Pharmacological Management of Anxiety and Depression in Older People

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9.1 Introduction: Pharmacological Treatments in Context

Depressive and anxiety disorders are commonly encountered in older patients in primary care. They may present with psychological or physical symptoms or a combination and may impact on the course and management of coexisting physical disorders. Depression and anxiety often coexist; up to a quarter of older people with anxiety disorders also meet criteria for major depression [1] and the presence of anxiety in depressed patients is associated with a greater risk of relapse [2]. Not surprisingly, therefore, their causes and treatments also overlap. Most anxiety disorders are diagnosed by the age of 40, but a few people will develop them after 65 years [3]; generalised anxiety and social phobia appear to be the more common disorders in older people. They typically run a cyclical course and are unlikely to remit completely, even with long-term treatment. Around two thirds of people with Alzheimer's disease experience anxiety symptoms and 5–6 % have diagnosable generalised anxiety disorder [4] so it is important to assess for cognitive impairment when deciding on management. Risk factors for anxiety in older people include female gender, multiple physical conditions, residing in a care home, and physical disability [3]. Anxiety is specifically linked to thyroid problems, respiratory and gastrointestinal disorders, and arthritis; anxiety disorders may also precede the onset of physical illness and worsen quality of life and disability [5].

Depression may also precede the onset of physical illness, such as Parkinson's disease [6]. Suffering with depression worsens the outcome of physical illness via reduced treatment adherence, increased disability, and higher mortality. Physical

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symptoms influence the course of depression; ongoing pain is particularly linked to the recurrence of depression [7]. While in younger adults antidepressants are as efficacious in people with comorbid physical illnesses as those without [8], in older people specific neurobiological changes such as cerebral white matter disease are associated with a poorer response to antidepressant treatment [9, 10]. Poorer response is also predicted by advanced age, higher levels of stress, poorer social support, younger age at first episode, higher anxiety, and poorer sleep [11]. Compared with younger patients, older people may take longer to respond to antidepressant medication and as many as half may not achieve remission with their first treatment [12]. There is marked variation in rate and stability of recovery ranging from rapid sustained improvement to partial response or lack or response.

Older patients may be reluctant to take antidepressant medication due a lack of understanding of depression, fear of drug dependence, and negative experiences with medication [13]. Stigma against seeking help for psychological problems may also be a barrier. It is worthwhile, therefore, exploring a patient's attitude and backing up treatment with factsheets and active monitoring [14]. The prescriber should be aware of relevant guidelines in the treatment of depression and anxiety. However, it is important to recognise that the evidence base for drug treatment of anxiety and depression in older people is significantly smaller than in younger adults as drug trials typically exclude patients with complex physical illness and those taking multiple medications [15]. For instance, there is a paucity of randomised controlled trials in anxiety disorders in older people not responding to first line treatments [16]. In addition, guidelines may not easily map onto the management of patients with complex multimorbidity [17]. Potential adverse effects will need to be taken into the equation and weighed against the negative consequences for physical and psychological health of leaving anxiety or depression untreated. Non-pharmacological treatments should always be considered. The best results are obtained by a collaborative approach between primary care and a depression case manager using both psychological and pharmacological interventions [18, 19], if such a service is available.

9.2 Drugs Used in the Treatment of Anxiety and Depression

Antidepressants are the principal group of medications used in the treatment of anxiety and depression. Their main therapeutic mechanisms of action are enhancement of the activity of the neurotransmitters serotonin (5-HT) and noradrenaline (norepinephrine); antidepressants can be subdivided into those acting solely on one neurotransmitter (single action) and those acting on both (dual action). The first antidepressants to be developed also acted on other neurotransmitter systems, such as cholinergic pathways, causing undesirable side effects. The diversity of actions of antidepressant drugs allows prescribers to individualise treatment decisions and to avoid specific side effects [20]. Specialist prescribers may also institute

Table 9.1 Main classes of antidepressant

Class	Examples
Serotonin reuptake inhibitors (SSRIs)	Sertraline, citalopram
Tricyclic antidepressants (TCAs)	Amitriptyline, imipramine, lofepramine
Serotonin/noradrenaline reuptake inhibitors (SNRIs)	Venlafaxine, duloxetine
Noradrenergic and specific serotonergic antidepressants (NaSSAs)	Mirtazapine
Serotonin antagonist/serotonin reuptake inhibitors (SARIs)	Nefazodone
Noradrenaline/dopamine reuptake inhibitors (NDRIs)	Bupropion
Monoamine oxidase inhibitors (MAOIs)	Phenelzine, tranylcypromine

Data from Stahl [20]

combinations of drugs to enhance efficacy and reduce adverse effects. The main classes of antidepressants currently in use are listed in Table 9.1.

9.2.1 Serotonin Reuptake Inhibitors (SSRIs)

SSRIs are single-action antidepressants and currently are the first line in the pharmacological treatment of depression and anxiety in late life. The group includes citalopram (and its isomer escitalopram), sertraline, fluoxetine, and paroxetine. SSRIs have a lower rate of cardiac conduction abnormalities in overdose than older antidepressants and a low propensity to cause seizures. However, frequent side effects include nausea, vomiting, dry mouth, insomnia, weight gain, and sexual dysfunction. Therefore they may not be suitable in patients with insomnia and agitation. SSRIs may also worsen parkinsonism. Naturalistic studies indicate that treatment of older adults with SSRIs is not associated with increased risk of completed or attempted suicide, in contrast with their use in adolescents. In fact, treatment reduces risk of suicide by over 50 % [21].

9.2.2 Tricyclic Antidepressants

These dual-action drugs were amongst the earliest antidepressants. The group includes amitriptyline, nortriptyline, dothiepin, clomipramine, and imipramine. As well as the desired action on serotonin and noradrenaline receptors, they also act at other receptors (acetylcholine, adrenergic, and histamine) giving rise to dry mouth, constipation, tachycardia, cognitive impairment, postural hypotension, and sedation. Nortriptyline has been well evaluated in older people with well-established efficacy and tricyclics retain a place in the treatment of depression and anxiety under specialist supervision.

9.2.3 Other Classes of Antidepressant

Venlafaxine and duloxetine are dual-action serotonin/noradrenaline reuptake inhibitors (SNRIs) that also have an inhibiting effect on the neurotransmitter dopamine. Some flexibility is offered by the use of venlafaxine which, at lower doses, functions as a single-action SSRI. SNRIs may be more beneficial than SSRIs in treatment-resistant depression [22]. Mirtazapine and nefazodone are dual-action antidepressants that have additional properties of postsynaptic serotonin antagonism which can reduce adverse effects such as sexual dysfunction and nausea associated with serotonin reuptake inhibition. They also antagonise alpha-adrenergic receptors causing adverse effects of postural hypotension and dizziness. Mirtazapine also has some histamine blocking effect, causing sedation and weight gain. Monoamine oxidase inhibitors were the original antidepressant class. Now generally avoided due to dietary restrictions and interactions, they still have a place in the treatment of atypical and treatment-resistant depression under specialist supervision.

9.2.4 Lithium

Lithium (as its carbonate or citrate salt) is a well-established and effective mood-stabilising treatment in the management of bipolar disorder, including the treatment of bipolar depression. Lithium can also be used in the augmentation of antidepressant treatment in patients with unipolar depression who have failed to respond to antidepressant treatment alone. From the limited number of studies of different augmentation strategies in older people, lithium has the strongest evidence of efficacy [23] and it also reduces suicide risk [24]. Prescribing with diuretics (particularly thiazides) and non-steroidal anti-inflammatory drugs should usually be avoided, but, otherwise, lithium can generally be used safely in older patients taking other drugs for comorbid medical conditions. Monitoring of serum levels, renal function, thyroid function, and weight is essential and particular care is necessary in patients with chronic renal impairment. Therefore, lithium should usually be initiated and monitored by a specialist.

9.2.5 Antipsychotics

Antipsychotic drugs are primarily used in the treatment of schizophrenia, other psychoses, and bipolar disorder. Their main action is through the blockade of dopaminergic pathways. Newer ("atypical") antipsychotics also interact with serotonin receptors and have a role in the specialist management of depressive illness to augment the effects of antidepressants [25] although extrapyramidal and metabolic side effects may limit their use in certain patients. There are only limited data to support the use of antipsychotics in the treatment of anxiety disorders [26], so given the risk of adverse effects in older people, their use should be limited to more severe or treatment-refractory cases, under specialist supervision. Antipsychotic use in people with dementia is associated with increased risk of stroke and death [27] and so should be limited to specialist prescribing.

9.2.6 Benzodiazepines

Benzodiazepines, such as lorazepam and diazepam, act by enhancing the effect of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). Although of benefit in the short-term management of severe anxiety, their side effects of sedation, falls and cognitive impairment, and the potential for dependence mean that long-term use is best avoided. However, under specialist supervision, they might be used in disabling anxiety that is refractory to a range of pharmacological and psychological interventions [28].

9.2.7 Buspirone

Buspirone is a partial serotonin agonist with some dopaminergic action that acts to reduce anxiety. It has the advantage over benzodiazepines of not suppressing breathing and lacks dependence risk. However its benefits in the long-term management of generalised anxiety are not clear and it appears to be ineffective in patients who have been dependent on benzodiazepines [29].

9.2.8 Pregabalin

Pregabalin is an anticonvulsant drug that decreases the release of glutamate and noradrenaline; unlike benzodiazepines, it does not act on GABA receptors. Although less commonly used than antidepressant drugs, it appears to be of benefit in the treatment of generalised anxiety disorder and social anxiety and may also relieve depressive symptoms. As it is excreted unmetabolised, it may be more suitable than other drugs for patients with hepatic impairment [28].

9.3 Pharmacological Considerations in Treating Older Patients

9.3.1 Drug Interactions

Knowledge of the interaction potential of antidepressants helps clinicians to predict and avoid certain drug combinations, making prescribing safer [30]. This applies particularly to older patients who often take a range of medications and in whom reduced serum albumin levels may give rise to interactions with other plasma-bound drugs such as warfarin. The hepatic cytochrome p450 enzymes are involved in the metabolism of a large proportion of psychotropic drugs which also can lead to the inhibition of warfarin metabolism in patients taking antidepressants. Therefore, patients taking warfarin who are starting antidepressant treatment will require closer anticoagulant monitoring. Sertraline and citalopram are the SSRIs least likely to interact with warfarin. SSRIs can also increase levels of tricyclic antidepressants so this combination should only

Table 9.2 Important drug interactions in older patients taking antidepressants

Drugs causing interaction	Effect of interaction
Antipsychotic drugs Loop and thiazide diuretics Antiepileptic drugs Antiparkinsonian drugs	Hyponatraemia
Anticoagulants Non-steroidal anti-inflammatory drugs	Increased bleeding
Erythromycin Tamoxifen Quinine Antiarrhythmic drugs	Impaired cardiac conduction
Other classes of antidepressant with serotonergic action	Serotonin syndrome

be used under specialist supervision. See Table 9.2 for a summary of important drug interactions.

9.3.2 Hyponatraemia

The prevalence of hyponatraemia in older people treated with antidepressants as a probable consequence of treatment is around 9 %. Mechanisms include syndrome of inappropriate antidiuretic hormone secretion (SIADH) and nephrogenic syndrome of inappropriate antidiuresis [31]. Although most often associated with SSRI treatment, hyponatraemia can occur with all classes of antidepressant. While routine monitoring of serum sodium in patients taking antidepressants is not recommended, the prescriber should consider monitoring in the presence of certain risk factors and potential interactions (see Tables 9.2 and 9.3) and when symptoms of confusion and fatigue are present. Management of hyponatraemia involves reviewing the indication for the antidepressant, review of other medications, fluid restriction, and possible trial of different classes of antidepressant. Left undetected, severe hyponatraemia can lead to seizures, permanent neurological damage, and death so discussion with a general physician is advised when serum sodium is lower than 125 mmol/l.

9.3.3 Risk of Bleeding

In patients taking SSRIs, a decrease in platelet serotonin release is thought to lead to reduced platelet aggregation, increasing the risk of gastrointestinal bleeding. Therefore, the prescriber should consider the addition of a proton pump inhibitor when an SSRI is prescribed with other medications that increase risk of gastric bleeding (non-steroidal anti-inflammatory drugs and anticoagulants) [32] and in patients drinking large amounts of alcohol. Concern has been expressed about the possibility of an increased risk of haemorrhagic stroke in people taking SSRIs, but,

Table 9.3 Risk factors for hyponatraemia in patients taking antidepressants

Previous hyponatraemia
Low weight
Psychosis
Heart failure
Severe renal impairment
Diabetes mellitus
Hypertension
Chronic obstructive pulmonary disease

based on current evidence, there is no reason to restrict their use in depressed older people with cerebrovascular risk factors or post-stroke depression [33].

9.3.4 Cardiac Effects

Antidepressants are associated with changes in cardiac conduction, with prolongation of the PR, QRS, and QT intervals. At clinical doses, these changes are most likely to occur with tricyclics; most SSRIs do not appear to be associated with an increased risk of adverse events in people with cardiac disease [34]. However, the SSRI citalopram and its isomer escitalopram are associated with significant risk of QT prolongation at higher clinical doses so that maximum daily doses of 20 mg and 10 mg, respectively, are recommended (www.hma.eu). Risk of QT prolongation is increased by prescribing with certain other drugs, including erythromycin, tamoxifen, and quinine. It should be remembered that treatment of depression may actually improve the prognosis of cardiovascular disease by reducing mortality associated with depression or through effects on platelet function and modification of arrhythmias [35].

9.3.5 Other Adverse Effects of Antidepressants

SSRIs can induce or worsen movement disorders such as tremor, dyskinesia, dystonia, and parkinsonism, so monitoring for side effects is recommended in patients with these problems. Sertraline may be the least likely to cause movement disorders [33]. Sexual side effects of SSRIs include delayed or absent orgasm; this may respond to a change to an alternative antidepressant such as mirtazapine. Older antidepressants (tricyclics and monoamine oxidase inhibitors) may worsen glycaemic control in patients with diabetes, while SSRIs and SNRIs appear to have no effect; mirtazapine is not known to affect glycaemic control but can produce weight gain. Although it has been suggested that serotonergic antidepressants can accelerate osteoporosis, there is no sound evidence for this [36]. Serotonin syndrome is a rare complication of treatment with serotonergic drugs manifesting as mental state changes, autonomic instability, and neuromuscular abnormalities; those at greater risk are patients taking more than one serotonergic drug [37].

9.3.6 Antidepressant Discontinuation Syndromes

Although antidepressants are not addictive, patients should be aware that abrupt cessation of treatment can produce unpleasant symptoms that may be similar to those of their anxiety or depression, such as irritability, nausea, and neuromotor changes. Apart from fluoxetine, which has a long half-life, antidepressants should be tapered and withdrawn over a 1-month period. On rare occasions, it may be appropriate to stop antidepressants suddenly (e.g. after a cardiac arrhythmia with a tricyclic antidepressant); on such occasions it would be prudent to seek specialist advice.

9.4 Making Prescribing Decisions for Depression in Older People

As in all clinical situations, the decision on whether or not to prescribe depends on a weighing-up of the potential pros and cons of treatment. Ideally, this should be a collaborative process with the clinician, the patient, and his/her relatives or friends. For some, a good assessment will itself be therapeutic, giving an opportunity for the clinician and patient to come to a shared understanding of the biological, psychological, and social factors impacting on the patient's condition. For mild depression, the patient may benefit from self-help strategies and addressing some of the stressors in their life. If the patient is found to have moderate depression, i.e. impacting on day-to-day functioning, they may have a view as to whether to pursue psychological or pharmacological therapy which may be based on some assumptions which might be helpful to explore. For example, some are wary to take antidepressants, believing that they are addictive; if this view is dispelled, it might persuade a patient to try antidepressants. Alternatively, a patient with a very medical view of depression may be encouraged to take a more psychological stance on considering his/her illness and may gain further insight and improve further than would have been possible with medication alone. In certain situations, following assessment, the primary care physician may recommend referral to a specialist service (see Table 9.4).

Evidence with younger adults indicates that 50 % of those in a depressive episode will respond to an antidepressant, compared to 30 % of those taking a placebo [38]. As with younger adults, antidepressant drugs are more likely to be of benefit if an older person's depression is of at least moderate severity [39]. The NICE clinical practice guideline for depression [14] advocates a stepwise approach to treatment, with active monitoring and psychological therapies being first-line treatments. Antidepressants are reserved for episodes of moderate or greater severity and for patients who have had a less intense low mood for 2 years or more (dysthymia) and those who have had previous episodes of severe depression. If antidepressants are started, NICE recommends an SSRI as first line, with a gastroprotective agent for older patients and/or those taking NSAIDs or aspirin. A Cochrane systematic review supports this approach, finding that SSRIs and tricyclics have similar efficacy in

Table 9.4 Indications for referral to a specialist older people's mental health service

Suspected bipolar affective disorder
Presence of delusions and hallucinations (psychotic depression)
Concurrent significant alcohol or substance abuse
Failure of anxiety or depression to respond to two different classes of antidepressant
Possibility of dementia
Significant risks (suicidality, self-neglect, risk to others)

older people but with SSRIs being better tolerated [40]. Sertraline and escitalopram are the better tolerated SSRIs [41].

Contrary to widely held beliefs, the beneficial effect of antidepressants is most pronounced in the first week of use, with continuing improvement seen for the first 6 weeks of treatment [42]. Guidelines suggest increasing the chosen antidepressant to recommended therapeutic dose and monitoring for 4 weeks to see if it is effective [38]. Subtherapeutic dosing has previously been found to be a significant cause of non-response in older people [43]. This may reflect low expectations on behalf of the prescriber or patient or fear of the harm; however, with newer antidepressants there is no reason to avoid recommended doses. When a first-line antidepressant trial has failed, subsequent prescribing choices are guided by the findings of the "STAR-D" study [44]. In this, with citalopram as first-line treatment, 30 % of participants achieved remission. After a switch to bupropion, venlafaxine, or sertraline, or augmenting with bupropion or buspirone about a further 25 % more remitted. In further treatment stages of change of drug class or augmentation, smaller proportions each time achieved remission. The NICE Depression Guideline [14] recommends that if there is an inadequate response or intolerable side effects with a first-line SSRI, treatment be changed to another SSRI or another better tolerated newer generation antidepressant such as mirtazapine. As a third-line strategy, a switch to a different class that is usually less well tolerated is indicated (e.g. venlafaxine, a tricyclic, or a MAOI). At all steps of the guideline, it is recommended that psychological therapies as an adjunct be considered. If some benefit is seen, but the patient is struggling with side effects, it may be appropriate to provide reassurance and to continue the drug (perhaps reducing the dose or offering non-pharmacological strategies to manage the side effect), as many side effects dissipate over time. If side effects persist or are intolerable, a second medication may be added to help, such as mirtazapine for sexual dysfunction. While first- and second-line treatments may be initiated in primary care, it would be usual for further interventions to be introduced under specialist supervision.

As well as switching between antidepressants, a specialist in secondary care may also suggest augmenting antidepressants with other drugs, particularly if some initial benefit has been seen. Agents used to augment antidepressants include lithium, mirtazapine, and atypical antipsychotics, including aripiprazole, olanzapine, quetiapine, and risperidone. Before starting lithium, a baseline ECG is recommended in patients with cardiovascular disease. Once stabilised, lithium levels are monitored

12 h post dose every 3 months, and renal function, thyroid function, and calcium monitored every 6 months. If a patient develops dehydration or altered renal function, more frequent monitoring is advised. Patients who have failed to respond to multiple courses of different antidepressants may be seen as being "treatment resistant" and some of the more complex strategies outlined above can be adopted. Before labelling a patient as "treatment resistant", however, it is prudent to review the diagnosis and to look at drug interactions, poor compliance, and comorbid substance abuse.

Depression is typically a recurrent disorder. Of those with one episode of major depression, 50–80 % will go on to have a second episode, and of those who have had two episodes, 80–90 % will have a third [35]. Risk factors for recurrence include being female, having a longer and more complex episode of depression, comorbid physical illness, recurrent dysthymia, psychosocial stressors, and poor social support. Guidelines for younger adults recommend continuing the antidepressant(s) at full therapeutic dose for 6–9 months from full remission of a first episode of depression in order to reduce the risk of relapse [14, 38]. In patients with recurrent depression, continuing antidepressants reduces the risk of relapse by two thirds [45] and NICE recommends continuing antidepressants for at least 2 years [14], but, again, this is based on studies with younger adults. A Cochrane review of continuation and maintenance studies of antidepressant treatment in older people did not find evidence of benefit based on a small number of trials [46]. The risks and benefits of continuing antidepressants must always be weighed up on an individual basis to allow the patient and doctor to make a decision about ongoing treatment. In the absence of contraindications, the prescriber is likely to base the decision on the available guidelines for younger adults and to consider long-term treatment when depression is severe or highly recurrent. A pathway for prescribing decisions is shown in Fig. 9.1.

St John's wort (*Hypericum perforatum*) is a commonly used herbal antidepressant that is available without prescription. The active ingredient and mechanism of action are unclear but they possibly involve inhibition of breakdown and reuptake of monoamines and action on serotonin receptors. St John's wort is generally well tolerated and has been found to be effective for mild to moderate depression and dysthymia [47]. However, the product is poorly regulated, the therapeutic dose is unknown, and it may interact with a number of other medications. Patients taking it may omit to mention it to their doctor assuming that, as a herbal medicine, it will be harmless. NICE does not recommend the use of St John's wort in the management of depression [14].

9.5 Case 1: Mr A, Initial Presentation of Depression

Mr A, a 70-year-old man, presents to his general practitioner (Dr X) with a month-long history of low mood, poor sleep, poor appetite, lack of motivation, and reduced enjoyment of his usual activities. He has no prior history of mental disorder and no physical illnesses.

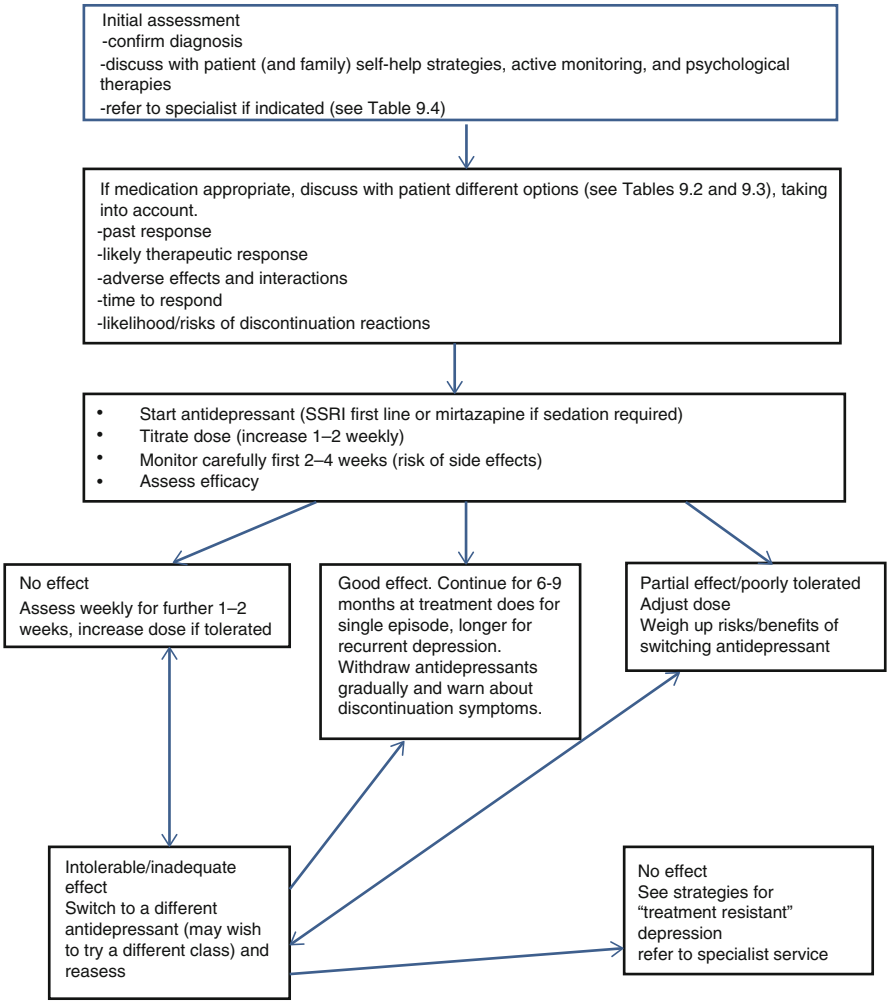

Fig. 9.1 Decision pathway for prescribing in depression

This would seem to be a depressive episode. A biopsychosocial assessment should confirm the diagnosis and identify precipitating and maintaining factors and risks.

Dr X completes a full assessment and diagnoses a moderate depressive episode with no major risks and no significant functional impairment. Dr X outlines treatment options, gives some written information about depression and sleep hygiene, and asks Mr A to make a follow-up appointment. Mr A returns the following week and is keen to be referred for psychological therapy but not sure about medication as he has heard it is addictive and would prefer to try a natural option like St John's wort. Dr X discusses the pros and cons of medication and St John's wort and addresses some of Mr A's misunderstandings. Mr A decides to try psychological

therapy alone (an online course while waiting for an assessment with the psychological therapy service). Dr X supports the decision and advises Mr A to return for a follow-up appointment in 2 weeks or sooner if necessary.

9.6 Case 2: Mr A, Starting an Antidepressant

Mr A returns to Dr X after a month as he feels no better and would like to consider starting an antidepressant. Dr X discusses the pros and cons of different medications. Although Mr A has difficulty getting to sleep, this has improved slightly with exercise and Mr A does not like the idea of taking mirtazapine due to the risks of daytime sedation and weight gain. They agree on a trial of sertraline, starting at 50 mg. Dr X discovers that Mr A occasionally takes ibuprofen for joint pain and advises him about the risk of gastrointestinal bleeding with both NSAIDs and SSRIs. Mr A agrees to try different analgesic options if required, rather than start a proton pump inhibitor as a gastroprotective agent. Dr X advises Mr A of possible side effects of sertraline and asks him to return in a week's time.

On return a week later, Mr A feels slightly better. He has had some symptoms of nausea and diarrhoea but these seem to be settling. One week later, Mr A still feels slightly better and asks to increase the dose of sertraline to see if this leads to any further improvement. Dr X increases the dose to 100 mg and asks Mr A to return again for a further appointment. Mr A feels a great deal better on 100 mg and decides to stay on this dose while continuing psychological treatment.

9.7 Case 3: Mr A, Stopping an Antidepressant

Mr A returns to Dr X after 5 months of treatment and asks about stopping the sertraline as he does not feel he needs it any longer. Dr X discusses the pros and cons of stopping the medication and the potential risk of relapse with Mr A. Mr A decides to continue for another couple of months until he has finished his course of psychological treatment before stopping the medication. The sertraline is reduced to 50 mg daily for 1 month and then discontinued.

NICE guidelines recommends continuing antidepressants for 6 months from remission of a first episode of depression [14] *although at present there is a lack of evidence specific to older people* [45].

9.8 Case 4: Mr A, Recurrence of Depression

Nine months later, Mr A returns with another episode of depression and feels worse than he did previously. He restarts sertraline and finds he needs a higher dose this time (150 mg). After 6 weeks of treatment, he feels much better and would like to reduce the dose and eventually stop the sertraline again. Dr X and Mr A discuss the increased risk of relapse; now Mr A has had two episodes of depression. Dr X

informs Mr A of the guidelines which recommend continuing it for 2 years for relapse prevention. Mr A decides to continue at 150 mg.

9.9 Case 5: Mrs B, a Patient Who Does Not Respond to Treatment

Mrs B presents with a first episode of moderate depression aged 75. She is not keen to try any psychological therapy and so starts a course of sertraline increasing the dose to 100 mg over 2 weeks. She does not notice any improvement in her symptoms and asks Dr X if she can try something else. Dr X discusses the pros and cons of different options with her, suggesting trying either mirtazapine or a different SSRI. Mrs B decides to try mirtazapine as she has been having trouble sleeping.

9.10 Case 6: Mrs B, No Response to a Change of Antidepressant

After 4 weeks, Mrs B has still not noticed any improvement in her symptoms. Dr X explores her problems further and discovers that she is using significant alcohol in order to help her sleep. He discusses the possibility of alcohol being a maintaining factor of her problems and suggests ways of cutting down her intake, offering specialist support and advice on sleep hygiene. Dr X explores again Mrs B's reticence towards psychological therapies but she remains unwilling to consider this as an option.

Mrs B manages to cut down her alcohol intake, but her depressive symptoms get worse, despite good compliance with mirtazapine 45 mg nightly. Dr X is concerned that Mrs B has been having more suicidal thoughts and is neglecting her self-care and refers her to the older adult community mental health team (CMHT). She sees a psychiatrist who adds venlafaxine to her mirtazapine and a community psychiatric nurse assesses Mrs B at home to support her through her recovery.

9.11 Case 7: Mr C, Depression After a Stroke

Dr X sees Mr C 2 weeks after his return from hospital following a large ischaemic cerebrovascular event. Mr C is receiving intensive support from the community physiotherapists but is not making as much progress as they would like as he lacks motivation to complete the rehabilitation exercises. The physiotherapist has discussed the case with Dr X as he is concerned Mr C may be depressed.

It is estimated that 40 % of patients who survive a stroke suffer from depression and that this slows down rehabilitation [48]. *There is also some evidence that, regardless of depressive symptoms, antidepressants may enhance recovery of motor skills in the rehabilitation process* [49]. *Although theoretically there is potential for SSRIs to worsen haemorrhagic stroke, in practice this does not seem to be the case*

and the benefits of antidepressants (*including SSRIs*) *outweigh the risks for both haemorrhagic and ischaemic stroke*[48], *with there currently being evidence for citalopram*, *fluoxetine, and nortriptyline* [35].

Mr C starts a course of fluoxetine (with omeprazole as he is already taking clopidogrel after his stroke) and finds his mood and motivation improve, with subsequent benefits for his recovery and rehabilitation.

9.12 Case 8: Mrs D, Depression After Previous Deliberate Overdoses

Mrs D has a history of recurrent depression with previous suicide attempts by overdose. She consults Dr X about starting antidepressants. She cannot recall what treatments have helped previously and her old records are not available. She currently has no specific plans to take an overdose but explains that previous overdoses have been impulsive and often after drinking alcohol.

Dr X considers the pros and cons of different medication options with Mrs D. Tricyclic antidepressants and venlafaxine are least safe in overdose so are best avoided. There would be a risk of oversedation if Mrs D were to take an overdose of mirtazapine, particularly if combined with alcohol. SSRIs would be the safest option but Mrs D will still need careful monitoring and possible referral to the CMHT. It is agreed that her neighbour will look after her stocks of medication.

9.13 Case 9: Mrs E, Hyponatraemia and Confusion with an SSRI

Mrs E is aged 85 and living in a nursing home. She has a history of heart failure following a myocardial infarction and a degree of renal impairment and takes (amongst other medications) bendroflumethiazide and omeprazole. She was started on fluoxetine by a colleague 2 weeks ago and the nursing home call Dr X as she appears muddled and lethargic. Dr X completes a full assessment and requests serum electrolytes. Mrs E is found to have a serum sodium of 127 mmol/L (normal range 135–145 mmol/L), which is the likely cause of her confusion and lethargy.

See Table 9.3 *for risk factors for developing hyponatraemia. When sodium is greater than 125 mmol/l*, *the patient can be monitored daily and the team may consider withdrawing the likely causal agent. If sodium drops below 125 mmol/l, it is prudent to seek specialist medical advice and to stop the SSRI. Fluid restriction alone may correct the sodium. It is possible to repeat a trial of an SSRI or to use a less serotonergic antidepressant*, *such as lofepramine* [35].

Dr X slowly withdraws the fluoxetine and monitors her sodium, but three days later it has dropped to 124 mmol/L. Mrs E is treated in a general hospital and returns to the nursing home. Dr X weighs up the pros and cons of further antidepressant treatment with Mrs E and her key nurse and they decide to avoid further antidepressants for the time being.

9.14 Case 10: Mr F, Sexual Dysfunction with an SSRI

Mr F presents to Dr X requesting to stop the fluoxetine he started a month ago. Dr X explores this further with him, and, although he reports some improvement in his depression, he has been suffering from erectile dysfunction and sees that this might be a side effect of the medication. Dr X discusses this further and Mr F recognises that the erectile dysfunction may also be linked to the depression, given that some of his difficulties occurred before starting fluoxetine. Dr X excludes other contributory factors to the erectile dysfunction, such as substance misuse, side effects of other medications, and diabetes. Dr X reassures Mr F that sexual dysfunction side effects of SSRIs are reversible and discusses different options with Mr F. Options include continuing on the same dose of fluoxetine and monitoring, trying a reduced dose, switching to or adding a different antidepressant with likely lower risk (e.g. mirtazapine), or considering adding sildenafil as an adjunct. Mr F decides to switch to mirtazapine which helps both his erectile dysfunction and his mood.

Bupropion is thought to be the antidepressant with the least likelihood of sexual dysfunction side effects, but it is currently not licensed for use as an antidepressant in the UK [35].

9.15 Case 11: Mrs G, Psychotic Depression

Mrs G's daughter asks Dr X to urgently assess her mother as she has rapidly lost weight. Dr X finds no physical cause for her weight loss. Mrs G has not been eating and explains to Dr X that her "insides have rotted away" and that she is somehow culpable for her grandaughter's recent miscarriage. Dr X explores this further and diagnoses Mrs G with a psychotic depression. Due to the severity of her illness, Dr X discusses her case with the CMHT who arrange an urgent assessment. Mrs G is supported in her home with daily visits from a care agency and frequent contact from the CMHT. She is started on olanzapine, an antipsychotic, and sertraline. Dr X continues to work closely with the mental health team and to manage her physical health, with regular reviews and blood tests as she begins to eat again. Over time, Mrs G's psychotic symptoms diminish and she is able to look after herself without the support of carers.

9.16 Case 12: Mr H, Depression with a Background of Bipolar Affective Disorder

Mr H presents to Dr X with a moderate depressive episode. He is known to have bipolar affective disorder with numerous previous admissions to hospital with mania. His last admission was 5 years ago, and he has been taking lithium since, but stopped it a year ago, with the support of the CMHT, as he was beginning to develop renal failure. Dr X discusses the case with the CMHT as there would be a risk of Mr

H developing another manic episode if he started antidepressant treatment. The CMHT psychiatrist assesses Mr H and discusses the pros and cons of different treatment options with him, including the possibility of trying quetiapine (an antipsychotic with an antidepressant action) or restarting lithium. Mr H agrees to try quetiapine and his depressive symptoms improve without any manic relapse.

9.17 Making Prescribing Decisions for Anxiety in Older People

Anxiety disorders are highly prevalent in older people although sufferers may be unlikely to seek help. Anxiety symptoms are associated with increased disability and mortality, increased burden on health service, and decreased cognitive and functional abilities [15]. As already described, anxiety often coexists with depression and chronic physical health conditions which may blind the clinician to identifying the anxiety disorder and offering appropriate treatment. Different types of anxiety disorder also often coexist – for example, a patient with generalised anxiety may also have a specific phobia. When considering more than one diagnosis, it is advisable to perform a thorough assessment of all symptoms in order to gain an understanding of the patient's experience, to treat the predominant disorder and then reassess the effect on other symptoms, and offer further treatment if necessary.

The largest evidence base in the management of anxiety disorders is for psychological interventions, particularly cognitive behavioural therapy (CBT) [50]; pharmacological therapy is reserved for patients who experience functional impairment or do not respond to psychological therapy. For treatment-refractory anxiety, the combination of pharmacotherapy and psychological therapy can be considered but there is little evidence to guide decisions [16]. Benzodiazepines are only recommended for short-term use in generalised anxiety disorder and extra caution should be taken when prescribing in the elderly due to risk of sedation and falls. Table 9.5 summarises current prescribing guidance. Patients whose anxiety does not respond to an SSRI are likely to be referred to a specialist for advice on further management.

9.18 Case 13: Mrs I, Generalised Anxiety Disorder

Mrs I presents to Dr X following an admission to hospital. She is highly anxious about falling and so has not felt able to leave the house since her discharge 2 months ago. She is frequently seeking reassurance from her daughter who asks if she can be started on benzodiazepines. Dr X assesses Mrs I and finds that she has numerous physical and psychological symptoms of anxiety and specific worries about falling consistent with generalised anxiety disorder. Dr X discusses different treatment options with Mrs I and her daughter and explains the risks of increased falls and dependence with benzodiazepines. Mrs I is too anxious to leave the house to attend

Table 9.5 Prescribing decisions for anxiety disorders

Anxiety disorder	Acute management	Long-term first-line management	Other drug treatments	Comments
Generalised anxiety disorder	Benzodiazepines (short-term use only – weeks)	Start with sertraline and then try another SSRI or venlafaxine Use low starting dose and increase gradually If lack of response, try pregabalin	Buspirone, beta blockers for somatic symptoms (with caution due to cardiovascular effects)	Continue treatment for a year. May prevent development of depression
Panic disorder	Benzodiazepines not recommended by NICE	SSRIs – as above	Imipramine or clomipramine if no improvement after 12 weeks (with caution due to cardiovascular effects)	Assess for comorbid depression and/or substance abuse
Post-traumatic stress disorder	Nil	SSRIs (paroxetine or sertraline) and then venlafaxine	Other antidepressants	Continue for 12 months
Obsessive compulsive disorder	Nil	SSRIs, clomipramine. May take up to 12 weeks to respond	Augment with antipsychotics or mirtazapine	May need higher dose of antidepressants than dose for depression. May take longer to remit. Continue for 12 months
Social phobia	Occasional short-acting benzodiazepines	SSRIs and then venlafaxine. Consider MAOIs (phenelzine, moclobemide)	Buspirone as adjunct to SSRIs, propranolol for performance anxiety (with caution due to cardiovascular effects)	Treat for at least 6 months

Data from National Institute for Health and Clinical Excellence [50] and Baldwin et al. [28]

a psychological therapy group and there is a waiting list for individual CBT at home. Mrs I and Dr X agree that she should start sertraline while waiting for the individual CBT. Mrs I responds well to sertraline and bibliotherapy about anxiety and the CBT model. After a month of treatment, she is able to leave the house and attends the group CBT with good effect.

9.19 Case 14: Mr J, Mixed Anxiety and Depression

Mr J presents 6 months after the death of his wife with symptoms of low mood and anxiety. After careful assessment Dr X diagnoses Mr J with a moderate depressive episode with prominent anxiety symptoms. Dr X and Mr J agree to initiate treatment with antidepressants and CBT. Mr J responds well to antidepressants and both his depressive and anxiety symptoms resolve.

9.20 Case 15: Mrs K, Anxiety in Chronic Disease

Mrs K frequently attends Dr X's practice with symptoms of breathlessness. Mrs K has a history of chronic obstructive pulmonary disease (COPD) with frequent exacerbations. Dr X diagnoses features of generalised anxiety disorder as well as poorly controlled COPD. Mrs K is not keen on taking medication and Dr X sees from old notes that many of her infective exacerbations of COPD have been complicated by her poor compliance with antibiotics and steroid regimes. Dr X refers Mrs K to the practice nurse for education about her COPD and intensive support in enabling her to manage her own symptoms. Mrs K's compliance with inhalers improves, her peak flow improves, and she has fewer exacerbations of her COPD, which improves her breathlessness and anxiety symptoms.

9.21 Suggested Topics for Clinical Audit in Primary Care

- Rates of follow-up appointments within 2 weeks of initiating antidepressant treatment
- Rates of 6-month review of antidepressant treatment with decision on whether to continue
- Identification of drug combinations associated with important interactions (SSRIs with NSAIDs or anticoagulants; lithium with diuretics)
- Monitoring of renal and thyroid function and lithium levels in patients taking lithium

9.22 Appendix 9.1: Suggested Reading for Patients

Age UK website, including printable factsheets on depression: www.ageuk.org.uk/health-wellbeing/conditions-illnesses/depression/

Mind website, including factsheets on depression and anxiety: www.mind.org.uk/information-support/types-of-mental-health-problems/depression

NHS Choices website: www.nhs.uk/conditions

9.22.1 Appendix 9.2: Recommended Reading for Prescribers

Cleare A, Pariante C, Young AH, et al. Evidence-based guidelines for treating depressive disorders with antidepressants: a revision of the 2008 British Association for Psychopharmacology guidelines. J Psychopharmacol 2015;29(5):459–525.

Baldwin DS, Anderson IM, Nutt DJ, et al. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: A revision of the 2005 guidelines from the British Association for Psychopharmacology. J Psychopharmacol (Oxf). 2014;28(5):403–39.

Taylor D, Paton C, Kapur S. The Maudsley prescribing guidelines in psychiatry. 11th edn. Chichester: Wiley-Blackwell; 2012.

Stahl S. The prescriber's guide: antidepressants. New York: Cambridge University Press; 2006.

References

1. Cairney J, Corna L, Veldhuizen S, et al. Comorbid depression and anxiety in later life: patterns of association, subjective well-being, and impairment. Am J Geriatr Psychiatry. 2008;16(3):201–8.
2. Andreescu C, Lenze E, Mulsant BH, et al. High worry severity is associated with poorer acute and maintenance efficacy of antidepressants in late-life depression. Depress Anxiety. 2009;26(3):266–72.
3. Wolitzky-Taylor KB, Castriotta N, et al. Anxiety disorders in older adults: a comprehensive review. Depress Anxiety. 2010;27(2):190–211.
4. Ferretti L, McCurry S, Logsdon R, et al. Anxiety and Alzheimer's disease. J Geriatr Psychiatry Neurol. 2001;14(1):52–8.
5. Sareen J, Jacobi F, Cox BJ, et al. Disability and poor quality of life associated with comorbid anxiety disorders and physical conditions. Arch Intern Med. 2006;166(19):2109–16.
6. de la Riva P, Smith K, Xie S, Weintraub D. Course of psychiatric symptoms and global cognition in early Parkinson disease. Neurology. 2014. doi:10.1212/WNL.0000000000000801.
7. Gerrits M, van Oppen P, Leone S, et al. Pain, not chronic disease, is associated with the recurrence of depressive and anxiety disorders. BMC Psychiatry. 2014;14:187.
8. Rayner L, Price A, Evans A, et al. Antidepressants for depression in physically ill people. Cochrane Database Syst Rev. 2010;3.
9. Alexopoulos G, Murphy C, Gunning-Dixon F, et al. Microstructural white matter abnormalities and remission of geriatric depression. Am J Psychiatry. 2008;165:238–44.
10. Sheline Y, Pieper C, Barch D, et al. Support for the vascular depression hypothesis in late-life depression: results of a two-site, prospective, antidepressant treatment trial. Arch Gen Psychiatry. 2010;67:277–85.
11. Dew MA, Reynolds III CF, Houck P, et al. Temporal profiles of the course of depression during treatment. Arch Gen Psychiatry. 1997;54:1016–24.
12. Roose SP, Schatzberg A. The efficacy of antidepressants in the treatment of late-life depression. J Clin Psychopharmacol. 2005;25(4 Suppl 1):S1–7.

13. Fawzi W, Abdel Mohsen MY, Hashem AH, et al. Beliefs about medications predict adherence to antidepressants in older adults. Int Psychogeriatr. 2012;24(01):159–69.
14. National Institute for Health and Clinical Excellence. The treatment and management of depression in adults (updated version). National Clinical Practice Guideline 90. 2010.
15. Gonçalves DC, Byrne GJ. Interventions for generalized anxiety disorder in older adults: systematic review and meta-analysis. J Anxiety Disord. 2012;26(1):1–11.
16. Barton S, Karner C, Salih F, et al. Clinical effectiveness of interventions for treatment-resistant anxiety in older people: a systematic review. Health Technol Assess Rep. 2014;18(50).
17. Greenlagh T, et al. Evidence based medicine: a movement in crisis? BMJ. 2014;348:18–21.
18. Hunkeler E, Katon W, Tang L, et al. Long term outcomes from the IMPACT randomised trial for depressed elderly patients in primary care. Br Med J. 2006;332:259–62.
19. Richards DA, Hill JJ, Gask L, et al. Clinical effectiveness of collaborative care for depression in UK primary care (CADET): cluster randomised controlled trial. BMJ. 2013;347:f4913.
20. Stahl S. Selecting an antidepressant by using mechanism of action to enhance efficacy and avoid side-effects. J Clin Psychiatry. 1998;59(18):23–9.
21. Barbui C, Esposito E, Cipriani A. Selective serotonin reuptake inhibitors and risk of suicide: a systematic review of observational studies. Can Med Assoc J. 2009;3:291–7.
22. Mazeh D, Shahal B, Aviv A, et al. A randomized single-blind comparison of venlafaxine with paroxetine in elderly patients suffering from resistant depression. Int Clin Psychopharmacol. 2007;22:371–5.
23. Cooper C, Katona C, Lyketsos K, et al. A systematic review of treatments for refractory depression in older people. Am J Psychiatry. 2011;168(7):681–8.
24. Cipriani A, Hawton K, Stockton S, Geddes J. Lithium in the prevention of suicide in mood disorders: updated systematic review and meta-analysis. BMJ. 2013;346:3646.
25. Sheffrin M, Driscoll H, Lenze EJ, et al. Pilot study of augmentation with aripiprazole for incomplete response in late-life depression: getting to remission. J Clin Psychiatry. 2009;70:208–13.
26. Depping A, Komossa K, Kissling W, Leucht S. Second-generation antipsychotics for anxiety disorders. Cochrane Database Syst Rev. 2010;(12):CD008120.
27. Banerjee S. The use of antipsychotic medication for people with dementia: time for action. London: Department of Health; 2009.
28. Baldwin DS, Anderson IM, Nutt DJ, et al. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology. J Psychopharmacol (Oxf). 2014;28(5):403–39.
29. Chessick C, Allen M, Thase M. Azapirones for generalized anxiety disorder. Cochrane Database Syst. Rev. 2006;(3):CD006115.
30. Spina E, Trifirò G, Caraci F. Clinically significant drug interactions with newer antidepressants. CNS Drugs. 2012;26(1):39–67.
31. Mannesse C, Jansen P, van Marum RP, et al. Characteristics, prevalence, risk factors, and underlying mechanism of hyponatraemia in elderly patients treated with antidepressants: a cross-sectional study. Maturitas. 2013;76:357–63.
32. de Abajo F. Effects of selective serotonin reuptake inhibitors on platelet function: mechanisms, clinical outcomes and implications for use in elderly patients. Drugs Aging. 2011;28(5):345–67.
33. Chemali Z, Chahine LM, Fricchione G. The use of selective serotonin reuptake inhibitors in elderly patients. Harv Rev Psychiatry. 2009;17(4):242–53.
34. Lespérance F, Frasure-Smith N, Koszycki D, et al. Effects of citalopram and interpersonal psychotherapy on depression in patients with coronary artery disease: the Canadian Cardiac Randomized Evaluation of Antidepressant and Psychotherapy Efficacy (CREATE) trial. JAMA. 2007;297:367–79.
35. Taylor D, Paton C, Kapur S. The Maudsley prescribing guidelines in psychiatry. 11th ed. Chichester: Wiley-Blackwell; 2012.
36. Gebara MA, Shea MLO, Lipsey KL, et al. Depression, antidepressants, and bone health in older adults: a systematic review. J Am Geriatr Soc. 2014;62(8):1434–41.

37. Buckley N, Dawson A, Ibister G. Serotonin syndrome. BMJ. 2014;348:33–5.
38. Cleare A, Pariante C, Young AH, et al. Evidence-based guidelines for treating depressive disorders with antidepressants: a revision of the 2008 British Association for Psychopharmacology guidelines. J Psychopharmacol 2015;29(5):459–525.
39. Nelson J, Delucchi K, Schneider L. Moderators of outcome in late-life depression: a patient-level meta-analysis. Am J Psychiatry. 2013;170:651–9.
40. Mottram P, Wilson K, Strobl J. Antidepressants for depressed elderly. Cochrane Database Syst Rev. 2006;(1):CD003491.
41. Cipriani A, Furukawa TA, Salanti G, et al. Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis. Lancet. 2009;373(9665):746–58.
42. Taylor MJ, et al. Early onset of selective serotonin reuptake inhibitor antidepressant action: systematic review and meta-analysis. Arch Gen Psychiatry. 2006;63:1217–23.
43. Heeren TJ, Derksen P, van Heycop Ten Ham BF, van Gent PP. Treatment, outcome and predictors of response in elderly depressed in-patients. B J Psychiatry. 1997;170:436–40.
44. Gaynes BD, Warden D, Trivedi MH, et al. What did the STAR*D teach us? Results from a large-scale, practical, clinical trial for patients with depression. Psychiatr Serv. 2009;60(11): 1439–45.
45. Geddes JR, Carney SM, Davies C, et al. Relapse prevention with antidepressant drug treatment in depressive disorders: a systematic review. Lancet. 2003;361:653–61.
46. Wilkinson P, Izmeth Z. Continuation and maintenance treatments for depression in older people (review). Cochrane Database Syst Rev. 2012;(11):CD006727. doi:10.1002/14651858.CD006727,pub2.
47. Linde K, Berner M, Egger M, Mulrow C. St John's wort for depression: meta-analysis of randomised controlled trials. Br J Psychiatry. 2005;186:99–107.
48. Sarkstein SE, Mizrahi R, Power BD. Antidepressant therapy in post-stroke depression. Expert Opin Pharmacother. 2008;9(8):1291–8.
49. Chollet D, Tardy J, Albucher J-F, Berard E, et al. Fluoxetine for motor recovery after acute ischaemic stroke (FLAME): a randomised placebo-controlled trial. Lancet Neurol. 2011;10: 123–30.
50. National Institute for Health and Clinical Excellence. Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults. Management in primary, secondary and community care. National Clinical Practice Guideline 113. www.niceorguk. 2011.