CLINICAL REVIEW

CME

Depression in older adults

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Depression is a major contributor to healthcare costs and is projected to be the leading cause of disease burden in middle and higher income countries by the year 2030.[w1] Depression in later life, traditionally defined as age older than 65, is associated with disability, increased mortality, and poorer outcomes from physical illness. Most clinicians will encounter older patients with depression in their day to day practice, but although treatment is as effective for older patients as for younger adults, the condition is often under-recognised and under-treated. According to WHO data, proportionately more people aged over 65 commit suicide than any other age group, and most have major depression. Older people who attempt suicide are more likely to die than younger people, while in those who survive, prognosis is worse for older adults.[1]

With a progressively ageing population worldwide, identification and treatment of depression in older adults becomes increasingly important, especially as older patients may have different presentations and needs than younger ones. We consider recent systematic reviews, meta-analyses, and randomised controlled trials to provide generalists with an understanding of current approaches to the diagnosis and management of patients who develop late life depression.

What is late life depression and who gets it?

Traditionally, the age of 65 has been used to differentiate between "older" and "younger" adults, although there is no set point at which an individual becomes "older" and assessment and care must be based on individual need. Arbitrary definitions of "late life" and differences between studies in terms of diagnostic criteria and populations sampled have produced varying reports of prevalence. Individuals with late life depression represent a hetero-

SOURCES AND SELECTION CRITERIA

We based the review on searches of PubMed, EMBASE, and the Cochrane Database of Systematic Reviews using the search terms "depression", "elderly", "aged", and "old age" published between 2006 and 2011 and limited to English language. We focused on well conducted systematic reviews, meta-analyses, and randomised controlled trials.

geneous group with symptoms that may fall anywhere on a spectrum ranging from sub-threshold mood disorder to major depression. A recent comprehensive meta-analysis using studies with moderate to high methodological quality showed that the point prevalence of major depression in over 75s ranged from 4.6% to 9.3%[2] whereas rates for sub-threshold depressive symptoms (those failing to reach diagnostic criteria) ranged from 4.5% to 37.4%. A related meta-analysis in people aged over 55 found that sub-threshold depressive symptomatology was two to three times more prevalent than major depression.[2] Most depressive episodes in late life will be a recurrence rather than a first ever episode[w2] and the increased female to male ratio is in line with that in younger adults.

Prevalence rates of depression are increased in brain disorders including dementia, Parkinson's disease, and stroke, and also in systemic disease, for example diabetes mellitus and cardiovascular disease (box 1). Prevalence estimates for depression in Alzheimer's disease cluster around 30% but range from 0% to 86%,[w3] reflecting the difficulty associated with definition and diagnosis of depression in dementia.

How is depression diagnosed in older patients?

Box 2 lists the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for diagnosis of a major depressive episode. Ideally diagnosis is based on clinical interview, observation of the patient's behaviour, and a collateral history from relatives and care givers. When taking a background history it is important to identify factors that may precipitate and maintain depression. The main risk factors for late life depression are comorbid physical illness, cognitive impairment, functional impairment, lack or loss of close social contacts, and a previous history of depression (box 1), according to the findings of large community based studies.

The risk assessment is important in any psychiatric presentation, and in patients with depression the main area of risk is suicide. Methodologically sound controlled studies have identified some key risk factors for suicide, listed in box 3.

SUMMARY POINTS

Depression in older adults is associated with an increased risk of death and disability

Cognitive and functional impairment and anxiety are more common in older than in younger adults with depression

Older adults with depression are at increased risk of suicide and are more likely than younger adults to complete suicide

Depression is associated with cognitive impairment and an increased risk of dementia

A selective serotonin reuptake inhibitor should be the first line pharmacological treatment for depression for most older adults, including those with chronic physical illness

Psychological and drug treatment is as effective in older as in younger adults

Subthreshold depressive symptoms that substantially affect older patients' lives are common and management with psychosocial and drug strategies may be effective and prevent further deterioration

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Box 1 | Risk factors for depression in elderly people[30]

Physical factors

Chronic disease, such as diabetes, ischaemic heart disease, heart failure, chronic obstructive pulmonary disease

Acute myocardial infarction

Organic brain disease: dementia, stroke, Parkinson's disease, cerebrovascular disease

Endocrine/metabolic disorders: thyroid disease, hypercalcaemia, B12 and folate deficiency

Malignancy

Chronic pain and disability

Psychosocial factors

Social isolation

Change in financial circumstances

Being a carer

Change of role and loss of social status

Bereavement and loss

Difficulty in adapting to illness/pain/disability

Poor defences against anxiety about death

History of depression

Being in institutional care

Box 2 | DSM-IV criteria for major depressive episode

Nearly every day for the preceding two weeks the patient has experienced five or more of:

Depressed mood for most of the day*

Decreased interest or pleasure in nearly all activities for most of the day*

Marked loss or gain of weight or markedly increased or decreased appetite

Excessive sleep or not enough sleep

Observable psychomotor agitation or retardation

Tiredness or loss of energy

Feelings of guilt or worthlessness

Poor concentration or indecisiveness

Thoughts of dying or suicide, suicide attempt

*One of these features must be present. Depressed mood for ≥2 weeks not meeting these criteria is defined as a minor depressive episode. Diagnostic and statistical manual of mental disorders (DSMIV), American Psychiatric Association, 1994

Box 3 | Risk factors for suicide in older people[1]

Older age, male sex

Social isolation

Bereavement

History of attempts

Evidence of planning

Chronic painful illness or disability

Drug or alcohol use

Sleep disorders

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tion of the patient health questionnaire, geriatric depression scale, hospital anxiety and depression scale, and the Cornell scale for depression in dementia (box 4).

Is depression more difficult to diagnose in older adults?

Several studies have shown that older adults are significantly less likely than younger ones to recognise depressive symptoms, which they attribute to normal ageing or physical illness, and that both patients and their doctors tend to view depression as a problem that can be explained away, rather than as an objective illness that warrants treatment.[w5] These findings suggest that older adults might be less able to identify, and therefore seek appropriate treatment for, common depressive symptoms.

In our clinical experience, late life depression differs qualitatively from depression in early life. Somatisation, hypochondriasis, psychomotor retardation or agitation, and psychosis more commonly form part of the clinical picture, although this tendency has not been uniformly demonstrated.[3] Furthermore, late life depression has been associated with cognitive impairment, physical disability, and anxiety, with a large community naturalistic study suggesting that clinically important anxiety coexists in around 50% of patients aged 55-85.[4]

Does depression increase the risk of dementia?

Most studies find that depression in late life is accompanied by measurable cognitive impairment, mediated by memory deficits, diminished executive function, and slowed information processing, which may resolve on remission of symptoms, or may persist even after effective treatment of mood. In the past, the term "depressive pseudodementia" was used to describe reversible dementia in depression, but this oversimplifies the complex spectrum of cognitive impairment.

Two systematic meta-analyses of high quality studies[5][6] report that late onset depression (after age 65) increases the risk of dementia twofold, but as yet no research has ascertained whether depression is a risk factor for dementia or represents a prodromal condition.[7]

Several mechanisms have been proposed to explain the relation between depression and dementia, including hypercortisolaemia, loss of hippocampal volume, neuro-inflammatory processes, increased Alzheimer-type pathology, reduced cognitive reserve, and vascular disease. None has yet been conclusively demonstrated, but the link is probably multifactorial and the mechanisms not mutually exclusive.

Of these potential mechanisms, vascular changes in the brain have attracted most attention. The key hypothesis is that disruption of prefrontal-striatal circuitry by

Older patients often have symptoms of depression that do not meet the criteria for a major depressive episode (box 2) but are nonetheless clinically important. Identification of the psychological and functional effects of these symptoms determines whether or not treatment is indicated and who may benefit from interventions.

Current guidance for the assessment and management of depression from the UK National Institute for Health and Clinical Excellence (NICE) (http://guidance.nice.org.uk/CG90/QuickRefGuide/pdf/English) recommends the use of rating scales to determine severity, although many are weighted towards the presence of somatic symptoms and may therefore overestimate depression in older people, in whom such symptoms are common.

A recent comparison of several assessment scales (patient health questionnaire, Beck depression inventory, hospital anxiety and depression scale) in a primary care population found that treatment and referral rates were identical even though each tool identified differing numbers of patients with moderate to severe depression. However, regardless of the tool used, rates for treatment in older people still remained lower than for younger adults.[w4] Many rating scales are in common use to assess depression but few are well validated in older people, with the excep-

Box 4 | Useful scales for depression

Geriatric depression scale (GDS-15)*

Specifically developed for use in geriatric patients; contains fewer somatic items; suitable only for patients with no, mild, or moderate cognitive impairment (>15/30 on mini-mental state examination)

Well validated in older people. Cut-off score in population over 60 of ≥5 indicates a case of depression: sensitivity 92%, specificity 54%[w12 w13]

Cornell scale for depression in dementia (CSDD)*

Suitable for patients with cognitive deficit, not diagnostic for depression but higher scores indicate greater need for further evaluation[w14]

Patient health questionnaire (PHQ-9)*

Self reported depression assessment tool scoring each of the nine DSM-IV criteria as 0 (not at all) to 3 (nearly every day)

Validated in adults over 60 in primary care in the United States and Netherlands. With cut-off score of >9 has sensitivity 88%, specificity 80%[w15 w16]

Beck depression inventory (BDI)

Self reported seven item scale

Not recommended for use in older people owing to focus on somatic symptoms[w17]

Hospital anxiety and depression scale (HADS)*

Self-rating scale containing two subscales measuring symptoms of depression (HADS-D) and anxiety (HADS-A) during previous week. Scores >8 for both HADS-A and HADS-D have sensitivity and specificity of 80% and predictive validity of 70%

HADS identifies equal numbers of patients with depression regardless of age[w18]

Montgomery and Åsberg depression rating scale (MADRS)

Clinician rated 10 item scale, measures severity of depressive symptoms; sensitive to change; mainly used to assess response to treatment but no agreement on cut-off score for remission (between ≤4 and ≤10), popular in Europe

*Validated in older adults

cerebrovascular pathology produces a syndrome of mood disorder and executive dysfunction. This syndrome is variously described as "vascular depression" or "depression executive dysfunction syndrome",[8] reflecting fundamental nosological differences. However, the concept is controversial, and a prospective population based post-mortem study of over 65s found no association between depression and cerebrovascular pathology.[9] Randomised controlled trials have shown that presence of "vascular depression"/"depression executive dysfunction syndrome" may predict a worse response to antidepressant drug treatment[10] and is associated with increased mortality.[11] There is currently no evidence to suggest that treating depression in early or late life reduces the incidence of dementia.

How is late life depression managed?

Given the association between medical morbidity and depression, exclusion of underlying causative or exacer-

Box 5 | Investigations to consider when depression is suspected

Full blood count

Urea and electrolytes

Liver function tests

Thyroid function tests

Vitamin B12

Folate

Fasting glucose

Bone profile

Further tests dictated by clinical presentation

bating factors is an important first step in the management of late life depression (box 1). Baseline investigations, for example routine blood tests, may be indicated (box 5).

In subsyndromal and mild depression, psychosocial interventions may be sufficient to cause an improvement. These include increasing social contact and adding structure to the day; for example, assistance in accessing local community events, day centres, or befriending services. Evidence from randomised trials suggests that depressive symptoms in older adults may improve with structured exercise programmes.[12] A RCT of a stepped care approach to the management of subthreshold depressive symptoms found that the intervention (watchful waiting, bibliotherapy based on cognitive behavioural therapy, problem solving therapy, and medication) was associated with a 50% reduction in depression and anxiety disorders at 12 months[13] compared with treatment as usual and was cost effective.[w6]

Current NICE guidance recommends that patients with mild or sub-threshold illness who do not respond well to initial supportive interventions are offered psychological therapy or antidepressant medication, while a combination of both interventions is recommended for those with moderate or severe illness.

When should I refer?

NICE guidance recommends that patients are referred to specialist services if they have not responded adequately to management options available in primary care; in severe depression, psychosis, or complex psychosocial situations; and where the degree of risk warrants specialist input. We also emphasise the need to refer older people with comorbid cognitive decline.

Services available in the UK vary geographically and are constantly evolving. A randomised controlled trial of home treatment versus conventional outpatient care for patients aged over 64 living independently and recruited from primary and secondary care services in Austria found significantly reduced depressive symptoms, improved global function, fewer admissions and lower costs of care in the home treatment arm at 3 and 12 months' follow-up.[14] Studies of collaborative care interventions, where care is delivered through integrated mental health and primary care providers, have also repeatedly reported improved outcomes compared with usual care[w7] although the effect appeared to be associated with prescription of antidepressant medication rather than better communication between primary care providers and mental health services.

Which medication should be prescribed?

Selective serotonin reuptake inhibitors (SSRIs) are well established as first line treatment for depression in older adults. A Cochrane review included 32 randomised controlled trials of antidepressant treatment in people aged 55 or over and reported that SSRIs and tricyclic antidepressants had similar efficacy, but that tricyclics were associated with more side effects and withdrawal from treatment.[15] It was not possible to compare efficacy for other antidepressant groups. Findings from a 2008 meta-analysis of second generation antidepressants in older adults (SSRIs,

selective serotonin and noradrenaline reuptake inhibitors, bupropion, and mirtazapine) found that treatment in studies lasting 10 weeks or longer was associated with an improved response, supporting the long held belief that response to antidepressants is delayed in older adults.[16] A recent meta-analysis showed an advantage of SSRIs or tricyclic antidepressants over placebo in the treatment of patients with depression in the context of chronic physical illness.[17] Furthermore, evidence from randomised controlled trials has shown that antidepressants are efficacious in depression after stroke[18] and myocardial infarction.[19] Interestingly, a 2007 meta-analysis of 10 randomised

controlled trials of prophylactic antidepressant treatment after stroke reported a significant reduction in the rate of post-stroke depression in treatment groups.[20] However, a large randomised controlled trial has recently shown that two commonly used antidepressants, sertraline and mirtazapine, were not appreciably different from placebo in treating depression in patients with Alzheimer's disease. This effect was sustained at 10 months' follow-up and side effects were increased in the antidepressant group.[21]

Overall, an SSRI is usually the safest choice in patients with physical illness; the most common drug interactions are mediated via cytochrome p450 enzymes, and citalopram, escitalopram, and sertraline are safest in this regard.

Common side effects of particular concern in the elderly are anticholinergic effects, postural hypotension, and sedation, all of which are more common with tricyclic antidepressants than with SSRIs.[20] The risk can be minimised by starting at a low dose and slowly titrating upward. The risk of hyponatraemia induced by antidepressants increases with age and is associated with female sex, low body weight, renal failure, prescription of other drugs associated with hyponatraemia (such as diuretics), and medical comorbidity.[w8 w9] Older patients prescribed SSRIs are also at increased risk of both upper and lower gastrointestinal bleeding.[w10] Monitoring of serum sodium levels may be necessary, and the risk of gastrointestinal bleeding can be reduced by prescribing proton pump inhibitors.

NICE guidance recommends that antidepressant treatment is continued for at least six months for a single episode and at least two years if patients are thought to be at risk of relapse. A meta-analysis of eight double-blind placebo controlled trials of maintenance antidepressant therapy between 6 and 36 months in people over 55, published in 2011, found that the optimal duration in older adults is uncertain.[22] We suggest that a practical approach is to regularly review depressive symptoms, side effects, comorbidity, and current psychosocial stressors and to involve the patient in the decision making process about ongoing drug treatment.

What if first line drug treatment doesn't work?

A 2011 systematic review and meta-analysis of inadequate response to treatment in older patients included 13 studies, most of which were open label.[23] The overall response rate for active treatment was 52%, and studies reporting positive results for augmentation of treatment with lithium or antipsychotics, and treatment with venlafaxine, duloxetine, selegiline, or phenelzine, were included. Lithium augmentation was the only treatment for which evidence of efficacy was replicated in more than two studies. We suggest that augmentation of treatment with antipsychotic medication should be used with particular caution in view of the susceptibility of older people to adverse drug reactions, and the paucity of data on safety.

Electroconvulsive therapy is sometimes used after inadequate response to drug treatment, although the usual indication is severe depressive illness in which life threatening refusal of food or fluid, risk of suicide, or psychotic features are present. Electroconvulsive therapy is a safe and effective treatment in the elderly despite an absence of methodologically sound evidence from randomised controlled trials.[24]

Can older adults benefit from psychological therapy?

Results from a 2009 meta-regression analysis suggest that psychological therapy—particularly cognitive behavioural therapy, interpersonal therapy, and problem solving therapy—is equally effective in older and younger adults with depression.[25] Combined psychological therapy and pharmacological therapy is more effective than psychological treatment alone for older people with depression.[26]

What is the outlook for older adults with depression?

A 2005 systematic review of studies comparing outcomes in depression in middle life with those in later life found that rates of remission were similar in both groups, but that late life depression was associated with higher rates of relapse.[27] A longitudinal primary care cohort study in the Netherlands reported that the median duration of a major depressive episode in late life was 18 months, with two thirds of patients taking three years to recover.[28] In the PRISM-E study, a large study of older patients with major depressive disorder, complete remission was attained in only 29% of patients at six month follow-up.[29] Factors associated with prolonged recovery in these studies included severity of depression at baseline, a family history of depression, comorbid anxiety, and general medical comorbidity.

A population based, age stratified, longitudinal study found that adults aged 70-84 years with depression have an increased risk of mortality compared with those who do not have depression, dying on average three years earlier. This risk holds beyond the effects of age, sex, and the presence of dementia, cardiovascular, and other somatic diseases, but did not persist in the oldest old—defined as those aged 85 to 101.[w11]

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