Drug Treatment in Old Age
Psychiatry
Drug Treatment in Old Age Psychiatry

Cornelius Katona MD FRCPsych
Professor of Psychiatry of the Elderly, Department of Psychiatry and Behavioural Sciences, University College London Medical School, London

Gill Livingston MB
Reader in Psychiatry of Older People, Department of Psychiatry and Behavioural Sciences, University College London Medical School, London

MARTIN DUNITZ
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Nowhere is it more important to get psychotropic drug prescribing ‘right’ than in old age psychiatry practice, given the increased vulnerability of older people to adverse drug effects and to dangerous interactions. Although there are many excellent textbooks dealing with psychiatric drug prescribing in general and with old age psychiatry, there is a remarkable lack of summary texts addressing the specific issues of psychotropic drug prescribing for older people.

We have attempted to produce a short, portable and practical book that should be helpful to psychiatrists (including those in training), to pharmacists and to physicians in medicine for older people. It should also be useful for nurses and psychologists working with older people because they are becoming increasingly involved in the practicalities of drug administration.

We have attempted to review the literature systematically and hope that the summary text we have produced is an accurate and up-to-date reflection of the current evidence base. In the interests of brevity, legibility and portability, we have chosen not to cite all the hundreds of references we have summarized. We have, however, appended a brief list of systematic reviews and more general papers and textbooks, which we hope will help guide readers who require more detailed information.

Writing the book has made us intensely aware that good prescribing is an art as well as a science. Prescribers need to be aware of the range of available drugs, their characteristics and limitations, and the problems
commonly encountered in their use. Equally important, they need to take into account the individual characteristics, wishes and knowledge of the patients involved and their families. We hope that, by summarizing the core knowledge currently available, this book will encourage good and individualized practice.

Cornelius Katona
Gill Livingston
Adherence and compliance: just keep taking the tablets

The scale of the problem
All tablets are ineffective if not taken. Adherence is often poor, with between 30% and 68% of patients discontinuing antidepressants and a further third taking too few, too many or irregularly. Patients who do not recover from depression are often those who have discontinued or never taken their medication.

Ways to increase adherence
The research into improving adherence is comparatively recent in its development. Factors identified as important in non-adherence for all age groups include patient attitudes, social circumstances, side effects of medication and the quality of the patient–doctor relationship. It is well established in the literature that a complex interplay of factors may be involved in an individual’s non-adherence to antidepressants. However, such awareness has not yet permeated the majority of research into adherence interventions. A review of 17 studies in younger adults found that 15 were focused on patient education. (Pampallona et al, 2002) Although such education improves patients’ knowledge, several studies have failed to demonstrate the translation of this into improved adherence or better outcome. Knowledge is not necessarily power.
The two exceptions to didactic information-based approaches to increasing adherence included some form of exploration of potential obstacles to adherence from a patient’s perspective. A trial of a cognitive–behavioural intervention combined with psychoeducation (compliance therapy) was compared with non-specific counselling for patients with psychosis on acute psychiatric admissions wards. This resulted in the development of a manual for use in this patient group. The second, published in 1999, was a trial of antidepressant drug counselling conducted by nurses in primary care compared with drug information leaflets. Both study interventions improved adherence in comparison to their control groups.

The literature on adherence interventions for the older population is fairly sparse. Only one small non-randomized study has specifically addressed the use of antidepressants in elderly people. It suggested that one-off family therapy sessions improve adherence.

Several other strategies have been explored for use with a variety of medical interventions in older people. Efforts to improve adherence with one-off treatments, using written educational material, have had mixed results; one study demonstrated increased uptake of influenza immunization with this method whereas another failed to demonstrate such an effect for colorectal cancer screening. For longer-term treatments, two patient education programmes conducted by pharmacists have shown a positive impact on adherence. A further study failed to demonstrate any benefit from adding a medication card to pharmacist-led patient education. It is of note, however, that most of the research on older people focuses on the mechanics of medication delivery, such as the successful use of calendar blister packs. This move away from emphasis on cognitive aspects of adherence may in part reflect stereotyping of older people as cognitively impaired.

The literature on adherence for both younger and older people suggests that patients often do an informal cost–benefit analysis to decide whether to take medication. This has been formalized in what is known as the health belief model (see Box 1 which lists the areas considered).

**Non-adherence to antidepressants**

Factors associated with non-adherence to antidepressants are lack of
education about the medication from the prescriber, and worry about experience of side effects. Tackling these factors may help ensure that people take their medication \((\text{Box 2})\). Our group has recently developed a form of concordance therapy for older people with depression combining elements of psychoeducation, motivation therapy and cognitive–behavioural therapy.

**Box 1  Health belief model.**

- Perceived threat of illness
- Internal cues to action, e.g. pain
- External cues to action, e.g. GP advice
- Perceived benefits of treatment
- Perceived costs of treatment

**Non-adherence to anti-psychotics**

Patients often do not take anti-psychotic medication \((\text{Box 3})\). The reasons may be similar to those mentioned above, e.g. unacceptable side effects. There may be additional factors; one study of younger people

**Box 2  Factors associated with increased adherence to antidepressants.**

- Prescribing tablets with fewer side effects
- Discussing the tablets with and educating the patient about the tablets
- Finding out and addressing patient’s worries about side effects.

**Box 3  Factors associated with adherence to anti-psychotics.**

- Less severe psychotic symptoms
- Good sense of relation to self or others
- Low agreement regarding purpose of treatment
has found that the most important predictor for not taking the tablets in this population was severity of psychotic symptoms. This may be related to disorganization, apathy or a lack of insight into having an illness.

**Dementia and non-adherence (Box 4)**

Non-adherence in dementia may be related to the inability to remember whether the tablets have been taken. There is also a marked similarity to the psychotic illnesses in that patients may not believe that they are ill, have difficulty in organizing themselves to take the tablets or are apathetic. People with dementia may benefit from some of the general strategies discussed in Box 5 such as a dosset box. Frequently, if the dementia is more than very mild, the patients need supervision because they will have difficulty learning to use a dosset box or finding it. Most supervision is done by the family at home or by paid carers if a person is institutionalized. Those people who live alone with care packages can be reminded by the carers to take their medication, but the carers are not

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**Box 4  Reasons for non-adherence in dementia.**

- Inability to remember whether tablets have been taken
- Patients believe that they are well
- Patients have difficulty organizing themselves to take the tablets
- Apathy

**Box 5  Strategies for managing general difficulties in taking medication.**

- Prescriber should ensure that regimen is as simple as possible
- Prescriber should review medication regularly to ensure that the patient is not on unnecessary tablets
- Dosset box
- Pharmacy-filled, dated, individualized containers
- Liquid medication
- Non-childproof containers
allowed to sort it out. This group of people will therefore require a pharmacist, district nurse or member of the family to put the medication into special packaging, a dosset box or other container.

**Difficulties in taking medication: general problems in older people (Box 6)**

We have discussed the reasons why people may choose not to take medication. In addition to these problems, older people more commonly have specific difficulties in taking medication related to specific or multiple morbidities. The difficulties may be related to a particular psychiatric problem such as dementia or psychosis and these are discussed above. There may also be difficulties related to physical illnesses, such as problems in swallowing or difficulty in getting the tablets out of the container. People with multiple morbidities may have very complex medication regimens which are difficult to follow even in those who are motivated to do so, cognitively intact and organized. Since many older patients with multiple illnesses are depressed or have dementia, these may be additional complications.

**Box 6  Factors associated with general difficulty in taking tablets.**

- Forgetting to take the tablets
- Difficulty in swallowing
- Difficulty in getting the tablets out of the container
- Complex medication regimens

**Strategies for tackling general problems in taking tablets (see Box 5)**

Many complex medication regimens do not need to be as difficult. It is the duty of the prescriber to ensure that the regimen is as simple as
possible, e.g. by ensuring that medication is not prescribed twice a day if it can be taken on a once-daily basis. Many patients have more and more tablets added without any being removed. It is also essential that prescribing doctors review medication regularly to ensure that the patient is not on unnecessary tablets. Patients who have difficulties in accessing drugs, e.g. because of muscular weakness or arthritis, may benefit from a more easily accessible container such as a dosset box or ticking the box on prescription that specifies non-childproof containers. Dosset boxes can also be very useful to sort out complex medication regimens, although they require to be filled manually. This may sometimes be done by relatives or district nurses.

An easier alternative may be the packaging service offered by most community pharmacists where all of a patient’s drugs are dispensed in an individualized pack that is labelled with the times and days of the week. Reviewing the packaging and number of tablets may help patients who have a degree of difficulty in swallowing. Some will require their medication in liquid form and this may not be readily available and may have to be specially made.

Paradoxically, patients who can swallow nothing may have no difficulty with tablets. They usually require nutrition through a percutaneous endoscopic gastrostomy (PEG) and medication can be given in the same way.
Definition and symptoms

Depression is common and disabling in old age, particularly in people who have co-morbid physical illness or are in institutional care. It is associated with high costs for health care and social care. Despite this, it is often missed, ignored or not managed adequately. Patients present when they need help but often they do not complain of low mood. This is partly a consequence of widely held ‘ageist’ assumptions that depression is intrinsic to the ageing process, and that treatment is inappropriate, excessively risky or unlikely to be effective. These assumptions are demonstrably untrue: most older people are not clinically depressed (despite their increased risk of loss and adversity); depression does not increase in prevalence with age and those who are depressed respond as well to the range of pharmacological and psychological treatment as do younger depressed patients.

Clinical features

Depression often presents in a less typical fashion in old age. The clinical features of depressive disorder may also be complicated by coexisting medical problems and/or cognitive impairment. This clearly has implications for the under- or misdiagnosis of depression in elderly people. Older patients tend to have an increase in somatic complaints, sleep
disturbance (initial insomnia) and agitation. Two main symptom clusters have been demonstrated: ‘affective suffering’, which includes low mood, tearfulness and the wish to die; and a ‘motivational’ cluster comprising loss of interest, poor concentration and lack of enjoyment (Box 7). Some depressive symptomatology is often found in older individuals who do not have frank depressive illness. The psychological symptoms most frequently elicited in such people include dysphoria, sleep disturbance, thoughts of death, anergy, impaired concentration, agitation and retardation.

**Box 7  Symptom clusters in depression in elderly people.**

*Affective suffering*
- Low mood
- Tearfulness
- The wish to die

*Motivational cluster*
- Loss of interest
- Poor concentration
- Lack of enjoyment

Age-related differences in symptom patterns have been reported in elderly people. Items relating to low self-esteem were more common in the ‘young old’, whereas the presence of hypochondriasis was positively correlated with age. Individuals whose first episode of depression occurred in late life are more likely to display cognitive impairment, although psychotic features occur less often. However, the latter finding may be a reflection of the greater average age (and therefore greater vulnerability to dementia) of those in the group with late first onset. Symptom patterns in depressed older people have been found to differ by sex. Depressed mood, guilt, anxiety and diurnal mood variation were found to be more common in women with depression than in men with depression.
Prevalence and associates of depression

Older individuals in the community appear to have a lower prevalence of major depression (as defined within the DSM [Diagnostic and Statistical Manual of Mental Disorders] system) than their younger counterparts whereas the prevalence of dysthymia (chronic mild depression) may be much higher. This probably reflects the differences in typical clinical features discussed above. Two recent comprehensive reviews (mainly of studies using interview schedules and diagnostic criteria designed specifically for use in older people) reported average prevalence rates of 13.5% and 12.3%. Most of the studies reviewed found rates in women nearly twice as high as in men.

The prevalence of depressive illness appears to be higher among those elderly people who attend their general practitioner (GP). Rates as high as 34% have been reported. Frequent attendance at the GP surgery may be a ‘marker’ of increased likelihood of depression. Similarly, the prevalence of depressive disorders among elderly people in long-term institutional care is in excess of 20%. In hospitalized elderly people, the prevalence of depression rises further, with a reported range between 12% and 45%.

Depression is more common in physically ill than in healthy older people. As physical illness and depression often both present with physical features (such as sleep disturbance, loss of appetite and pain), the use of screening tests that use biological symptoms can lead to false positives. The main risk factors for depression appear to be the severity of physical illness, the degree of disability, coexisting cognitive impairment and a positive past psychiatric history. Physical disability seems to be particularly strongly associated with depression in institional settings. Depression in older medical patients frequently becomes chronic, and in turn appears to have an adverse effect on the physical prognosis, especially in terms of likelihood of successful rehabilitation. In addition, older medical patients with depression consume more healthcare resources, have longer admissions and a higher mortality, and are more likely to be transferred to residential care. However, depression in older medical patients is frequently overlooked by medical staff, despite high
rates of depressive symptomatology. Its detection may be facilitated by simple screening tests.

The most striking vulnerability factors for depression identified in community surveys are social, including poverty, bereavement and social isolation. Life events often precipitate depression in old age. Several community studies have emphasized the importance of the concept of loss in understanding the depression of old age. The availability of a confidant(e) may act as a buffer against such loss-related depression, particularly in women. Those individuals who are separated, divorced or widowed exhibit more depressive illness than single or married individuals. Several studies have found that being a caregiver for someone with dementia or depression is associated with an increased risk of depression in the caregiver; this is particularly marked in women, in spouse caregivers, where the pre-morbid relationship was poor and where there are prominent behavioural problems such as aggression.

The management of depression in old age

**Depression is underdetected and undertreated**

Only a small minority of older patients with depression receive treatment. A community study found that only 13% of those with depression were being treated with antidepressants; at follow-up the figure remained virtually the same at 14%. Similarly, only 10% of patients with depression identified by consecutive primary care attenders were receiving treatment for depression, although in 95% of cases their GPs were able to identify them as depressed. Even when older people are prescribed antidepressants, the doses given are frequently subtherapeutic.

There are several possible reasons for this underprescribing (Box 8). Depression in older patients may be missed owing to its frequent manifestation as symptoms not immediately identified as depressive, such as anxiety or somatic complaints. It may also not be diagnosed if the symptoms displayed are viewed as a ‘normal’ response to ageing, physical impairment or living alone. Doctors may be reluctant to prescribe medication to older patients because of concerns about adverse effects and
lack of knowledge about the different side effects of the various agents; this may account for the common prescription of medication at subtherapeutic doses. As a result, GPs may conceptualize depression in old age as a legitimate and unavoidable consequence of ageing and associated adversity, which is recognizable but not seen as treatable.

Box 8 Reasons for undertreatment of depression in old age.

- Prominent anxiety or somatic complaints
- Symptoms seen as ‘normal’ response to:
  - ageing
  - physical impairment
  - living alone
- Depression seen as legitimate consequence of ageing and adversity
- Lack of knowledge about drug side effects in old age
- Fear of adverse effects

Goals of treatment of depression (Box 9 and Figure 1)

Depression is associated with suicide and the first responsibility of the clinician is to assess the risk of suicide and to prevent suicide with appropriate management. The next aim is to achieve a significant reduction in symptom severity. This should not, however, be seen as
adequate; a more important goal within the acute treatment phase is full remission of symptoms – which is achieved much less often than symptom reduction.

As depression is a chronic and recurring illness, the goals of treatment are alleviation of symptoms leading not only to eventual remission but also to preventing relapse (during the period of recovery) and recurrence (after a period of being well). These phases are illustrated in Figure 1. This means that continuation treatment is essential after alleviation of symptoms and that maintenance treatment should be considered to prevent recurrence. Depression is associated with a decrease in social functioning, interpersonal relationships and self-care. Restoration of functioning is another important goal of treatment.

**Acute treatment**

Drug trials usually use a 50% reduction in the depression severity scale as a measure of response, i.e. 50% reduction in the score on the Hamilton Scale. This indicates that the patient has improved but not necessarily that

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*Figure 1 Graphic representation of the phases of treatment for depressive disorder (after Frank et al 1991).*
he or she is well. Other drug trials use the end-point of ‘remission’, which is achieved only when the patient is no longer depressed according to usual criteria used to diagnose depression or has only negligible depressive symptoms (< 7 on the Hamilton Scale). Clinically the goal of treatment should be remission rather than simply improvement, not only because this will reduce individual suffering but also because incompletely treated depression is associated with a much higher rate of recurrence. Even with the best treatment, antidepressant monotherapy is not always successful. It is therefore important to have a rational strategy about how to manage those who are resistant to initial treatment. This is discussed below.

Difficulties in prescribing antidepressants for older adults

Antidepressants are undeniably more hazardous in old age, because of age-related pharmacokinetic changes and the high frequency in older people of coexistent medical problems and co-administered drugs that may interact adversely with antidepressants. Some of the adverse effects of antidepressants, particularly falls, are potentially much more serious in old age.

Age-related reductions in creatinine clearance, hepatic blood flow and plasma protein levels in older patients typically result in higher plasma levels of many drugs, including tricyclic antidepressants (TCAs). This is less so for new antidepressants and often no dose adjustment is necessary. The elimination half-life of some selective serotonin re-uptake inhibitors (SSRIs) such as paroxetine and citalopram is significantly increased in old age; this is much less marked for other SSRIs (fluoxetine or fluvoxamine). It must, however, be borne in mind that there is considerable variability in drug absorption, distribution, metabolism and excretion between individuals caused, for example, by genetically determined differences in cytochrome P450 isoenzyme levels.

The same side effects may be more hazardous in older compared with younger adults. Both TCAs and monoamine oxidase inhibitors (MAOIs)
have a propensity to produce adverse effects that are likely to be more
dangerous in older patients. These include anticholinergic, antihistaminic
and anti-adrenergic effects. Vulnerability to falls relates mainly to the
potency of older TCAs, which act as α₁-adrenergic receptor blockers which
thereby aggravate postural hypotension. An increase in falls and fractures
is perhaps the most hazardous consequence of these. In addition, MAOIs
require dietary restriction, and TCAs may have a quinidinelike effect and
cause tachycardia and prolongation of the Q–T interval. The anticholinergic
side effects can lead to urinary retention, constipation and glaucoma.
Not all antidepressants within a class have identical side effects, e.g. nor-
triptyline causes relatively little postural hypotension and is widely used
in old age psychiatry practice in the USA, and lofepramine is relatively free
of anticholinergic side effects, causes little cognitive impairment and is
very safe in overdose. Much of the data about efficacy has to be extrapo-
lated from work that includes very few or no older people. There are few
trials that are exclusively in older people and they tend to have relatively
low numbers (see below). In particular few data are available on the pure
noradrenaline re-uptake inhibitor (NARI) reboxetine (which is not at
present recommended for use in older people) and the serotonin
(5-hydroxytryptamine or 5HT) antagonist SSRI nefazodone.

Antidepressant-induced hyponatraemia caused by inappropriate antidi-
uretic hormone secretion occurs almost exclusively in older people. It is a
rare but potentially serious complication that can lead to acute confusion
and then to seizures. Older patients with co-morbid medical disorders are
the group at risk of this relatively rare complication.

In addition to the age-related pharmacological differences outlined
above, older people are more likely to have significant physical and/or
cognitive co-morbidity which antidepressant drugs may affect adversely.

Interaction with other medication is a more frequent problem as
patients age. This is considered in more detail below.

**General factors relating to choice of antidepressant in older people**

Several factors (*Box 10*) should be taken into account when choosing an
antidepressant. They will vary with individual patients. There is no one
drug or class of drug that will suit all older patients and the prescription