani 2009). It is important to continue first-line

treatment for a sufficient duration (at least 6 weeks), before increasing the dose or adding a second antidepressant, if needed (Rush 2007). Antipsychotic medication and lithium are good options for augmentation. Given the paucity of evidence for psychological therapies, combination or augmentation with pharmacological agents is likely to be more clinically effective than the addition of a psychological intervention. However, for those who are psychologically minded, these may be useful strategies.

References and further reading

Alexopoulos GS, Meyers BS, Young RC, et al (1997) 'Vascular depression' hypothesis. *Archives of General Psychiatry* **54**: 915–22.

Alexopoulos GS, Canuso CM, Gharabawi GM, et al (2008) Placebo-controlled study of relapse prevention with risperidone augmentation in older patients with resistant depression. *American Journal of Geriatric Psychiatry* **16**: 21–30.

*Alexopoulos GS, Kelly RE (2009a) Research advances in geriatric depression. *World Psychiatry* **8**: 140–9.

Alexopoulos GS, Reynolds CF, Bruce ML, et al (2009b) Reducing suicidal ideation and depression in older primary care patients: 24-month outcomes of the PROSPECT study. *American Journal of Psychiatry* **166**: 882–90.

Alexopoulos GS (2011) Pharmacotherapy for late-life depression. *Journal of Clinical Psychiatry* **72**(1): e04.

Allan CL, Ebmeier KP (2011a) The use of ECT and MST in treating depression. *International Review of Psychiatry* **23**: 400–12.

Allan CL, Herrmann LL, Ebmeier KP (2011b) Transcranial magnetic stimulation in the management of mood disorders. *Neuropsychobiology* **64**: 163–9.

Allan C, Kalu U-G, Sexton CE, et al (2012) Transcranial stimulation in depression. *British Journal of Psychiatry* **200**: 10–1.

American Psychiatric Association (1994) *Diagnostic and Statistical Manual of Mental Disorders (4th edn) (DSM-IV)*. APA.

*Anderson IM, Ferrier IN, Baldwin RC, et al (2008) Evidence-based guidelines for treating depressive disorders with antidepressants: a revision of the 2000 British Association for Psychopharmacology guidelines. *Journal of Psychopharmacology* **22**: 343–96 (available at www.bap.org.uk/pdfs/antidepressants.pdf).

Apler A (2011) Citalopram for major depressive disorder in adults: a systematic review and meta-analysis of published placebo-controlled trials. *BMJ Open* **1**(2): e000106.

*Bains J, Birks JS, Dening TR (2002) The efficacy of antidepressants in the treatment of depression in dementia. *Cochrane Database of Systematic Reviews* issue 4: CD003944.

Banerjee S, Hellier J, Dewey M, et al (2011) Sertraline or mirtazapine for depression in dementia (HTA-SADD): a randomised, multicentre, double-blind, placebo-controlled trial. *Lancet* **378**: 403–11.

Beekman AT, Copeland JR, Prince MJ (1999) Review of community prevalence of depression in later life. *British Journal of Psychiatry* **174**: 307–11.

Beekman AT, Geerlings SW, Deeg DJ, et al (2002) The natural history of late-life depression: a 6-year prospective study in the community. *Archives of General Psychiatry* **59**: 605–11.

Bondareff W, Alpert M, Friedhoff AJ, et al (2000) Comparison of sertraline and nortriptyline in the treatment of major depressive disorder in late life. *American Journal of Psychiatry* **157**: 729–36.

Bose A, Li D, Gandhi C (2008) Escitalopram in the acute treatment of depressed patients aged 60 years or older. *American Journal of Geriatric Psychiatry* **16**: 14–20.

BOX 1 Clinical summary

- Recognise late-life depression as a treatable illness
- Pay careful attention to medical and medication history
- Use a systematic approach to treatment
- Continue antidepressants for 2 years to prevent relapse
- Adopt a holistic approach to care, including psychological and social support

Brown MN, Lapane KL, Luisi AF (2002) The management of depression in older nursing home residents. *Journal of the American Geriatric Society* **50**: 69–76.

Carney S, Geddes J (2003) Electroconvulsive therapy. *BMJ* **326**: 1343–4.

Ciechanowski P, Wagner E, Schmaling K, et al (2004) Community-integrated home-based depression treatment in older adults: a randomized controlled trial. *JAMA* **291**: 1569–77.

*Cipriani A, Furukawa TA, Salanti G, et al (2009) Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis. *Lancet* **373**: 746–58.

Cipriani A, La Ferla T, Furukawa TA, et al (2010) Sertraline versus other antidepressive agents for depression. *Cochrane Database of Systematic Reviews* **14**(4): CD006117.

Coupland C, Dhiman P, Morriss R, et al (2011) Antidepressant use and risk of adverse outcomes in older people: population based cohort study. *BMJ* **343**: d4551.

Dew MA, Whyte EM, Lenze EJ, et al (2007) Recovery from major depression in older adults receiving augmentation of antidepressant pharmacotherapy. *American Journal of Psychiatry* **164**: 892–9.

Djernes JK, Gulmann NC, Foldager L, et al (2011) 13 year follow up of morbidity, mortality and use of health services among elderly depressed patients and general elderly populations. *Australian and New Zealand Journal of Psychiatry* **45**: 654–62.

Dodd S, Horgan D, Malhi GS, et al (2005) To combine or not to combine? A literature review of antidepressant combination therapy. *Journal of Affective Disorders* **89**: 1–11.

Fayssoil A, Issi J, Guerbaa M, et al (2011) Torsade de pointes induced by citalopram and amiodarone. *Annales de Cardiologie et d'Angéiologie (Paris)* **60**: 165–8.

Howland RH (2011) A critical evaluation of the cardiac toxicity of citalopram: part 1. *Journal of Psychosocial Nursing and Mental Health Services* **49**(11): 13–6.

Jung YE, Jun TY, Kim KS, et al (2011) Hyponatremia associated with selective serotonin reuptake inhibitors, mirtazapine, and venlafaxine in Korean patients with major depressive disorder. *International Journal of Clinical Pharmacology and Therapeutics* **49**: 437–43.

Kalu UG, Sexton CE, Loo CK, et al (2012) Transcranial direct current stimulation in the treatment of major depression: a meta-analysis. *Psychological Medicine* **42**: 1791–800.

Kasper S, de Swart H, Friis Andersen H (2005) Escitalopram in the treatment of depressed elderly patients. *American Journal of Geriatric Psychiatry* **13**: 884–91.

Kennedy SH, Milev R, Giacobbe P, et al (2009) Canadian Network for Mood and Anxiety Treatments (CANMAT) clinical guidelines for the management of major depressive disorder in adults. IV. Neurostimulation therapies. *Journal of Affective Disorders* **117 (suppl 1)**: S44–53.

Kivela SL, Luukinen H, Koski K, et al (1998) Early loss of mother or father predicts depression in old age. *International Journal of Geriatric Psychiatry* **13**: 527–30.

Knight BG (2009) *Psychotherapy and Older Adults Resource Guide* (online only). American Psychological Association (http://www.apa.org/pi/aging/resources/guides/psychotherapy.aspx).

Kok R, Heeren T, Nolen W (2011) Continuing treatment of depression in the elderly: a systematic review and meta-analysis of double-blinded randomized controlled trials with antidepressants. *American Journal of Geriatric Psychiatry* **19**: 249–55.

Krishna M, Jauhari A, Lepping P, et al (2011) Is group psychotherapy effective in older adults with depression? A systematic review. *International Journal of Geriatric Psychiatry* **26**: 331–40.

Lenox-Smith AJ, Jiang Q (2008) Venlafaxine extended release versus citalopram in patients with depression unresponsive to a selective serotonin reuptake inhibitor. *International Clinical Psychopharmacology* **23**: 113–9.

Llewellyn-Jones RH, Baikie KA, Smithers H, et al (1999) Multifaceted shared care intervention for late life depression in residential care: randomised controlled trial. *BMJ* **319**: 676–82.

Loo CK, Alonzo A, Martin D, et al (2012) Transcranial direct current stimulation for depression: 3-week, randomised, sham-controlled trial. *British Journal of Psychiatry* **200**: 52–9.

Mark TL, Joish VN, Hay JW, et al (2011) Antidepressant use in geriatric populations: the burden of side effects and interactions and their impact on adherence and costs. *American Journal of Geriatric Psychiatry* **19**: 211–21.

McDougall FA, Matthews FE, Kvaal K, et al (2007) Prevalence and symptomatology of depression in older people living in institutions in England and Wales. *Age and Ageing,* **36**: 562–8.

Meyers BS, Flint AJ, Rothschild AJ, et al (2009) A double-blind randomized controlled trial of olanzapine plus sertraline vs olanzapine plus placebo for psychotic depression: the study of pharmacotherapy of psychotic depression (STOP-PD). *Archives of General Psychiatry* **66**: 838–47.

Morghen S, Gentile S, Ricci E, et al (2011) Rehabilitation of older adults with hip fracture: cognitive function and walking abilities. *Journal of the American Geriatric Society* **59**: 1497–502.

*Nelson JC, Delucchi K, Schneider LS (2008) Efficacy of second generation antidepressants in late-life depression: a meta-analysis of the evidence. *American Journal of Geriatric Psychiatry* **16**: 558–67.

Nelson J, Devanand D (2011) A systematic review and meta-analysis of placebo-controlled antidepressant studies in people with depression and dementia. *Journal of the American Geriatrics Society* **59**: 577–85.

National Collaborating Centre for Mental Health (2006) *Dementia: Supporting People with Dementia and Their Carers in Health and Social Care (NICE Clinical Guideline 42)*. National Institute for Health and Clinical Excellence.

National Collaborating Centre for Mental Health (2009a) *Depression: The Treatment and Management of Depression in Adults (Updated Edition) (National Clinical Practice Guideline 90)*. British Psychological Society/Royal College of Psychiatrists.

National Collaborating Centre for Mental Health (2009b) *Depression in Adults with a Chronic Physical Health Problem: Treatment and Management (National Clinical Practice Guideline 91)*. British Psychological Society/Royal College of Psychiatrists.

O'Connor DW, Gardner B, Presnell I, et al (2010) The effectiveness of continuation-maintenance ECT in reducing depressed older patients' hospital re-admissions. *Journal of Affective Disorders* **120**: 62–6.

Reynolds CF, Frank E, Perel JM, et al (1999) Nortriptyline and interpersonal psychotherapy as maintenance therapies for recurrent major depression: a randomized controlled trial in patients older than 59 years. *JAMA* **281**: 39–45.

Reynolds CF, Dew MA, Pollock BG, et al (2006) Maintenance treatment of major depression in old age. *New England Journal of Medicine* **354**: 1130–8.

Reynolds CF, Dew MA, Martire LM, et al (2010) Treating depression to remission in older adults: a controlled evaluation of combined escitalopram with interpersonal psychotherapy versus escitalopram with depression care management. *International Journal of Geriatric Psychiatry* **25**: 1134–41.

Reynolds CF, Butters MA, Lopez O, et al (2011) Maintenance treatment of depression in old age: a randomized, double-blind, placebo-controlled evaluation of the efficacy and safety of donepezil combined with antidepressant pharmacotherapy. *Archives of General Psychiatry* **68**: 51–60.

Roose SP, Miyazaki M, Devanand D, et al (2004) An open trial of venlafaxine for the treatment of late-life atypical depression. *International Journal of Geriatric Psychiatry* **19**: 989–94.

Roose SP, Schatzberg AF (2005) The efficacy of antidepressants in the treatment of late-life depression. *Journal of Clinical Psychopharmacology* **25** (suppl 1): S1–7.

Rosenberg PB, Drye LT, Martin BK, et al (2010) Sertraline for the treatment of depression in Alzheimer disease. *American Journal of Geriatric Psychiatry* **18**: 136–45.

Rush AJ, Trivedi MH, Wisniewski SR, et al (2006) Bupropion-SR, sertraline, or venlafaxine-XR after failure of SSRIs for depression. *New England Journal of Medicine* **354**: 1231–42.

Rush AJ (2007) STAR*D: what have we learned? *American Journal of Psychiatry* **164**: 201–4.

Rush AJ, Trivedi MH, Stewart JW, et al (2011) Combining medications to enhance depression outcomes (CO-MED): acute and long-term outcomes of a single-blind randomized study. *American Journal of Psychiatry* **168**: 689–701.

Sacchetti E, Trifiro G, Caputi A, et al (2008) Risk of stroke with typical and atypical anti-psychotics: a retrospective cohort study including unexposed subjects. *Journal of Psychopharmacology* **22**: 39–46.

Sackeim HA, Dillingham EM, Prudic J, et al (2009) Effect of concomitant pharmacotherapy on electroconvulsive therapy outcomes: short-term efficacy and adverse effects. *Archives of General Psychiatry* **66**: 729–37.

Schwarzbach M, Luppa M, Sikorski C, et al (2013) The relationship between social integration and depression in non-demented primary care patients ages 75 years and older. *Journal of Affective Disorders* **145**: 172–8.

Scogin F, McElreath L (1994) Efficacy of psychosocial treatments for geriatric depression: a quantitative review. *Journal of Consulting and Clinical Psychology* **62**: 69–74.

Seitz DP, Gill SS, Conn DK (2010) Citalopram versus other antidepressants for late-life depression: a systematic review and meta-analysis. *International Journal of Geriatric Psychiatry* **25**: 1296–305.

Sirey JA, Bruce ML, Alexopoulos GS (2005) The Treatment Initiation Program: an intervention to improve depression outcomes in older adults. *American Journal of Psychiatry* **162**: 184–6.

Steptoe A, Marmot M (2003) Burden of psychosocial adversity and vulnerability in middle age: associations with biobehavioral risk factors and quality of life. *Psychosomatic Medicine* **65**: 1029–37.

Steunenberg B, Beekman AT, Deeg DJ, et al (2007) Mastery and neuroticism predict recovery of depression in later life. *American Journal of Geriatric Psychiatry* **15**: 234–42.

Teri L, Logsdon RG, Uomoto J, et al (1997) Behavioral treatment of depression in dementia patients: a controlled clinical trial. *Journals of Gerontology, Series B: Psychological Sciences and Social Sciences* **52**: P159–66.

Teri L, Gibbons LE, McCurry SM, et al (2003) Exercise plus behavioral management in patients with Alzheimer disease: a randomized controlled trial. *JAMA* **290**: 2015–22.

Tew JD, Mulsant BH, Haskett RF, et al (1999) Acute efficacy of ECT in the treatment of major depression in the old-old. *American Journal of Psychiatry* **156**: 1865–70.

Thase ME, Friedman ES, Biggs MM, et al (2007) Cognitive therapy versus medication in augmentation and switch strategies as second-step treatments: a STAR*D report. *American Journal of Psychiatry* **164**: 739–52.

Turnheim K (2003) When drug therapy gets old: pharmacokinetics and pharmacodynamics in the elderly. *Experimental Gerontology* **38**: 843–53.

Volicer L, Frijters DH, Van der Steen JT (2012) Relationship between symptoms of depression and agitation in nursing home residents with dementia. *International Journal of Geriatric Psychiatry* **27**: 749–54.

Waring WS, Graham A, Gray J, et al (2010) Evaluation of a QT nomogram for risk assessment after antidepressant overdose. *British Journal of Clinical Pharmacology* **70**: 881–5.

Watanabe N, Omori IM, Nakagawa A, et al (2011) Mirtazapine versus other antidepressive agents for depression. *Cochrane Database of Systematic Reviews* issue 12: CD006528.

Weintraub D, Rosenberg PB, Drye LT, et al (2010) Sertraline for the treatment of depression in Alzheimer disease: week-24 outcomes. *American Journal of Geriatric Psychiatry* **18**: 332–40.

Wilkins V, Kiosses D, Ravdin L (2010) Late-life depression with comorbid cognitive impairment and disability: nonpharmacological interventions. *Clinical Interventions in Aging* **5**: 323–31.

Wilson KC, Mottram PG, Vassilas CA (2008) Psychotherapeutic treatments for older depressed people. *Cochrane Database of Systematic Reviews* (1): CD004853.

World Health Organization (1992) *The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines.* WHO.

*An asterisk denotes recommended further reading.

MCQs

Select the single best option for each question stem

1 What percentage of older people living in institutions have depression?

a 5%

b 10%

c 20%

d 25%

e 30%.

2 The SSRI with the best evidence for efficacy and effectiveness in late-life depression is:

a citalopram

b escitalopram

c sertraline

d fluoxetine

e paroxetine.

3 Olanzapine can be used where clinical benefits outweigh the risks; preferably, it is used to augment antidepressants in patients with:

a no significant medical history

b diabetes

c heart disease

d history of stroke

e cognitive impairment.

4 To prevent relapse, pharmacotherapy should be continued for:

a 3 months

b 6 months

c 1 year

d 2 years

e indefinitely.

5 In what proportion of people is depression comorbid with dementia?

a 10%

b 20%

c 30%

d 40%

e 50%.