Mental Illness in the Oldest-Old

17

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Introduction

There is comparatively limited data on psychiatric illness in the elderly and even less so in the oldest-old. Whilst there are broad similarities in clinical presentation and management between the oldest-old and their younger counterparts, some qualitative differences between these groups highlight the need for clinicians to modify their diagnostic and management approaches.

Psychiatry differs from most other branches of medicine in that it is based largely on the description and treatment of syndromes. Whilst research is gradually closing in on many of the biological substrates associated with psychiatric conditions, for now at least there are no definitive investigative markers with which to confirm the presence of a specific mental illness. A diagnosis of major depression or schizophrenia is based on clinical assessment, not a blood test or cerebral scan. Given the great potential for symptomatic overlap between different conditions, this can make for challenging diagnostic waters and underscores the particular importance of performing a careful history and mental state examination as part of a methodical diagnostic and management approach in this group.

Historically, distinction was made between psychological conditions that were *secondary* to "organic" disease (i.e. demonstrated physical conditions) and those that were *primary*, due to "functional or non-organic" disease (i.e. occurring in the absence of demonstrable physical illness and so assumed to have some other aetiology). This is obviously a limiting and artificial categorisation, particularly in the oldest-old where multiple physical comorbidities and polypharmacy are largely the norm and any distinction between "primary or non-organic" and "secondary or organic" becomes increasingly blurred. Nevertheless, a broad appreciation of the interplay between the "psychological" and the "physical" can still assist in diagnostic formulation and therefore in directing best initial management. This relationship could be considered as follows:

A physical problem (or its treatment) causes psychological symptoms.
A psychological problem (or its treatment) causes physical symptoms.
A separate condition causes both psychological and physical symptoms.

Common Psychiatric Presentations

The major neuropsychiatric syndromes encountered in the oldest-old include the *mood disorders* (depression and mania), *anxiety disorders*, *psychotic disorders*, and *cognitive disorders* (covered elsewhere in this text). On encountering these symptoms in the elderly patient, the clinician should consider whether they are:

1. Due to an acute, potentially reversible medical issue
2. Due to an acute, reversible, or transient stress
3. Part of a more sustained, pervasive disorder

Psychological Disturbance Due to an Acute, Potentially Reversible Medical Issue

The elderly present with underlying vulnerability in the form of age-related systemic changes, multiple medical comorbidities, and frequent polypharmacy. Even relatively minor homeostatic disturbances can result in significant psychological and behavioural symptoms. Potentially treatable causes of psychological symptoms are shown in Table 17.1.

Psychological Disturbance Due to an Acute, Reversible, or Transient Stress

Distinguishing these conditions from other psychiatric disorders is important, as symptom course, impact on function, and level of associated risk are different. It will also

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Table 17.1 Potentially treatable causes of psychological symptoms

Delirium
Depression, mania, anxiety, psychosis [1]
Neurological conditions
Pain (of any kind)
Epilepsy (especially complex partial seizures): mood disorders, psychosis, cognitive changes
Normal pressure hydrocephalus: apathy, inertia, cognitive changes [2]
Endocrine disease [3]
Hypothyroidism: depression, cognitive changes, psychosis
Hyperthyroidism: anxiety, mania/mixed affective states, psychosis
Cushing's syndrome: fatigue, depression, cognitive changes
Addison's disease: apathy, depression
Metabolic or nutritional problems [3]
B12/folate deficiency: can contribute to depression
Anaemia: fatigue, can contribute to depression
Hypercalcaemia: depression, cognitive changes
Hypoglycaemia: anxiety, irritability, cognitive changes
Respiratory
Obstructive sleep apnoea: can present with amotivation, lethargy, dysphoria
Cancer (direct and indirect effects): mood changes, psychosis
Prescribed medication
Opiates/benzodiazepines: depression, anxiety, cognitive changes
Antihypertensives: depression, anxiety (beta-blockers, calcium blockers)
Corticosteroids: depression, anxiety, cognitive changes, or mania/psychosis (esp. higher doses)
Anti-Parkinsonian medication (dopaminergic): psychosis, anxiety/depression (during "off" cycles), pathological gambling
Anti-epileptic medications: depression, cognitive changes
Substance use
Caffeine: anxiety, insomnia
Nicotine: anxiety
Alcohol: depression, anxiety, cognitive changes

Information sources: American Psychiatric Association [1]; Lovestone [2]; Harrison & Kopelman [3]

affect management; identifying these conditions does not mean no intervention is required, only that a different range of treatment approaches may be more appropriate. Common time-limited psychological reactions to intermittent stress include grief and loss, other "adjustment disorders", to specific life stresses, and transient demoralisation, anxiety, or misperceptions in cognitive impairment and dementia [4].

Psychological Disturbance Due to a More Sustained, Pervasive Disorder

Sometimes depression, mania, anxiety, and psychosis presenting in the elderly are part of a more pervasive, entrenched constellation of symptoms that may not respond to simple general measures and require a more elaborate treatment approach. In the elderly, these may be either:

1. A relapse of a pre-existing condition (with its onset earlier in life)
2. A new condition of late onset

Pathogenesis involves a combination of underlying predisposing vulnerability factors interacting over time with any number of accumulating stresses, eventually manifesting clinically as disease. These include genetic, medical, psychological, social, and cultural influences. The extent and manner in which they combine in a particular individual can influence the way symptoms manifest.

Studies of mood and psychotic disorders in the elderly that have had their first onset earlier in life consistently show stronger associations with a positive family history. In contrast, disorders presenting for the very first time in old age have fewer genetic links. Late-onset conditions have weaker direct association with stressful psychosocial triggers and instead are more commonly associated with underlying neurological signs and medical problems, particularly cerebrovascular disease [5–16] Table 17.2.

Late-onset mental illness is more commonly associated with cognitive deficits. Neurocognitive assessment has demonstrated varying degrees of impaired executive function, processing speed, and attention, memory, and language function, reflecting predominantly frontosubcortical changes [23–32]. Imaging studies have shown reductions in caudate or hippocampal neuronal volume in depression and in bipolar disorder. The pathological basis remains unclear. Theories include a

Table 17.2 Other medical conditions associated with late-onset psychological symptoms

Cerebrovascular disease
Generalised (in the form of accumulating small vessel disease or silent lacunar infarcts) or localised (ischaemic or haemorrhagic stroke), often on a background of vascular risk factors
Other neurological conditions
Parkinson's disease: depression, anxiety, cognitive changes, psychosis [16–18]
Dementia
(behavioural and psychological symptoms of dementia – BPSD)
Given the widespread, progressive neurochemical and structural impacts on the brain, any array of psychopathology is possible and occurs in as many as 90% of cases. Depression, anxiety, or psychosis (often with persecutory beliefs or hallucinations) are common. Mania and excitability are reported. Agitation and aggression or withdrawal and apathy can occur [19, 20]. Whilst these psychiatric features can occur in any type of dementia, some symptom patterns may more commonly accompany specific dementia types. Lewy body disease commonly presents with vivid visual hallucinations. Frontal dementias (of any cause) may have significant cross-sectional symptomatic overlap with either depression (apathy, diminished communication, and indifference) or mania (social disinhibition, impulsivity, and hyperactivity) [21, 22]

Information sources: Nilsson et al. [16]; Zhang et al. [17]; Schneider et al. [18]; Brodaty et al. [19]; van der Linde et al. [20]; Pose et al. [21]; Wylie et al. [22]

process of CNS neuroinflammation (associated with elevated inflammatory markers including white cells, cytokines, and CRP), reduced neurogenesis (associated with decreased brain-derived neurotrophin factor), and cumulative damage caused by repetitive stress-induced high-cortisol states [33–39]. Other studies emphasise the role of cerebrovascular disease in the pathogenesis of both mental illness and cognitive impairment. Certainly, cognitive changes are far more likely in the presence of underlying cerebrovascular disease, which is also associated with poorer treatment response [10–12, 15, 36, 40, 41]. Regardless of underlying aetiological factors, several pervasive psychiatric syndromes are commonly encountered in the elderly and are discussed below.

Major Depression

In the oldest-old, the prevalence of significant depression has been reported as ranging from around 5–32% [42–44]. Perhaps not surprisingly, there is a higher risk in those living alone or isolated from loved ones, those with poor physical health or impaired IADLs, and those with cognitive impairment [43, 45–47]. In general, depression in the very old presents in a similar fashion to other age groups. However the depressed elderly may present with less typical clinical features including higher rates of sub-threshold depressive features and "depression without sadness", somatic preoccupation or unexplained physical symptoms, and apathy. This may affect diagnostic accuracy, particularly when using narrower definitions or excluding high-risk subpopulations (those with cognitive impairment or dwelling in residential facilities) [47–52].

Numerous attempts have been made to classify depressive subtypes. One hierarchical model proposes three broad subgroups: non-melancholic depression (where anxiety is common, and mood disturbance is more closely linked to the underlying temperament and personality), melancholic depression (with more distinctive mood, sleep, and psychomotor changes), and psychotic depression (melancholia along with distortions in beliefs and perception that often have a mood-congruent quality) [53]. All require treatment.

Hypomania and Mania

Bipolar disorder in the elderly is uncommon, estimated at 0.1–0.5% prevalence in over 65-year-olds (compared with 1.4% in young adults) although rates are much higher in inpatient populations [54, 55]. Many cases may represent relapse of an early-onset illness, either of a previously established bipolar disorder or through a recurrent depression that has switched to mania for the first time in late life, often after a latency of some decades. New-onset cases of mood elevation have associations with the various medical, cerebrovascular, and cognitive factors described earlier. Whilst the clinical features are broadly similar at any age, mania in the elderly is arguably less intense and more likely associated with longer duration of symptoms [54]. In mania, symptoms last at least a week, cause significant functional impairment, and can be so severe that psychosis (including grandiose or paranoid delusions and marked thought disorder) occurs. At least one lifetime episode of mania enables a diagnosis of bipolar I disorder. In hypomania symptoms can be briefer (4 days) and are generally less severe (so overall function remains mostly intact). Hypomania can occur in bipolar I disorder (if mania has previously occurred) but otherwise if associated with a history of previous major depression would enable a diagnosis of bipolar II disorder [4].

Anxiety Disorders

Anxiety disorders are prevalent in the elderly at 15%, with even higher rates of less specific anxiety symptoms [56, 57]. Almost all begin earlier in life, following a relapsing-remitting course across the lifespan with a tendency to flare-up in response to life stresses (psychosocial and physical), often recurring in the elderly at the very time when long-established coping structures are starting to fail. Risk factors include female gender, being single, multiple medical comorbidities (including vascular disease), and certain temperamental traits (neuroticism and perfectionism) [58–60]. Only a minority will have new-onset anxiety in late life. This could be in the context of an adjustment disorder or in the setting of cognitive decline or medical illness. More prominent agitation and dysphoria would raise suspicion of anxiety secondary to a major depression, although depression and anxiety often co-exist independently in the oldest-old [61]. Common anxiety disorders include generalised anxiety disorders (GADs), phobias, panic disorder, obsessive compulsive disorder (OCD), and post-traumatic stress disorder (PTSD) [4].

In the elderly, GAD is the most common form, is highly comorbid with other psychiatric illnesses (especially depression), and is possibly more common in some medical illnesses (such as stroke or Parkinson's disease) [61–63]. Phobias are also common. Specific phobias in the elderly more often involve fears around the natural environment (lightning, heights) than younger adults. They also have high rates (around 60% in some samples) of fear of falling, a multifactorial condition more frequent in the setting of balance problems or after a previous fall, which can be associated with generalised anxiety and depression [64–68]. Agoraphobia can be the product of fear of falling, fear of social embarrassment (e.g. in incontinence), or of having a panic attack in public. It can result in social isolation, physi-

cal deconditioning (and worsening mobility), and reduced quality of life.

Panic disorder, OCD, and PTSD are much less common and often associated with physical illness or cognitive impairment [69]. Some studies suggest more frequent obsessions around sin, more compulsive hand-washing, and more severe hoarding in older people with OCD compared to their younger counterparts [70, 71]. New traumas in late life (such as falls, cancer scares, traumatic bereavements, and frightening delirium experiences) can present with PTSD-like anxiety features, whilst physical, cognitive, and psychosocial stresses in old age can also reignite PTSD from earlier-life traumas (including childhood and military experiences).

Psychotic Disorders

Psychotic disorders are characterised by varying patterns of "positive symptoms": distortion in beliefs (delusions), perception (illusions, hallucinations), and thought form. Delusions are strongly held convictions outside of social or cultural norms, either entirely false or unrealistic, and largely impervious to reason. There are many different forms, including persecutory, grandiose, somatic, nihilistic, and referential. Perceptual distortions in the absence (hallucinations) or presence (illusions) of an external trigger may occur in any sensory modality. Formal thought disorder, inferred through the expression of language, may be subtle (such as the divergent loss of goal in tangentiality) or prominent (such as loosening of the associated connectedness between different ideas or topics or the more dramatic loss of grammatical cohesion in "word salad"). "Negative symptoms" (flattening of affective expression, avolition, alogia, ambivalence, and reduced attention) can occur in some forms of psychosis.

Psychosis is common in old age. This is usually a secondary psychosis (as discussed earlier), although primary psychotic disorders also occur. Secondary psychotic syndromes in the elderly include delirium, dementia, and mood disorders. The primary psychotic syndromes include delusional disorder, schizophrenia, and schizoaffective disorder [4]. Whilst there is much symptomatic overlap irrespective of the underlying cause of psychosis, some patterns are often evident and hint at likely aetiology.

Primary psychotic illnesses with their onset early in life follow a variable course and can persist into old age. Depending on the severity of the illness and the efficacy of previous treatment, one may expect to see the psychosocial impacts of many decades of a chronic or relapsing-remitting illness. The toll of many years of antipsychotic dopaminergic blockade or mood stabiliser use will also often be evident in the form of extrapyramidal side effects, tardive syndromes, metabolic disease, or renal and electrolyte abnormality.

Primary psychotic conditions can also have their onset in late life. There is a clear female preponderance. Higher rates have been reported in populations who experience marginalisation, discrimination, or communication difficulties such as migrants and the hearing or vision impaired. Clinically they may meet traditional criteria for schizophrenia or delusional disorder, or fall somewhere in between. They have been variously referred to as late paraphrenia, late-onset (after age 40) schizophrenia, and very late-onset (after age 60) schizophrenia-like psychosis, reflecting the lack of clarity in definition, classification, and phenomenology in the literature, in what is likely a very heterogeneous group of patients [72, 73]. Persecutory beliefs occur in the majority, often in the form of "partition delusions" (the belief of being monitored or affected by someone through the walls, floor or ceiling, either directly or with gas, radiation, or electricity). Auditory hallucinations are common. Disorder of thought form is rare and affect is usually preserved. Mild cognitive deficit may be evident [32, 74–76].

Suicide in the Elderly

Suicide is significantly more common in males, with two peaks across the lifespan: one in middle age and a second in the oldest-old. Australian rates in 2015 were 31.5/100,000 men aged 45–49 and 39.3/100,000 men over 85 [77]. Depression is a prominent risk factor, especially when anxiety is comorbid, yet in a concerning majority of cases, it will remain undetected prior to the attempt [78–81]. Higher rates are reported in the presence of physical illness (especially cancer and cardiovascular disease) or disability, in social isolation, and in temperaments characterised by introversion, anxious, and obsessional features [78, 79, 82–84]. A disrupted sense of self following traumatic loss, loneliness, intolerable anxiety, loss of control or autonomy, and hopelessness have been described as common underlying themes [84–86].

Key Elements of the Psychiatric Assessment in the Elderly

History and Examination

1. Obtain collateral information (from family, friends, caregivers) especially in the presence of cognitive impairment, where recollection and articulation of symptoms can become limited. In addition to aiding diagnosis, this provides valuable information regarding premorbid personality style, baseline function, and extent of existing social and supportive structures.

2. Explore risk in all its forms:
   - Risk to self (through deliberate self-harm, misadventure, self-neglect)
   - Risk to reputation or financial security
   - Risk from others (through neglect or deliberate abuse)
   - Risk to others (through aggression or negligence)

   The nature and extent of risk will strongly influence choice of treatment setting.
3. Clarify whether this is the first presentation of psychological illness or relapse of a longstanding recurrent illness. Look for underlying triggers and risk factors (including family history, underlying cerebrovascular risk factors, a history of relevant medical conditions, or use of medications commonly associated with mental disturbance).
4. Be mindful of the high prevalence of sub-syndromal or somatic presentations of depression and anxiety in this age group.
5. Always ask about substance use. Misuse or abuse of alcohol or prescription medications (especially benzodiazepines and opiates) or excessive caffeine intake is easily overlooked.
6. Always perform a bedside cognitive assessment.

Medical Investigation

Whilst there is no standardised approach to selection of investigations, a reasonable initial "aged care psychiatry screen" would include (Table 17.3).

The use of reliable, valid rating scales is no substitute for careful clinical assessment but may add weight to diagnostic impressions. The Geriatric Depression Scale is a commonly used self-rating 30-item questionnaire that is quick and simple to administer; a shorter 15-item version may be preferable in the presence of fatigue or mild cognitive impairment. In dementia, the Cornell Scale for Depression in Dementia, which combines patient and carer interviews, is preferred and also has validity in patients without dementia [91–93].

Table 17.3 Initial investigative screen

Investigation	Details
Electrolytes Renal and liver function Calcium, magnesium Fasting blood sugar Fasting lipids	Derangement can be associated with psychological disturbance Renal or hepatic impairment can impact on pharmacokinetics Lithium is eliminated by the kidneys and can cause renal impairment Antidepressants and mood stabilisers commonly cause hyponatraemia in the elderly Metabolic syndromes can result from atypical antipsychotics
Thyroid function	Derangement can be associated with psychological disturbance Lithium can affect thyroid function
Full blood count	Anaemia can impact on energy and mood Some psychotropic medications can cause neutropenia
Iron studies	Deficiency can cause anaemia and has associations in neuroleptic malignant syndrome [88]
Vit B12 and folate	Deficiency has been associated with depression, reduced antidepressant response, and cognitive impairment [89, 90]
Vit D	Deficiency associated with depression
Urine microscopy/ culture	Infections are common and can cause dramatic psychological disturbances
Cerebral imaging CT or MRI	Quantify extent and location of any vascular disease or atrophy Exclude other pathology
Electrocardiogram	As part of the general vascular risk work up Many psychotropics are associated with QTc prolongation

Information source: Dodd et al. [87]; Rosebush & Mazurek [88]; Robinson et al. [89]; Nahas &Sheikh [90]

Treatment

The burden of untreated mental illness, at any age, is readily apparent. The anguish of "psychological pain" is as profound as physical pain. It impacts on self-confidence, identity, relationships, and function; active mental illness impairs our ability to maintain meaningful connections with who we are, what we do, and who we do it with.

There are also hidden risks of untreated illness. Depression is an established independent risk factor for coronary heart disease, impacts on recovery and increases adverse outcomes following heart attack. It has been shown to increase risk of stroke. Similar evidence is growing for anxiety disorders. Mental illness generally carries increased mortality risk via medical illness and suicide [78, 94–96]. Therapy aims to reduce suffering and disability, improve quality of life, and where possible reduce morbidity and mortality.

General Treatment Approaches

Treatment of any acute medical issues identified during the initial physical assessment should occur, along with rationalisation of any polypharmacy (and where possible tapering of agents detrimental to mental state). Given the interaction between psychological distress, psychosocial risk factors, and physical problems in the oldest-old, there are several initial broad management approaches that have relevance regardless of the presenting flavour of mental disturbance and can be promoted by any clinician Box 17.1.

Box 17.1 General Treatment Measures

Supportive contact

Facilitating access to practical supports such as transport and assistance around the home, and supportive interaction with an empathic clinician.

Regular exercise

Aerobic exercise has shown benefits in both prevention and treatment of depression. It has positive effects in anxiety and can help improve sleep [97–99]. Both aerobic and anabolic exercise have been shown to increase cortical volume and improve memory and executive function in mild cognitive impairment [100–102].

Sunlight and sleep hygiene

Dysregulation of circadian rhythms can have significant impacts on sleep and mental well-being. A dose of direct morning sunlight soon after waking can be beneficial, along with broader healthy sleep hygiene habits [97, 103].

Manage substance use

The negative impacts (psychologically and physically) of alcohol and benzodiazepines should be addressed. Nicotine and caffeine can aggravate anxiety and impair quality of sleep.

Healthy diet

Encouraging good hydration and a healthy balanced diet is important in brain health. Regular intake of omega-3 fatty acids can be beneficial in cerebrovascular health and in depression. Folate has shown benefits in augmentation of antidepressants [90, 104, 105].

Socialisation and diversional activity

Encourage regular engagement in pleasurable diversional activities across the week, alone and in company, in and out of the home.

Education and "self-help" resources

Psychoeducation helps empower individuals, is a fundamental element of informed consent, and facilitates collaborative management.

Information sources: Nagas et al. [90]; Malhi et al. [97]; Ensai et al. [98]; Schuch et al. [99];Suo et al. [100]; Fiatarone et al. [101]; Colcombe et al. [102]; Wirz-Justice et al. [103]; Lin et al. [104]; Opie et al. [105].

Focused Approaches: Psychological/ Behavioural Therapies

In combination with general treatment approaches, non-pharmacological strategies may be all that is required for some types of disorder. They can be delivered individually or in a group setting. One of the more rigorously studied interventions is cognitive behavioural therapy (CBT), which comprises a wide array of psychological and behavioural strategies delivered in a systematic and structured manner, aiming to modify unhelpful patterns of thinking or action that may be contributing to ongoing symptoms or distress, with a focus on "here and now" issues. There is a considerable body of evidence for efficacy of CBT in insomnia, chronic pain, substance use, depression, delusions, and hallucinations in some psychoses, and it is particularly effective in anxiety disorders (often as stand-alone treatment), although limited data exists for the oldest-old [106, 107]. Success in therapy requires a degree of motivation and commitment to the process.

Focused Approaches: Biological Therapies

Biological treatment options include medication and neurostimulation and are generally similar to other age groups. Despite the inherent risks of adverse effects, rates of antidepressant, antipsychotic, and sedative prescription are significantly higher in the oldest-old than any other group, particularly in aged care residential settings [108]. As always, obtaining informed consent should be the first step.

Depression

Antidepressants are indicated in moderate-severe depression, when they are often combined with CBT. Generally, different antidepressant classes have shown comparable efficacy (around 50–60%) in most studies, and choice of agent will be influenced more by tolerability, although some studies have suggested superior efficacy for venlafaxine or tricyclic antidepressants over SSRIs. Some studies suggest less benefit for late-onset depression in the setting of vascular disease and in dementia [23, 97, 109, 110].

SSRIs (selective serotonin reuptake inhibitors) are a reasonable first-line choice. Early side effects usually settle within 1–2 weeks. Alternatives would include SNRIs (serotonin and noradrenaline reuptake inhibitors, particularly if depression is more severe or if there is comorbid neuropathic pain), NaSSA (noradrenaline and specific serotonin antidepressant), agomelatine, or NARI (noradrenaline reuptake inhibitor) (Tables 17.4 and 17.5).

Whilst early benefits may be seen within a few weeks, onset can be considerably delayed (10–12 weeks) in the elderly; it is important to resist the temptation to change treatment too early and instead allow an adequate therapeutic trial. If intolerable or ineffective, options would include changing dose or changing antidepressant class. Thereafter, options would include a switch in class to a second- or third-line antidepressant or augmentation with a different agent (lithium, atypical antipsychotics, thyroxine) [97] [Table 17.6].

In major depression with psychosis, an antipsychotic will often be added to the antidepressant early in treatment. In bipolar depression, antidepressants can induce a mood swing into mania or rapid mood cycling. Initial monother-

apy with a mood stabiliser (lithium, valproate, lamotrigine) or second-generation antipsychotic may suffice; alternatively an antidepressant may be used in combination with a mood stabiliser [97].

All antidepressants (but especially SSRI/SNRI) can cause hyponatraemia. Serotonergic antidepressants have the potential to cause serotonin syndrome, especially if combined with other serotonergic agents.

Neurostimulation therapy is an ever-developing field. Electroconvulsive therapy is a well-established antidepressant treatment superior to medication, with remission rates of around 60–90% [113–115]. Whilst often used in cases of medication intolerance or inadequacy, it can be used as first line for its more rapid onset of effect if there are acute risks (active suicidality or poor oral intake) or in melancholic and psychotic subtypes where it is particularly effective. It also has demonstrated benefits in the treatment of mania, schizophrenia, and several neurological conditions (catatonia, Parkinson's disease, neuroleptic malignant syndrome). As long as the patient can tolerate a general anaesthetic and the cardiovascular effects of treatment (rapid changes in heart rate and blood pressure) and has no relative contraindications (very recent MI or CVA, raised intracranial pressure or space-occupying lesion, retinal detachment), the treatment can be used safely in the oldest-old, where response rates are similar but relapse rates high [115, 116]. Side effects are usually minor (headache, nausea); however, the main concern is the potential for cognitive problems (acute confusion, anterograde and retrograde memory problems, executive dysfunction); in the vast majority these are time-limited and resolve once clear of the treatment course; however, some will experience persisting deficits into the longer term. Whilst ECT remains unsurpassed in terms of efficacy in depression, other emerging promising neurostimulation modalities include transcranial magnetic stimulation (TMS), which has the advantage of no anaesthetic or cognitive impacts.

Mania

Medications used to treat mania comprise a diverse collection of agents from different pharmacological groups (Table 17.7).

In mania, any medication that could be contributing to mood elevation should be weaned and an anti-manic agent commenced. If ineffective, options include a switch in agent, trial of second-line treatments (such as carbamazepine), or use of combinations. ECT can also be effective and should be used early if symptoms are severe [97].

Table 17.4 SSRIs

Name	Advantages/disadvantages	Adverse effects
Sertraline Citalopram Escitalopram	Minimal CYP isoenzyme activity (so less drug interactions)	GIT symptoms (nausea, diarrhoea, constipation, cramps) Headache Sexual dysfunction Agitation, sweating, insomnia QTc prolongation (citalopram) Hyponatraemia common in the elderly Osteoporosis and falls Bleeding risk (platelet dysfunction) Extrapyramidal side effects (less common)
Paroxetine	Higher propensity for anticholinergic side effects. Can be difficult to wean (due to short half-life and often marked rebound anxiety)	
Fluoxetine	Very long half-life	
Fluvoxamine	Potentially less sexual side effects Can be sedating	

Information sources: Katona & Livingston [110]; Taylor et al. [111]; Draper & Berman [112]

Table 17.5 Other first-line antidepressant options

Class/name	Advantages/disadvantages	Adverse effects
SNRI Venlafaxine Desvenlafaxine Duloxetine	May be more effective in severe depression or melancholia May be more effective in pain	Similar to SSRIs Hypertension at higher doses
NaSSA Mirtazapine Mianserin	Can be beneficial for insomnia and anorexia Sexual dysfunction uncommon	Sedation (at low dose) Increased appetite/weight (Mirtazapine) Oedema, restless legs Neutropaenia
Melatonergic agonist Agomelatine	Can be beneficial for insomnia Sexual dysfunction uncommon	Can cause hepatic problems
NARI Reboxetine	Can be activating	Sweating, tachycardia, dry mouth Insomnia Nausea, constipation Urinary hesitancy

Information sources: Malhi et al. [97]; Katona & Livingston [110]; Taylor et al. [111]

Table 17.6 Second-line antidepressants

Name	Advantages/disadvantages	Adverse effects
Tricyclic antidepressants (TCA) Nortriptyline Dothiepin Doxepin Amitriptyline Clomipramine	Can be more effective in melancholic depression Nortriptyline has less anticholinergic/hypotensive effects (so preferable in elderly)	Sedation, weight gain Anticholinergic side effects (confusion, dry mouth, constipation, urinary hesitancy, risks in glaucoma) Cardiovascular effects (hypotension, tachycardia, QTc prolongation, increased morbidity in IHD) Seizures in high doses Risk in overdose
Monoamine oxidase inhibitors Phenelzine Tranylcypromine	Risk of tyramine reaction (hypertensive crisis) with some medication, foods, and alcohol. Dietary restriction required	Dizziness, sedation Hypotension Constipation, urinary retention Hepatotoxicity

Information sources: Malhi et al. [97]; Katona & Livingston [110]; Taylor et al. [111]

Table 17.7 First-line anti-manic medications

Name	Advantages/disadvantages	Adverse effects
Lithium	Efficacy for both antidepressant augmentation and anti-manic effects Can reduce suicidality Higher risk of toxicity in the elderly due to reduced renal function and fluid balance and can occur within traditional therapeutic serum ranges Regular monitoring of serum trough levels, renal and thyroid function, calcium is required	Diarrhoea, vomiting Neurotoxicity Fine tremor, Parkinsonism Polyuria, polydipsia (nephrogenic diabetes insipidus) Weight gain Psoriasis Renal impairment Hypothyroidism, Hyperparathyroidism Cardiac effects (sick sinus syndrome, T wave flattening)
Valproate	Monitoring of serum trough levels to avoid toxicity	Nausea, vomiting, headache Weight gain Sedation Neutropaenia, thrombocytopaenia Hyponatraemia Tremor, Parkinsonism
Second-generation antipsychotics Olanzapine Quetiapine Risperidone Aripiprazole	Can be used as anti-manic monotherapy, or for sedative/antipsychotic augmentation (of lithium or valproate)	Sedation Cardiovascular effects (hypotension, QTc prolongation) Metabolic effects (less with aripiprazole) Anticholinergic effects (less with risperidone) Extrapyramidal effects (least with quetiapine) Neutropaenia

Information sources: Malhi et al. [97]; Katona & Livingston [110]; Taylor et al. [111]

Anxiety

Antidepressants have efficacy in anxiety disorders. SSRIs or SNRIs may be used as first line and often augment psychological approaches [58]. Anxious patients are often somatically hypervigilant and can misattribute symptoms of anxiety to medication side effects; careful explanation can often prevent premature abandonment of treatment or unnecessary multiple trials. In some cases, addition of other anxiolytics in low dose (including atypical antipsychotics and pregabalin) early in the course of treatment may help control some symptoms of arousal until the antidepressant agent has achieved response [117, 118]. Benzodiazepines should be avoided if possible or used in low doses for brief periods only.

Psychosis

In the elderly, antipsychotics carry a considerable risk of side effect burden. As always, this risk needs to be weighed against the risk of untreated symptoms and the likelihood the antipsychotic will improve things. In dementia, non-pharmacological options should always be the primary therapeutic focus, with antipsychotic medication reserved for

Table 17.8 Side effects of antipsychotic medications

Extrapyramidal (EPSE) (especially in Lewy body/Parkinson's disease) Dystonia, Parkinsonism Akathisia Tardive dyskinesia	*Neuroleptic malignant syndrome* (in <2%) Autonomic and thermoregulatory instability Tachycardia Hypertension Hyperthermia Diaphoresis, tachypnoea Neurological changes Muscle rigidity Tremor Confusion, stupor, coma Investigations Raised creatine kinase Leucocytosis Renal/electrolyte/ hepatic abnormality
Metabolic and endocrine Weight gain, dyslipidaemia Impaired glucose tolerance, diabetes Hyperprolactinaemia (and increased risk of osteoporosis and breast cancer) Hyponatraemia	
Anticholinergic Dry mouth, blurred vision Constipation, urinary retention Confusion	
Cardiovascular Hypotension QTc prolongation	
Other Sedation Gastrointestinal (nausea, diarrhoea, constipation, raised liver enzymes) Sexual dysfunction	

Information sources: Katona & Livingston [110]; Taylor et al. [111]; Galletly et al. [121]; Musselman et al. [122]

more persistent psychotic symptoms associated with distress, problematic behaviours, or elevated risk. Late-onset schizophrenia tends to respond to much smaller antipsychotic doses than early-onset forms [73, 119, 120].

Atypical (second-generation) antipsychotics are generally preferred for their more tolerable side effect profile. Nevertheless, they also carry risk of adverse effects (Table 17.8). Furthermore studies have shown in some populations (dementia) an increased risk of mortality (especially through pneumonia and cardiac problems) and morbidity (including cerebrovascular disease) [119]. Apart from clozapine (rarely used in the elderly), quetiapine has the least potential for EPSE. Aripiprazole has fewer metabolic side effects, and risperidone has fewer anticholinergic side effects (Table 17.8). Whilst oral preparations are preferable, in cases of poor compliance, injectable depot administration may be utilised.

Clinical Relevance

- Mental illness in the elderly can be due to relapse of early-onset disease or a new late-onset process.
- Medical causes of psychological disease in the oldest-old are very common. Identification and treatment is always the first priority.
- Depression in the elderly commonly presents with somatic or sub-syndromal features.
- Whilst treatment approaches are similar to younger populations, medication should be introduced slowly in low doses.
- Antidepressants and antipsychotics carry a significant side effect burden, and their potential benefit must outweigh this risk.
- Electroconvulsive therapy is most effective for melancholic or psychotic depression subtypes and can be safely used in the elderly.
- In dementia, non-pharmacological strategies for behavioural and psychological symptoms are first line.
- Elderly males have the highest suicide rates. Exploring suicide and other risks is an essential part of the basic assessment.

Multiple Choice Questions

1. In the treatment of depression, a reasonable first-line antidepressant agent would be:
   A. Lithium
   B. An SSRI
   C. A tricyclic antidepressant
   D. Oxazepam
   E. All of the above
2. A patient you are treating for late-onset psychosis presents with abrupt onset of confusion, fever, muscle stiffness, and new hypertension. A reasonable initial approach would include:
   A. Supportive nursing measures
   B. Withholding of their regular antipsychotic
   C. Medical work up including full blood count, renal and liver function, creatine kinase
   D. Obtaining additional information from family or friends
   E. All of the above
3. ECT would be considered early in the setting of:
   A. Acute paranoid psychosis
   B. Recurrent disabling panic attacks
   C. Parkinson's disease
   D. Melancholic depression
   E. All of the above
4. Which of the following form part of the basic assessment of any elderly patient?
   A. Cognitive screen
   B. Physical examination and investigation
   C. Careful assessment of risk including suicidality
   D. Obtaining a corroborative history
   E. All of the above

Answers to MCQs

1. B
2. E
3. D
4. E

References

1. American Psychiatric Association. Practice guideline for the treatment of patients with delirium. Am J Psychiatry. 1999;156(5 Supp):1–20.
2. Lovestone S. Other disorders of the nervous system. In: David AS, Fleminger S, Kopelman MD, Lovestone S, Mellers JDC, editors. Lishman's organic psychiatry. A textbook of neuropsychiatry. 4th ed. West Sussex: Wiley-Blackwell; 2009. Chap 14.
3. Harrison NA, Kopelman MD. Endocrine diseases and metabolic disorders. In: David AS, Fleminger S, Kopelman MD, Lovestone S, Mellers JDC, editors. Lishman's organic psychiatry. A textbook of neuropsychiatry. 4th ed. West Sussex: Wiley-Blackwell; 2009. Chap 10.
4. American Psychiatric Association: diagnostic and statistical manual of mental disorders, 5th ed. Arlington: American Psychiatric Association; 2013.
5. Gallagher D, Mhaolain AN, Greene E, Walsh C, Denihan A, Bruce I, et al. Late life depression: a comparison of risk factors and symptoms according to age of onset in community dwelling older adults. Int J Geriatr Psychiatry. 2010;25:981–7.
6. Hayes JC, Krishnan KRR, George LK, Blazer DG. Age of first onset of bipolar disorder: demographic, family history, and psychosocial correlates. Depress Anxiety. 1998;7:76–82.
7. Almeida OP, Howard RJ, Levy R, David AS. Psychotic states arising in late life (late paraphrenia). The role of risk factors. Br J Psychiatry. 1995;166(2):215–28.
8. Grace J, O'Brien JT. Association of life events and psychosocial factors with early but not late onset depression in the elderly: implications for possible differences in aetiology. Int J Geriatr Psychiatry. 2003;18:473–8.
9. Hickie I, Simons L, Naismith S, Simons J, McCallum J, Pearson K. Vascular risk to late-life depression: evidence from a longitudinal community study. ANZ J Psychiatry. 2003;37: 62–5.
10. Subramaniam H, Dennis M, Byrne E. The role of vascular risk factors in late onset bipolar disorder. Int J Geriatr Psychiatry. 2007;22:733–7.
11. Wijeratne C, Malhi GS. Vascular mania: an old concept in danger of sclerosing? A clinical overview. Acta Psychiatr Scand. 2007;116(Suppl.434):35–40.
12. Tamashiro JH, Zung S, Zanetti MV, de Castro CC, Vallada H, Busatto GF, et al. Increased rates of white matter hyperintensities in late-onset bipolar disorder. Bipolar Disord. 2008;10: 765–75.
13. Taylor WD, MacFall JR, Steffens DC, Payne ME, Provenzale JM, Krishnan KR. Localization of age-associated white matter hyperintensities in late-life depression. Prog Neuro-Psychopharmacol Biol Psychiatry. 2003;27(3):539–44.
14. Flint AJ, Rifat SL, Eastwood MR. Late-onset paranoia: distinct from paraphrenia? Int J Geriatr Psychiatry. 1991;6(2):103–9.
15. Sachdev P, Brodaty H. Quantitative study of signal hyperintensities on T2-weighted magnetic resonance imaging in late-onset schizophrenia. Am J Psychiatry. 1999;156(12):1958–67.
16. Nilsson FM, Kessing LV, Sørensen TM, Andersen PK, Bolwig TG. Affective disorders in neurological diseases: a case register-based study. Acta Psychiatr Scand. 2003;108:41–50.
17. Zhang N, Liu W, Ye M, Cohen AD, Zhang Y. The heterogeneity of non-motor symptoms of Parkinson's disease. Neurol Sci. 2015;36:577–84.
18. Schneider F, Althaus A, Backes V, Dodel R. Psychiatric symptoms in Parkinson's disease. Eur Arch Psychiatry Clin Neurosci. 2008;258(Supp5):55–9.
19. Brodaty H, Draper B, Saab D, Low L, Richards V, Paton H, Lie D. Psychosis, depression and behavioural disturbances in Sydney nursing home residents: prevalence and predictors. Int J Geriatr Psychiatry. 2001;16:504–12.
20. van der Linde RM, Dening T, Matthews FE, Brayne C. Grouping of behavioural and psychological symptoms of dementia. Int J Geriatr Psychiatry. 2014;29:562–8.
21. Pose M, Cetkovich M, Gleichgerrcht E, Ibanez A, Torralva T, Manes F. The overlap of symptomatic dimensions between frontotemporal dementia and several psychiatric disorders that appear in late adulthood. Int Rev Psychiatry. 2013;25(2):159–67.
22. Wylie MA, Shnall A, Onyike CU, Huey ED. Management of frontotemporal dementia in mental health and multidisciplinary settings. Int Rev Psychiatry. 2013;25(2):230–6.
23. Alexopoulos G, Kelly R. Research advances in geriatric depression. World Psychiatry. 2009;8:140–9.
24. Bagulho F. Depression in older people. Curr Opin Psychiatry. 2002;15:417–22.
25. Rock PL, Roiser JP, Riedel WJ, Blackwall MD. Cognitive impairment in depression: a systematic review and meta-analysis. Psychol Med. 2014;44(10):2029–40.
26. Thomas AJ, O'Brien JT. Depression and cognition in older adults. Curr Opin Psychiatry.; Jan. 2008;21(1):8–13.
27. Gildengers AG, Mulsant BH, Al Jurdi RK, Beyer JL, Greenberg RL, Gyulai L, Moberg PJ, Sajatovic M, Ten Have T, Young RC, The GERIBD Study Group. The relationship of bipolar disorder lifetime duration and vascular burden to cognition in older adults. Bipolar Disord. 2010;12:851–8.
28. Porter RJ, Robinson LJ, Malhi GS, Gallagher P. The neurocognitive profile of mood disorders – review of the evidence and methodological issues. Bipolar Disord. 2015;17(Suppl. 2):21–40.
29. Schouws SN, Comijs HC, Stek ML, Dekker J, Oostervink F, Naarding P, et al. Cognitive impairment in early and late bipolar disorder. Am J Geriatr Psychiatry. 2009;17(6):508–15.
30. Chowdhury R, Ferrier IN, Thompson JM. Cognitive dysfunction in bipolar disorder. Curr Opin Psychiatry. 2003;16:7–12.
31. Almeida OP, Howard RJ, Levy R, David AS, Morris RG, Sahakian BJ. Cognitive features of psychotic states arising in late life (late paraphrenia). Psychol Med. 1995;25(4):685–98.
32. Hassett A. A descriptive study of first presentation psychosis in old age. ANZ J Psychiatry. 1999;33:814–24.
33. Zhou H, Li R, Ma Z, Rossi S, ZU X, Li J. Smaller gray matter volume of hippocampus/parahippocampus in elderly people with subthreshold depression: a cross-sectional study. BMC Psychiatry. 2016;16:219.
34. Hickie I, Naismith S, Ward PB, Turner K, Scott E, Mitchell P, et al. Reduced hippocampal volumes and memory loss in patients with early- and late-onset depression. Br J Psychiatry. 2005;186:197–202.
35. Sawyer K, Corsentino E, Sachs-Ericsson N, Steffens D. Depression, hippocampal volume changes, and cognitive decline in a clinical sample of older depressed outpatients and non-depressed controls. Aging and Ment Health. 2012;16(6):753–62.
36. Kohler S, Thomas A, Lloyd A, Barber R, Almeida O, O'Brien JT. White matter hyperintensities, cortisol levels, brain atrophy and continuing cognitive deficits in late-life depression. Br J Psychiatry. 2010;196:143–9.
37. Beyer JL, Kuchibhatla M, Payne M, Moo-Young M, Cassidy F, MacFall J, et al. Caudate volume measurement in older adults with bipolar disorder. Int J Geriatr Psychiatry. 2004;19:109–14.

38. Alexopoulos G, Morimoto SS. The inflammation hypothesis in geriatric depression. Int J Geriatr Psychiatry. 2011;26:1109–18.
39. Hurley LL, Tizabi Y. Neuroinflammation, neurodegeneration, and depression. Neurotox Res. 2013;23:131–44.
40. Aizenstein HJ, Baskys A, Boldrini M, Butters MA, Diniz BS, Jaiswal MJ, et al. Vascular depression consensus report – a critical update. BMC Med. 2016;14:161.
41. Breitner JC, Husain MM, Figiel GS, Krishnan KR, Boyko OB. Cerebral white matter disease in late-onset paranoid psychosis. Biol Psychiatry. 1990;28(3):266–74.
42. Paivarinta A, Verkkoniemi A, Niinisto L, Kivela SL, Sulkava R. The prevalence and associates of depressive disorders in the oldest-old Finns. Soc Psychiatry Psychiatr Epidemiol. 1999;34:352–9.
43. Stek ML, Gussekloo J, Beekman AT, van Tilburg W, Westendorp RG. Prevalence, correlates and recognition of depression in the oldest old: the Leiden 85-plus study. J Affect Disord. 2004;78(3):193–200.
44. Petersson S, Mathillas J, Wallin K, Olofsson B, Allard P, Gustsfson Y. Risk factors for depressive disorders in very old age: a population-based cohort study with a 5-year follow-up. Soc Psychiatry Psychaitr Epidemiol. 2014;49:831–9.
45. Jopp DS, Park MS, Lehrfeld J, Paggi M. Physical, cognitive, social and mental health in near-centenarians and centenarians living in New York City: findings from the Fordham Centenarian Study. BMC Geriatr. 2016;16:1.
46. Wilson K, Mottram P, Sixsmith A. Depressive symptoms in the very old living alone: prevalence, incidence and risk factors. Int J Geriatr Psychiatry. 2007;22:361–6.
47. Hybels CF, Landerman LR, Blazer DG. Age differences in symptom expression in patients with major depression. Int J Geriatr Psychiatry. 2012;27:601–11.
48. Snowden J. Is depression more prevalent in old age? ANZ J Psychiatry. 2001;35(6):782–7.
49. Zarit SH, Femia EE, Gatz M, Johansson B. Prevalence, incidence and correlates of depression in the oldest old: the OCTO study. Aging Ment Health. 1999;3(2):119–28.
50. O'Connor DW. Do older Australians truly have low rates of anxiety and depression? A critique of the 1997 National Survey of mental health and wellbeing. ANZ J Psychiatry. 2006;40:623–31.
51. Brodaty H, Luscombe G, Parker G, Wilhelm K, Hickie I, Austin MP, et al. Increased rate of psychosis and psychomotor change in depression with age. Psychol Med. 1997;27(5):1205–13.
52. Brodaty H, Cullen B, Thompson C, Mitchell P, Parker G, Wilhelm K, et al. Age and gender in the phenomenology of depression. Am J Geriatr Psychiatry. 2005;13(7):589–96.
53. Parker G. Classifying depression: should paradigms lost be regained? Am J Psychiatry. 2000;157(8):1195–203.
54. Depp CA, Jeste DV. Bipolar disorder in older adults: a critical review. Bipolar Disord. 2004;6:343–67.
55. Dols A, Kupka RW, van Lammeren A, Beekman AT, Sajatovic M, Stek ML. The prevalence of late-life mania: a review. Bipolar Disord. 2014;16:113–8.
56. Bryant C, Jackson H, Ames D. The prevalence of anxiety in older adults: methodological issues and a review of the literature. J Affect Disord. 2008;109(3):233–5.
57. Golden J, Conroy RM, Bruce I, Denihan A, Greene E, Kirby M, Lawlor BA. The spectrum of worry in the community-dwelling elderly. Aging Ment Health. 2011;15(8):985–94.
58. Wolitzky-Taylor KB, Castriotta N, Lenze EJ, Stanley MA, Craske MG. Anxiety disorders in older adults: a comprehensive review. Depress Anxiety. 2010;27:190–211.
59. Chang WH, Chen WT, Lee IH, Chen PS, Yang YK, Chen KC. Coexisting anxiety disorders alter associations with physical disorders in the elderly: a Taiwan cross-sectional nationwide study. Psych Clin Neurosci. 2016;70:211–7.
60. Handley AK, Egan SJ, Kane RT, Rees CS. The relationships between perfectionism, pathological worry and generalised anxiety disorder. BMC Psychiatry. 2014;14:98.
61. Van der Weele GM, Gussekloo J, MWM DW, AJM DC, Van der Mast RC. Co-occurrence of depression and anxiety in elderly subjects aged 90 years and its relationship with functional status, quality of life and mortality. Int J Geriatr Psychiatry. 2009;24:595–601.
62. Flint AJ. Epidemiology and comorbidity of anxiety disorders in the elderly. Am J Psychiatry. 1994;151(5):640–9.
63. Flint AJ. Generalised anxiety disorder in elderly patients. Epidemiology, diagnosis and treatment options. Drugs Aging. 2005;22(2):101–14.
64. Fredrikson M, Annas P, Fischer H, Wik G. Gender and age differences in the prevalence of specific fears and phobias. Behav Res Ther. 1996;34(1):33–9.
65. Arfken CL, Lach HW, Birge SJ, Miller JP. The prevalence and correlates of fear of falling in elderly persons living in the community. Am J Public Health. 1994;84(4):565–70.
66. Ribeiro O, Santos AR. Psychological correlates of fear of falling in the elderly. Educ Gerontol. 2015;41:69–78.
67. Payette MC, Bélanger C, Benyebdri F, Filiatrault J, Bherer L, Bertrand JA, et al. The association between generalized anxiety disorder, subthreshold anxiety symptoms and fear of falling among older adults: preliminary results from a pilot study. Clin Gerontol. 2017;40(3):197–206.
68. Visschedijk JHM, Caljouw MAA, Bakkers E, van Balen R, Achterberg W. Longitudinal follow-up study on fear of falling during and after rehabilitation in skilled nursing facilities. BMC Geriatr. 2015;15:161.
69. Koychev I, Ebmeier KP. Anxiety in older adults often goes undiagnosed. Practitioner. 2016;260(1789):17–20.
70. Kohn R, Westlake RJ, Rasmussen SA, et al. Clinical features of obsessive-compulsive disorder in elderly patients. Am J Geriatr Psychiatry. 1997;5:211–5.
71. Ayers CR, Saxena S, Golshan S, Loebach Wetherall J. Age at onset and clinical features of late life compulsive hoarding. Int J Geriatr Psychiatry. 2010;25:142–9.
72. Roth M, Kay DWK. Late paraphrenia: a variant of schizophrenia manifest in late life or an organic clinical syndrome? A review of recent evidence. Int J Geriatr Psychiatry. 1998;13:775–84.
73. Howard R, Rabins PV, Seeman MV, Jeste DV, The International Late-Onset Schizophrenia Group. Late-onset schizophrenia and very-late-onset schizophrenia-like psychosis: an international consensus. Am J Psychiatry. 2000;157:172–8.
74. Howard R, Castle D, O'Brien J, Almeida O, Levy R. Permeable walls, floors, ceilings and doors. Partition delusions in late paraphrenia. Int J Geriatr Psychiatry. 1992;7:719–24.
75. Sato T, Bottlender R, Schröter A, Möller HJ. Psychopathology of early-onset versus late-onset schizophrenia revisited: an observation of 473 neuroleptic-naive patients before and after first-admission treatments. Schizophr Res. 2004;67(2–3):175–83.
76. Almeida OP, Howard RJ, Levy R, David AS. Psychotic states arising in late life (late paraphrenia) psychopathology and nosology. Br J Psychiatry. 1995;166(2):205–14.
77. Australian Bureau of Statistics. Age-specific death rates for intentional self-harm, by sex, 2015. Cat no. 3303.0; 2016.
78. Snowden J, Baume P. A study of suicides of older people in Sydney. Int J Geriatr Psychitry. 2002;17:261–9.
79. Harwood D, Hawton K, Hope T, Jacoby R. Psychiatric disorder and personality factors associated with suicides in older people: a descriptive and case-control study. Int J Geriatr Psychiatry. 2001;16:155–65.
80. Oude Voshaar RC, van der Veen DC, Hunt I, Kapur N. Suicide in late-life depression with and without comorbid anxiety disorders. Int J Geriatr Psychiatry. 2016;31:146–52.

81. Suominen K, Isometsä E, Lönnqvist J. Elderly suicide attempters with depression are often diagnosed only after the attempt. Int J Geriatr Psychiatry. 2004;19(1):35–40.
82. Harris EC, Barraclough BM. Suicide as an outcome for medical disorders. Medicine. 1994;73(6):281–96.
83. Shelef A, Hiss J, Cherkashin G, Berger U, Aizenberg D, Baruch Y, Barak Y. Psychosocial and medical aspects of older suicide completers in Israel: a 10-year survey. Int J Geriatr Psychiatry. 2014;29:846–51.
84. Chan J, Draper B, Banerjee S. Deliberate self-harm in older adults: a review of the literature from 1995 to 2004. Int J Geriatr Psychiatry. 2007;22:720–32.
85. Bonnewyn A, Shah A, Bruffarts R, Schoevaerts K, Rober P, Van Parys H, Demyttenaere K. Reflections of older adults on the process preceding their suicide attempt: a qualitative approach. Death Stud. 2014;38:612–8. https://doi.org/10.1080/07481187.2013.835753.
86. Westefeld JS, Casper D, Galligan P, Gibbons S, Lustgarten S, Rice A, et al. Suicide and older adults: risk factors and recommendations. J Loss Trauma. 2015;20:491–508. https://doi.org/10.1080/15325024.2014.949154.
87. Dodd S, Malhi G, Tiller J, Schweitzer I, Hickie I, Khoo JP, et al. A consensus statement for safety monitoring guidelines of treatments for major depressive disorder. ANZ J Psychiatry. 2011;45(9):712–25.
88. Rosebush PI, Mazurek MF. Serum iron and neuroleptic malignant syndrome. Lancet. 1991;338(8760):149–51.
89. Robinson DJ, O'Luanaigh C, Tehee E, O'Connell H, Hamilton F, Chin AV, et al. Associations between holotranscobalamin, vitamin B12, homocysteine and depressive symptoms in community-dwelling elders. Int J Geriatr Psychiatry. 2011;26:307–13.
90. Nahas R, Sheikh O. Complementary and alternative medicine for the treatment of major depressive disorder. Can Fam Physician. 2011;57:659–63.
91. Sharp L, Lipsky M. Screening for depression across the lifespan: a review of measures for use in primary care settings. Am Fam Physician. 2002;66(6):1001–8.
92. Debruyne H, Van Buggenhout M, Le Bastard N, Aries M, Audenaert K, De Deyn PP, et al. Is the geriatric depression scale a reliable screening tool for depressive symptoms in elderly patients with cognitive impairment? Int J Geriatr Psychiatry. 2009;24:556–62.
93. Alexopoulos GS, Abrams RC, Young RC, Shanoian CA. Cornell scale for depression in dementia. Biol Psychiatry. 1988;23:271–84.
94. Cohen BE, Edmondson D, Kronish IM. State of the art review: depression, stress, anxiety, and cardiovascular disease. Am J Hypertens. 2015;28(11):1295–302.
95. Liebetrau M, Steen B, Skoog I. Depression as a risk factor for the incidence of first-ever stroke in 85-year-olds. Stroke. 2008;39(7):1960–5.
96. Scott KM. Depression, anxiety and incident cardiometabolic diseases. Curr Opin Psychiatry. 2014;27(4):289–93.
97. Malhi G, Bassett D, Boyce P, Bryant R, Fitzgerald P, Fritz K, et al. Royal Australian and New Zealand college of psychiatrists clinical practice guidelines for mood disorders. ANZ J Psychiatry. 2015;49(12):1–185.
98. Ensari I, Greenlee TA, Motl RW, Petruzzello SJ. Meta-analysis of acute exercise effects on state anxiety: an update of randomised controlled trials over the past 25 years. Depress Anxiety. 2015;32(8):624–34.
99. Schuch FB, Deslandes AC, Stubbs B, Gosmann NP, Silva CT, Fleck MP. Neurobiological effects of exercise on major depressive disorder: a systemic review. Neurosci Biobehav Rev. 2016;61:1–11.
100. Suo C, Singh MF, Gates N, Wen W, Sachdev P, Brodaty H, et al. Therapeutically relevant structural and functional mechanisms triggered by physical and cognitive exercise. Mol Psychiatry. 2016;21(11):1633–42.
101. Fiatarone Singh MA, Gates N, Saigal N, Wilson GC, Meiklejohn J, Brodty H, et al. The study of mental and resistance training (SMART) study-resistance training and/or cognitive training in mild cognitive impairment: a randomised, double-blind, double-sham controlled trial. JAMA. 2014;15:873–80.
102. Colcombe SJ, Erickson KI, Scalf PE, Kim JS, Prakash R, McAuley E, et al. Aerobic exercise training increases brain volume in aging humans. J Gerontol A Biol Sci Med Sci. 2006;61(11):1166–7.
103. Wirz-Justice A, Benedetti F, Berger M, Lam RW, Martiny K, Terman M, et al. Chronotherapeutics (light and wake therapy) in affective disorders. Psychol Med. 2005;35(7):939–44.
104. Lin PY, Mischoulon D, Freeman MP, Matsuoka Y, Hibbeln J, Belmaker RH, et al. Are omega-3 fatty acids antidepressants or just mood-improving agents? The effect depends upon diagnosis, supplement preparation, and severity of depression. Mol Psychiatry. 2012;7:1161–3.
105. Opie RS, Itsiopoulos C, Parletta N, Sanchez-Villegas A, Akbaraly TN, Ruusunen A, et al. Dietary recommendations for the prevention of depression. Nutr Neurosci. 2017;20(3):161.
106. Hofman SG, Asaani A, Vonk IJJ, Sawyer AT, Fang A. The efficacy of cognitive behavioural therapy: a review of meta-analyses. Cogn Ther Res. 2012;36:427–40.
107. Hendriks GJ, Oude Voshaar RC, Keijsers GPJ, Hoogduin CAL, Van Balkom AJLM. Cognitive-behavioural therapy for late-life anxiety disorders: a systematic review and meta-analysis. Act Psychiatr Scand. 2008;117:403–11.
108. Hollingworth SA, Lie DC, Siskind DJ, Byrne GJ, Hall WD, Whiteford HA. Psychiatric drug prescribing in elderly Australians: time for action. ANZ J Psychiatry. 2001;45:705–8.
109. Banerjee S, Hellier J, Romeo R, Dewey M, Knapp M, Ballard C, et al. Study of the use of antidepressants for depression in dementia: the HTA-SADD trial--a multicentre, randomised, double-blind, placebo-controlled trial of the clinical effectiveness and cost-effectiveness of sertraline and mirtazapine. Health Technol Assess. 2013;17(7):1–166.
110. Katona C, Livingston G. Drug treatment in old age psychiatry. London: Martin Dunitz; 2003.
111. Taylor D, Paton C, Kapur S. The Maudsley prescribing guidelines. 10th ed. London: Informa Healthcare; 2009.
112. Draper B, Berman K. Tolerability of selective serotonin reuptake inhibitors. Issues relevant to the elderly. Drugs Aging. 2008;25(6):501–19.
113. NSW Government Health. Electroconvulsive therapy: ECT minimum standards of practice in NSW, 2016 Jan. Document Number PD2011_003.
114. Van der Wurff FB, Stek ML, Hoogendijk WJG, Beekman ATF. The efficacy and safety of ECT in depressed older adults, a literature review. Int J Geriatr Psychiatry. 2003;18:894–904.
115. Burke D, Shannon J, Beveridge A. Electroconvulsive therapy use in a 97-year-old woman. Aust Psychiatry. 2007;15(5):427–30.
116. Flint AJ, Gagnon N. Effective use of electroconvulsive therapy in late-life depression. Can J Psychiatr. 2002;47(8):734–41.
117. Albert U, Carmassi C, Cosci F, De Cori D, Di Nicola M, Ferrari S, et al. Role and clinical implications of atypical antipsychotics in anxiety disorders, obsessive-compulsive disorder, trauma-related, and somatic symptom disorders: a systematized review. Int Clin Psychopharmacol. 2016;31(5):249–58.
118. Frampton J. Pregabalin: a review of its use in adults with generalized anxiety disorder. CNS Drugs. 2014;28:835–54.
119. Royal Australian and New Zealand College of Psychiatrists, Faculty of Psychiatry of Old Age and Committee for Therapeutic Interventions and Evidence-based Practice. Antipsychotic medi-

cations as a treatment of behavioural and psychological symptoms of dementia. 2016, Aug. PPG10.
120. Palmer BW, McClure FS, Jeste DV. Schizophrenia in late life: findings challenge traditional concepts. Harvard Rev Psychiatry. 2001;9:51–8.
121. Galletly C, Castle D, Dark F, Humberstone V, Jablensky A, Killackey E, et al. Royal Australian and New Zealand college of psychiatrists clinical practice guidelines for the management of schizophrenia and related disorders. ANZ J Psychiatry. 2016;50(5):1–117.
122. Musselman ME, Saely S. Diagnosis and treatment of drug-induced hyperthermia. Am J Health-Syst Pharm. 2013;70: 34–42.