

SAMPLE CHAPTER FROM:

Depression

Management of Depression in Primary and Secondary Care

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2 Depression

This guideline is concerned with the treatment and management of people with depression in primary and secondary care. Although the terminology and diagnostic criteria used for this heterogeneous group of related disorders has changed over the years, this guidance relates only to those identified by *The ICD-10 Classification of Mental and Behavioural Disorders* (ICD-10) (WHO, 1992), namely, depressive episode (F32), recurrent depressive episode (F33) and mixed anxiety and depressive disorder (F41.2). It should be noted that a sizeable quantity of the research forming the evidence base from which much of this guideline is drawn has used a similar classificatory system – the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* of the American Psychiatric Association (DSM-IV) (APA, 1994). The guideline does not address the management of related affective disorders such as bipolar disorder or dysthymia, nor does it provide specific guidance for post-natal depression.

2.1 The disorder

2.1.1 Symptoms, presentation and pattern of illness

Depression refers to a wide range of mental health problems characterised by the absence of a positive affect (a loss of interest and enjoyment in ordinary things and experiences), low mood and a range of associated emotional, cognitive, physical and behavioural symptoms. Distinguishing the mood changes between major depression and those occurring 'normally' remains problematic: persistence, severity, the presence of other symptoms and the degree of functional and social impairment form the basis of that distinction.

Commonly, mood and affect in a major depressive illness are unreactive to circumstance, remaining low throughout the course of each day, although for some people mood varies diurnally, with gradual improvement throughout the day only to return to a low mood on waking. Arguably as common, a person's mood may be reactive to positive experiences and events, although these elevations in mood are not sustained, with depressive feelings re-emerging, often quickly (Andrews & Jenkins, 1999).

Behavioural and physical symptoms typically include tearfulness, irritability, social withdrawal, reduced sleep, an exacerbation of pre-existing pains, and pains secondary to increased muscle tension and other pains (Gerber *et al.*, 1992), lowered appetite (sometimes leading to significant weight loss), a lack of libido, fatigue and diminished activity, although agitation is common and marked anxiety frequent. Along with a loss of interest and enjoyment in everyday life, feelings of guilt, worthlessness and deserved punishment are common, as are lowered self-esteem, loss of confidence, feelings of helplessness, suicidal ideation and attempts at self-harm or suicide. Cognitive changes include poor concentration and reduced attention, pessimistic and recurrently negative thoughts about oneself, one's past and the future, mental slowing and rumination (Cassano & Fava, 2002).

Depression is often accompanied by anxiety, and in these circumstances one of three diagnoses can be made: (1) depression, (2) anxiety, or (3) mixed depression and anxiety, dependent upon which constellation of symptoms dominates the clinical picture. In addition, the presentation of depression varies with age, the young showing more behavioural symptoms and older adults more somatic symptoms and fewer complaints of low mood (Serby & Yu, 2003).

Major depression is generally diagnosed when a persistent and unreactive low mood and an absence of positive affect are accompanied by a range of symptoms, the number and combination needed to make a diagnosis being operationally defined (ICD-10, WHO, 1992; DSM-IV, APA, 1994), although some people show an atypical presentation with reactive mood, increased appetite, weight gain and excessive sleepiness (Quitkin *et al.*, 1991).

In addition, those with a more severe and typical presentation, including marked physical slowness (or marked agitation) and a range of somatic symptoms, are often referred to as melancholic depressions, or depression with melancholia.

People with severe depressions may also develop psychotic symptoms (hallucinations and/or delusions), most commonly thematically consistent with the negative, self-blaming cognitions and low mood typically encountered in major depression, although others may develop psychotic symptoms unrelated to the patient's mood (Andrews & Jenkins, 1999). In the latter case, these mood-incongruent psychotic symptoms can be hard to distinguish from those that occur in other psychoses such as schizophrenia.

2.1.2 Course and prognosis

The average age of the first episode of a major depression occurs in the mid-20s and although the first episode may occur at any time, from early childhood through to old age, a substantial proportion of people have their first depression in childhood or adolescence (Fava & Kendler, 2000). And just as the initial presentation and form of a depressive illness varies considerably, so too does the prodromal period. Some individuals experience a range of symptoms in the months prior to the full illness, including anxiety, phobias, milder depressive symptoms and panic attacks; others may develop a severe major depressive illness fairly rapidly, not uncommonly following a major stressful life event. Sometimes somatic symptoms dominate the clinical picture leading the clinician to investigate possible underlying physical illness until mood changes become more obvious.

Although it is generally thought that depression is usually a time-limited disorder lasting up to six months with complete recovery afterwards, in the WHO study of mental disorders in 14 centres across the world, 66% of those suffering from depression were still found to satisfy criteria for a mental disorder a year later, and for 50% the diagnosis was depression. It is probable that widely differing rates between the clinics studied in these countries reflect true differences in prevalence in these clinics rather than differing concepts of depression between countries (Simon *et al.*, 2002). In the WHO study, episodes of depression that were either untreated by the GP or missed entirely had the same outlook as treated episodes of depression; however, they were milder at index consultation (Goldberg *et al.*, 1998). In a meta-analysis of 12 studies of depressed older adults, the outcomes for people with depression in the community were on average poor:

after two years, 20% had died and nearly 40% were still depressed (Cole *et al.*, 1999).

While around half of those affected by depression will have no further episodes, depressive illnesses, as with many other mental health problems such as schizophrenia, have a strong tendency for recurrence. At least 50% of people following their first episode of major depression will go on to have at least one more episode (Kupfer, 1991), with early onset depression (at or before 20 years of age) particularly associated with a significantly increased vulnerability to relapse (Giles *et al.*, 1989).

After the second and third episodes, the risk of further relapse rises to 70% and 90% respectively (Kupfer, 1991). Thus, while the outlook for a first episode is good, the outlook for recurrent episodes over the long term can be poor, with many patients suffering symptoms of depression over many years (Akiskal, 1986). Sometimes, recurrent episodes of depression will follow a seasonal pattern, receiving the label seasonal affective disorder.

The term 'treatment-resistant depression', used to describe depression that has failed to respond to two or more antidepressants at an adequate dose for an adequate duration given sequentially, is not especially helpful. It does not take into account depressive subtypes, makes no distinction between chronicity, relapse or recurrence, and fails to take into account what psychosocial factors may be preventing recovery or indeed whether the patient has had an adequate course of an appropriate psychotherapeutic treatment (Andrews & Jenkins, 1999).

2.1.3 Impairment and disability

Depression is the most common mental disorder in community settings, and is a major cause of disability across the world. In 1990 it was the fourth most common cause of loss of disability-adjusted life years in the world, and by 2020 it is projected to become the second most common cause (World Bank, 1993). In 1994 it was estimated that about 1.5 million disability-adjusted life years were lost each year in the west as a result of depression (Murray *et al.*, 1994). It is even more common in the developing world (for review, see Institute of Medicine *et al.*, 2001).

Apart from the subjective suffering experienced by people who are depressed, the impact on social and occupational functioning, physical health and mortality is substantial. The impact on physical health puts depression on a par with all the major chronic and disabling physical illnesses such as diabetes, arthritis and hypertension (Cassano & Fava, 2002). Depressive illnesses substantially reduce a person's ability to work effectively, with losses in personal and family income (and, therefore, tax revenues), and unemployment (with loss of skills from the workplace). Wider social effects include: greater dependence upon welfare and benefits with the inevitable impact upon self-esteem and self-confidence; social impairments, including reduced ability to communicate during the illness; disturbed relationships during and subsequent to an episode; and longer term changes in social functioning, especially for those who have a recurrent disorder. The stigma associated with mental health problems generally (Sartorius, 2002), and the public view that depression suggests a person is unbalanced, neurotic and irritating (Priest *et al.*, 1996), may account for the reluctance of depressed people to seek help (Bridges & Goldberg, 1987).

Mental disorders account for as much of the total disability in the population as physical disorders (Ormel & Costa e Silva 1995), and there is a clear dose-response relationship between illness severity and the extent of disability (*ibid.*). Depression and disability show synchrony of change (Ormel *et al.*, 1993), and onsets of depression are associated with onsets of disability, with an approximate doubling of both social and occupational disability (Ormel *et al.*, 1999).

Depression can also exacerbate the pain and distress associated with physical diseases, as well as adversely affecting outcomes. For example, in people with myocardial infarction (MI), death rates are significantly greater for those who are depressed following an MI, not only in the immediate post-MI period, but for the subsequent year (Lesperance & Frasere-Smith, 2000). In one community study, patients with cardiac disease who were depressed had an increased risk of death from cardiac problems compared with those without depression, and depressed people without cardiac disease also had a significantly increased risk of cardiac mortality (Pennix *et al.*, 2001). Similar findings for a range of physical illnesses also suggest an increased risk of death when comorbid depression is present (Cassano & Fava, 2002).

Suicide accounts for just under 1% of all deaths, and nearly two-thirds of this figure occur in depressed people (Sartorius, 2001). Sometimes depression may also lead to acts of violence against others, and may even include homicide. However, more common, and a greater cause of disability for people who are depressed, is the impact of depressive illnesses on social and occupational function (Ormel *et al.*, 1999). Marital and family relationships are frequently negatively affected, and parental depression may lead to neglect of children and significant disturbances in children (Ramachandani & Stein, 2003). The vocational consequences are discussed below.

2.2 Incidence and prevalence

The estimated point prevalence for major depression among 16- to 65-year-olds in the UK is 21/1000 (males 17, females 25), but, if the less specific and broader category of 'mixed depression and anxiety' (F41.2, ICD-10, WHO, 1992) was included, these figures rise dramatically to 98/1000 (males 71, females 124). In mixed depression and anxiety, it can be seen that the gender ratio is more skewed to females (Meltzer *et al.*, 1995a and b).

Prevalence rates are greatly influenced by gender, age and marital status. In the same survey, for example, female preponderance was marked during the reproductive years, but after the age of 55 the sex ratio actually reverses. Prevalence is highest among the separated (56/1000 female, 111/1000 male), next highest among widowed males (70/1000) and divorced females (46/1000), with the lowest prevalence among the married (17/1000 and 14/1000 respectively). Female prevalence is higher among the single and cohabiting than among the married, but male rates are low for all of these. Lone parents have higher rates than couples, and couples with children higher rates than those without (*ibid.*).

Ethnic status and gender also interact: prevalence rates for males from minority ethnic groups were not greatly different from those for white males, but female rates differed remarkably, the highest rates being found amongst Asians and Orientals (51/1000), the next highest for whites (24/1000) and the lowest rates for West Indians or Africans

(6/1000) (Meltzer *et al.*, 1995a). However, these estimates are based on relatively small samples of people from minority ethnic groups.

Gender and a number of socio-economic factors also significantly affect prevalence rates differentially: unemployed women have over twice the prevalence of depression of unemployed men (56/1000 vs 27/1000), whereas the rates are low for both sexes in full-time employment (11/1000 vs 12/1000 respectively), with part-time women workers in between (22/1000). Social classes 3 and below have higher rates than classes 1 and 2 for both sexes, and those living in rented accommodation have substantially higher rates than those living in their own home. There are clear trends for years of education for males, with those finishing education later having progressively lower rates for depression; these effects are less for females. Rates are higher in town than country, with 'semi-rural' being intermediate (Meltzer, 1995a and b).

Rates for the homeless living in leased accommodation and hostels are very high indeed, with prevalence rates of 130/1000 for ICD depression, and 270/1000 for all forms of depression (Meltzer, 1995b). Another study, of the roofless homeless, showed that 60% were depressed (Gill *et al.*, 1996). Those who are depressed consume no more alcohol than the non-depressed, but their cigarette consumption is higher (Meltzer *et al.*, 1995b). It should be emphasised that the direction of causality in these associations is unclear. Depression also affects asylum seekers, with one-third of asylum seekers in Newham being diagnosed with depression (Gammell *et al.*, 1993), considerably higher than the rate in the population.

Further confirmation of the social origins of depression was found in a general practice survey in which 7.2% (range: 2.4% to 13.7%, depending upon the practice) of consecutive attendees had a depressive disorder. Neighbourhood social deprivation accounted for 48.3% of the variance among practices, and the variables that accounted for most of that variance were: the proportion of the population having no or only one car; and neighbourhood unemployment (Ostler *et al.*, 2001).

The rates for depression considered so far have looked at depression at a point in time. Annual period prevalence produces much higher figures, with male rates ranging between 24 and 34/1000 and females rates between 33 and 71/1000 in Puerto Rico, Edmonton, Canada, and Christchurch, New Zealand (Jenkins *et al.*, 2003). Even higher rates are obtained for one-year prevalence using the International Composite Interview Schedule in the US of 77/1000 for males, and 129/1000 for females (Kessler *et al.*, 1994). It is probable that widely differing rates between the clinics studied in these countries reflect true differences in prevalence in these clinics rather than differing concepts of depression between countries (Simon *et al.*, 2002). In any event, the evidence overwhelmingly supports the view that the prevalence of depression, however it is defined, varies considerably according to gender and a wide range of social, ethnic and economic factors.

2.3 Diagnosis

Diagnostic criteria and methods of classification of depressive illnesses have changed substantially over the years, although the advent of operational diagnostic criteria has improved the reliability of diagnosis. ICD-10 uses an agreed list of 10 depressive symptoms, and divides the common form of major depressive episode into four groups: not depressed (fewer than four symptoms), mild (four symptoms), moderately depressed (five to six symptoms), and severe (seven symptoms or more, with or without various psychotic symptoms). Symptoms must be present for at least two weeks. These definitions have been used in the report that follows. The more severe the episode of depression, the less likely it is that remission will occur spontaneously. Patients with mild episodes in primary care settings will frequently remit, but such episodes may well be persistent, and may also be a transitional state as a more severe illness develops. Mild depression is also a vulnerability factor, rendering patients more likely to develop a more severe illness in the presence of life stress. However, it is doubtful whether the severity of a depressive illness can realistically be captured in a single symptom count although there is some evidence for this (Faravelli *et al.*, 1996): clinicians will wish to consider family and previous history, as well as the degree of associated disability, in making this assessment. In addition, some symptoms may have greater weight than others in establishing severity levels (Faravelli *et al.*, 1996).

Although reliability of diagnosis has improved, there has been no parallel improvement in the validity of diagnosis (Dohrenwend, 1990), partly as a result of the breadth of the diagnostic category – major depression – partly the result of the lack of physical tests available to confirm a diagnosis of depression, and partly because our understanding of the aetiology and underlying mechanisms of depression remain putative and lacking in specificity.

The symptom-focused, diagnostic approach adopted in much contemporary research, and which underpins the evidence base for this guideline, will distinguish between types of depression (e.g. unipolar versus bipolar), severity (mild, moderate and severe), chronicity, recurrence and treatment resistance. However, depressed people also vary greatly in their personalities, premorbid difficulties (e.g. sexual abuse), psychological mindedness and current relational and social problems – all of which may significantly affect outcomes. It is also common for depressed people to have a comorbid diagnosis, such as anxiety, social phobia, panic and various personality disorders (Brown *et al.*, 2001). As noted above, gender, ethnic and socio-economic factors account for large variations in the population rates of depression, and few studies of pharmacological, psychological or indeed other treatments for depression control for or examine these variations. Indeed, there is increasing concern that 'depression' may be too heterogeneous in biological, psychological and social terms to enable clarity on which specific interventions will be effective – for which problem, for which person, and in which context.

Differential diagnosis of depression can be difficult; of particular concern are patients with bipolar disorder presenting with depression. The issue of differential diagnosis in this area will be dealt with in the forthcoming NICE guideline on bipolar disorder.

2.4 Aetiology

The enormous variation in the presentation, course and outcomes of depressive illnesses is reflected in the breadth of theoretical explanations for their aetiology, including genetic (Kendler & Prescott, 1999), biochemical and endocrine (Goodwin, 2000), psychological (Freud, 1917), and social (Brown & Harris, 1978) processes and/or factors. No doubt an emphasis upon physical, and especially endocrine, theories of causation has been encouraged by the observation that some physical illnesses do increase the risk of depression, including diabetes, cardiac disease, hyperthyroidism, hypothyroidism, Cushing's syndrome, Addison's disease and hyperprolactinaemic amenorrhoea (Cassano & Fava, 2002).

Whatever theories of causation have gained credence none has been convincingly accepted. Most now believe that all these factors influence an individual's vulnerability to depression, although it is likely that for different people living in different circumstances, precisely how these factors interact and influence that vulnerability will vary between individuals (Harris, 2000). Nevertheless, the factors identified as likely to increase a person's vulnerability to depression include gender (see above), genetic and family factors, adverse childhood experiences, and personality factors. In the stress-vulnerability model (Nuechterlein & Dawson, 1984), these 'vulnerability factors' interact with current social circumstances, such as poverty and social adversity, with stressful life events acting as the trigger for a depressive episode (Harris, 2000). Physical illness is also regarded as an important stressful life event.

A family history of depressive illness accounts for around 39% of the variance of depression in both sexes (Kendler *et al.*, 2001), and early life experiences such as a poor parent-child relationship, marital discord and divorce, neglect, physical abuse and sexual abuse almost certainly increase a person's vulnerability to depression in later life (Fava & Kendler, 2000). Personality traits such as 'neuroticism' also increase the risk of depression when faced with stressful life events (Fava & Kendler, 2000). However, different personalities have different expectancies of stressful life events, and some personalities have different rates of dependent life events, which are directly related to their personality – such as breaking up a relationship (Hammen *et al.*, 2000).

The role of current social circumstances in increasing the risk of depression, such as poverty, homelessness, unemployment and chronic physical or mental illness cannot be doubted even from a brief examination of the epidemiology of depression (see above). However, in the UK, predictive factors for depression in women in Camberwell, south-east London, include: having three or more children under the age of 14 years living at home; not having a confiding relationship with another person; and having no paid employment outside the home (Brown & Harris, 1978).

The neatness of this model, in which vulnerabilities interact with stressful life events, such as separation or loss of a loved one, triggering a depressive episode, is not always supported by the 'facts': some episodes of depression occur in the absence of a stressful event, and conversely many such events are not followed by a depressive disorder. Having said that, the presence of some factors protects against depression following a stressful life event, such as having a supportive confiding relationship with another person (Brown & Harris, 1978), or befriending (Harris *et al.*, 1999).

2.5 Use of health service resources and other costs

As the most common psychiatric disorder, and one that has a strong tendency for recurrence and chronicity, depression is ranked as the fourth leading cause of burden among all diseases and is expected to show a rising trend during the coming 20 years (WHO, 2001). One in four women and one in ten men in the UK are likely to suffer a period of depression serious enough to require treatment (National Depression Campaign, 1999). Due to its high prevalence and treatment costs, its role as probably the most important risk factor for suicide (Knapp & Ilson, 2002), and the cost of antidepressant drug overdose and its great impact on the productivity of people with the disease, depression places enormous economic burden not just on the health care system but also on the broader society. On average, depressed patients lose 11 days over a six-month period, compared with two to three days for individuals without this condition (Lepine *et al.*, 1997). It is also of interest that the cost of health and social service utilisation is almost 1.5-fold higher for older adults with depression compared with their younger counterparts (Hughes *et al.*, 1997).

A recent review identified three studies that investigated the economic burden of depression in the UK (Berto *et al.*, 2000). The study by Jonsson and Bebbington (1993) focused only on the direct costs of depression in the UK without giving detailed breakdown of the results. They calculated the direct costs of depression to be about £222 million in 1990, but this is likely to be a substantial underestimate. For example, West (1992) estimated the direct costs of depression in the UK to be £333 million at 1990 prices, of which £55 million are drug costs, £250 million hospitalisation costs, and £28 million are GP surgery consultation costs based on data from England and Wales.

In the third study reviewed, Kind and Sorensen (1993), using a different methodology, calculated the cost of depression for England and Wales in the year 1990 from a broader societal perspective. They estimated the direct care costs at £417 million, of which £47 million were drug treatment costs, £143 million were primary healthcare costs, £40 million were social services costs, £177 million were inpatient care costs, and outpatient attendances accounted for £9 million. For hospital admissions they included reasons such as depression, attempted suicide, poisoning and mental illness. These authors also went a step further by attempting to measure productivity forgone due to premature deaths and morbidity arising as a consequence of depression. They estimated that 155 million working days were lost in 1990 at a cost of £2.97 billion.

In a study comparing community-based and hospital-based treatment of anxious depression in Manchester (Goldberg *et al.*, 1996), lost productivity costs due to morbidity were on average £2,574 per patient to be compared with £424 for total service costs during six months. This study included lost marketed output as well as lost domestic output. It is of interest that the indirect costs were six times as great as the direct costs to the NHS.

These studies highlight the important facts that drug costs account for only approximately 11 to 19% of the direct costs and that the cost of lost productivity due to depression far outweighs the health service costs.

Although no recent economic burden estimates exist for the UK, it is likely that the overall economic impact of depression has increased substantially over the last decade: statistics reveal that the age-standardised prevalence of treated depression in primary

care grew from 19.9/1000 males and 50.5/1000 females in 1994 to 29.0/1000 males and 70.1/1000 females in 1998 (Office for National Statistics, 2000) and that the number of GP consultations for depressive disorders more than doubled from four million to nine million during these years (National Depression Campaign Survey, 1999). Also the number of prescriptions for antidepressants increased by 11.2% between 1998 and 1999 (Compufile Ltd, 1999). This may reflect increasing trends in the prevalence and/or in the recognition and treatment of major depressive disorder.

In 1993, Henry reported that the majority of cases of major depression were diagnosed by general practitioners, who issued 95% of all prescriptions for antidepressants (Henry, 1993). Freemantle & Mason (1995) and Freemantle (1998) calculated that 76.5% of the GP antidepressant prescribing volume was for TCAs and related drugs, which accounted for 36.7% of the total cost of prescription for depression in primary care in England in the year 1993/94. In the same period, SSRIs accounted for 23.2% of the total volume of prescribing at 62.6% of the total cost. Both the sale and cost shares of MAOIs were less than 1%. In 1996, GPs prescribed 160 million pounds' worth of antidepressants. This figure has further increased as newer and more expensive antidepressants have become available (Eccles *et al.*, 1999).

Without doubt, depression places a major direct economic burden on patients, carers and the healthcare system, and its indirect economic consequences are shown to be even greater. Furthermore, its healthcare costs continue to increase substantially. Efficient service provision could greatly reduce this burden and ensure that best care is delivered within the budget constraint.

2.6 Treatment and management in the NHS

Treatment for depressive illnesses in the NHS is hampered by the unwillingness of many people to seek help for depression and the failure to recognise depression, especially in primary care. The improved recognition and treatment of depression in primary care is central to the WHO strategy for mental health (WHO, 2001).

2.6.1 Detection, recognition and referral in primary care

Of the 130 cases of depression (including mild cases) per 1000 population only 80 will consult their GP. The most common reasons given for reluctance to contact the family doctor were: did not think anyone could help (28%); a problem one should be able to cope with (28%); did not think it was necessary to contact a doctor (17%); thought problem would get better by itself (15%); too embarrassed to discuss it with anyone (13%); afraid of the consequences (e.g. treatment, tests, hospitalisation, being sectioned – 10%) (Meltzer *et al.*, 2000). The stigma associated with depression cannot be ignored in this context (Priest *et al.*, 1996).

Of the 80 depressed people per 1000 population who do consult their GP, 49 are not recognised as depressed, mainly because most such patients are consulting for a somatic symptom, and do not consider themselves mentally unwell, despite the presence of symptoms of depression (Kisely *et al.*, 1995). This group also have milder illnesses (Goldberg *et al.*, 1998; Thompson *et al.*, 2001). And of those that are recognised as

depressed, most are treated in primary care and about one in four or five are referred to secondary mental health services. There is considerable variation between individual GPs in their referral rates to the mental illness services, but those seen by the mental illness service are a highly selected group – they are skewed towards those who do not respond to antidepressants, more severe illnesses, single women and those below the age of 35 (Goldberg & Huxley, 1980).

General practitioners are immensely variable in their ability to recognise depressive illnesses, with some recognising virtually all the patients found to be depressed at independent research interview, and others recognising very few (Goldberg & Huxley, 1992; Üstün & Sartorius, 1995). The communication skills of the GP make a vital contribution to determining their ability to detect emotional distress, and those with superior skills allow their patients to show more evidence of distress during their interviews, thus making detection easy. Those doctors with poor communication skills are more likely to collude with their patients, who may not themselves wish to complain of their distress unless they are asked directly about it (Goldberg & Bridges, 1988a; Goldberg *et al.*, 1993).

Attempts to improve the rate of recognition of depression by GPs using guidelines, lectures and discussion groups have not improved recognition or outcomes (Thompson *et al.*, 2000), although similar interventions combined with skills training may improve detection and outcomes in terms of symptoms and level of functioning (Tiemens *et al.*, 1999; Ostler *et al.*, 2001). The inference that these health gains are the result of improved detection and better access to specific treatments, while having face validity, has been contested. For example, Ormel *et al.* (1990) suggested that the benefits of recognition of common mental disorders could not be attributed entirely to specific mental health treatments. Other factors like *acknowledgement of distress*, *reinterpretation of symptoms*, *providing hope and social support* were suggested to contribute to better patient outcomes.

This view has gained confirmation from a Dutch study in which providing skills training for GPs did not improve detection but did improve outcomes. Moreover, about half of the observed improvement in patient outcomes was mediated by the combined improvements in process of care. In combination with the strong mediating effect of empathy and psycho-education they suggest that other, probably also non-specific, aspects of the process of care must be responsible for the training effect on symptoms and disability (Van Os *et al.*, 2002). In addition, the communication skills needed by GPs can be learned and incorporated into routine practice with evident improvement in patient outcomes (Gask *et al.*, 1988; Roter *et al.*, 1995).

In summary, those with more severe disorders, and those presenting psychological symptoms to their doctor, are especially likely to be recognised as depressed, while those presenting with somatic symptoms for which no cause can be found are less likely to be recognised. The evidence suggests that this very undesirable state of affairs, in which large numbers of people each year suffer depression, with all the personal and social consequences and suffering involved, could be changed. With 50% of people with depression never consulting a doctor, 95% never entering secondary mental health services, and many more having their depression going unrecognised and untreated, this is clearly a problem for primary care.

2.6.2 Assessment and co-ordination of care

Given the low detection and recognition rates, it is essential that primary care and mental health practitioners have the required skills to assess the patients with depression, their social circumstances and relationships, and the risk they may pose to themselves and to others. This is especially important in view of the fact that depression is associated with an increased suicide rate, a strong tendency for recurrence and high personal and social costs. The effective assessment of a patient, including risk assessment and the subsequent co-ordination of their care (through the use of the Care Programme Approach in secondary care services), is highly likely to improve outcomes, and should, therefore, be comprehensive.

- 2.6.2.1 All healthcare professionals involved in diagnosis and management should have a demonstrably high standard of consultation skills, so that a structured approach can be taken to the diagnosis and subsequent management of depression. (GPP)
- 2.6.2.2 In older adults with depression, their physical state, living conditions, and social isolation should be assessed. The involvement of more than one agency is recommended where appropriate. (GPP)
- 2.6.2.3 When depressive symptoms are accompanied by anxious symptoms, the first priority should usually be to treat the depression. Psychological treatment for depression often reduces anxiety, and many antidepressants also have sedative/anxiolytic effects. When the patient has anxiety without depression, the NICE guideline on management of anxiety should be followed. (GPP)
- 2.6.2.4 In deciding on a treatment for a depressed patient, the healthcare professional should discuss alternatives with the patient, taking into account other factors such as past or family history of depression, response of any previous episodes to intervention, and the presence of associated problems in social or interpersonal relationships. (GPP)
- 2.6.2.5 Healthcare professionals should always ask patients with depression directly about suicidal ideas and intent. (GPP)
- 2.6.2.6 When a patient with depression is assessed to be at high risk of suicide, the use of additional support such as more frequent direct contacts with primary care staff or telephone contacts should be considered. (C)
- 2.6.2.7 Healthcare professionals should advise patients and carers to be vigilant for changes in mood, negativity and hopelessness, and suicidal ideas, particularly during high-risk periods, such as during initiation of and changes to medication and increased personal stress. Patients and carers should be advised to contact the appropriate healthcare practitioner if concerned. (GPP)
- 2.6.2.8 Healthcare professionals should assess whether patients with suicidal ideas have adequate social support and are aware of sources of help. They should advise them to seek appropriate help if the situation deteriorates. (GPP)

- 2.6.2.9 Where a patient presents considerable immediate risk to self or others, urgent referral to a specialist mental health service should be arranged. (GPP)
- 2.6.2.10 When a patients' depression has failed to respond to various strategies for augmentation and combination treatments, referral to a clinician with a specialist interest in treating depression should be considered. (GPP)
- 2.6.2.11 The assessment of patients with depression referred to specialist mental health services should include a full assessment of their symptom profile and suicide risk and, where appropriate, previous treatment history. Assessment of psychosocial stressors, personality factors and significant relationship difficulties should also be undertaken, particularly where the depression is chronic or recurrent. (GPP)
- 2.6.2.12 In specialist mental health services, after a thorough review of previous treatments for depression has been undertaken, consideration should be given to re-introducing previous treatments that have been inadequately delivered or adhered to. (GPP)
- 2.6.2.13 Medication in secondary-care mental health services should be initiated under the supervision of a consultant psychiatrist. (GPP)
- 2.6.2.14 Inpatient treatment should be considered for people with depression who are at significant risk of suicide or self-harm. (C)
- 2.6.2.15 Where a patients' depression has resulted in loss of work or disengagement from other social activities over a longer term, a rehabilitation programme addressing these difficulties should be considered. (C)

The nature and course of depression is significantly affected by psychological, social and physical characteristics of the patient and their circumstances. These factors have a significant impact upon both the initial choice of treatment and the probability of a patient benefiting from that intervention.

- 2.6.2.16 When assessing a person with depression, healthcare professionals should consider the psychological, social, cultural and physical characteristics of the patient and the quality of interpersonal relationships. They should consider the impact of these on the depression and the implications for choice of treatment and its subsequent monitoring. (GPP)

The need for more effective assessments for people who are depressed also requires that healthcare professionals must have the requisite level of skill and ensure continued competence in the use of those skills.

- 2.6.2.17 Healthcare professionals should ensure they maintain their competence in risk assessment and management. (GPP)

This is particularly important if an individual receives help and treatment in both primary and secondary care.

- 2.6.2.18 Where a patient's management is shared between primary and secondary care, there should be clear agreement between individual healthcare professionals on the responsibility for the monitoring and treatment of that patient, and the treatment plan should be shared with the patient and, where appropriate, families and carers. (GPP)

2.6.3 Non-specific effects of treatment and the placebo

Among those seeking care with depression, those put on waiting lists do improve steadily with time. Posternak & Miller (2001) studied 221 patients assigned to waiting lists in 19 treatment trials of specific interventions, and found that 20% improved in between four and eight weeks, and 50% improved in six months. They estimate that 60% of placebo responders, and 30% of responders to antidepressants, may experience spontaneous resolution of symptoms (if untreated). An earlier study by Coryell *et al.* (1994) followed up 114 patients with untreated depression for six months: the mean duration of episode was six months, with 50% remission in 25 weeks. It should be noted that there is a high relapse rate associated with depression (see Section 2.1.2 above).

Despite their greater severity and other differences, Furukawa *et al.* (2000) showed that patients treated by psychiatrists with antidepressants did better than this: the median time to recovery was three months, with 26% recovering in one month, 63% in six months; 85% in one year, and 88% in two years.

Although there is insufficient space to allow proper discussion, the placebo effect in trials of psychiatric drugs is often so large that specific pharmacological effects can be hard to identify, especially when given to people who fall into one of the larger, more heterogeneous diagnostic categories. The treatment of depression is a clear example of this (Kirsch *et al.*, 2002a). Drug, and some other, treatments for depression, when compared with wait list controls in the treatment of mild to moderate depression, all produce a substantial and roughly equal fall in depressive symptoms. But, when antidepressants are compared with placebo for this diagnostic group, the clinical improvements resulting from antidepressants over and above that for placebo is not clinically significant (Kirsch *et al.*, 2002b). Given the recent focus upon publication bias, especially with regard to drug company funded trials (Lexchin *et al.*, 2003; Melander *et al.*, 2003) there is the possibility that some drug (or other) treatments for depression may offer no advantage, on average, over placebo, for patients with mild depression. Nevertheless, it is likely that with greater definition of subgroups of people with depression, benefits over placebo may well be demonstrable. Further discussion of the placebo effect in the treatment of depression can be found in the evidence chapters.

2.6.4 Pharmacological treatments

The mainstay of the pharmacological treatment of depression for the last 40 or more years has been antidepressants. Tricyclic antidepressants (TCAs) were introduced in the 1950s, the first being imipramine (Kuhn, 1958). The mode of action of this class of drugs thought to be responsible for their mood-elevating properties is their ability to block the synaptic reuptake of monoamines, including noradrenaline (NA), 5-hydroxytryptamine (5HT) and dopamine (DA). In fact the TCAs predominantly affect the reuptake of NA and 5HT rather than DA (Mindham, 1982). The antidepressant properties of MAOIs were discovered by chance in the 1950s in parallel with TCAs.

Although the introduction of the TCAs was welcome, given the lack of specific treatments for people with depression, the side effects resulting from their ability to influence anticholinergics, histaminergic and other receptor systems reduced their acceptability. Moreover, overdose with TCAs (with the exception of lofepramine) carries a high mortality and morbidity, particularly problematic in the treatment of people with suicidal intentions.

In response to the side effect profile and the toxicity of TCAs in overdose, new classes of antidepressants have been developed, including: the specific serotonin reuptake inhibitors (SSRIs) such as fluoxetine; drugs chemically related to, but different from, the TCAs, such as trazodone; and a range of other chemically unrelated antidepressants including mirtazapine (*BNF*, 4.3). Their effects and side effects vary considerably, although their mood-elevating effects are again thought to be mediated through increasing intra-synaptic levels of monoamines, some primarily affecting NA, some 5HT and others affecting both to varying degrees and in different ways.

Other drugs used either alone or in combination with antidepressants include lithium salts (*BNF*, 4.2.3), and the antipsychotics (*BNF*, 4.2), although the use of these drugs is usually reserved for people with severe, psychotic or chronic depressions, or as prophylactics. A full review of the evidence base for the use of the different types of antidepressants is presented in Chapter 8.

In addition, there is preliminary evidence that pharmacogenetic variations may affect the efficacy and tolerability of antidepressant drugs. It is likely that future research on this topic will lead to the development of clinically meaningful pharmacogenetic markers, but at the moment the data is insufficient to make recommendations.

2.6.5 Psychological treatments

In 1917 Freud published *Mourning and Melancholia*, probably the first modern psychological theory on the causes, meaning and psychological treatment of depression. Since that time, numerous theories and methods for the psychological treatment of psychological disorders have been elaborated and championed, although psychological treatments specifically for depression were developed only over the last 30 to 40 years, and research into their efficacy is more recent still (Roth & Fonagy, 1996). Many, but not all, such therapies are derived from Freudian psychoanalysis, but address the difficulties of treating people with depression using a less rigid psychoanalytic approach (Fonagy, 2003). In any event, the emergence of cognitive and behavioural approaches to the treatment of mental health problems has led to a greater focus upon the evidence base and the development of psychological treatments specifically adapted for people with depression (for example, see Beck *et al.*, 1979).

Psychological treatments for depression currently claiming efficacy in the treatment of people with depressive illnesses and reviewed for this guideline in Chapter 6 include: cognitive behavioural therapy (CBT); behaviour therapy (BT); interpersonal psychotherapy (IPT); problem-solving therapy (PST); counselling; short-term psychodynamic psychotherapy; and couple-focused therapies. Psychological treatments have expanded rapidly in recent years and generally have more widespread acceptance from patients (Priest *et al.*, 1996). In the last 15 years in the UK there has been a very significant expansion of psychological treatments in primary care for depression, in particular primary care counselling.

2.6.6 Service-level and other interventions

Given the complexity of healthcare organisations, and the variation in the way care is delivered (inpatient, outpatient, day hospital, community teams, etc.), choosing the right service configuration for the delivery of care to specific groups of people has gained increasing interest with regard to both policy (for example, see Department of Health, 1999b), and research (e.g. evaluating day hospital treatment, Marshall *et al.*, 2001). Research using RCT designs has a number of difficulties; for example, using comparators such as 'standard care' in the US make the results difficult to generalise or apply to countries with very different types of 'standard care'.

Service-level interventions considered for review in this guideline include: organisational developments, crisis teams, day hospital care, and non-statutory support and other social supports. Other types of interventions also reviewed for this guideline include: exercise, guided self-help, computerised cognitive behavioural therapy (CCBT) and screening.

2.6.7 Stepped care

In Figure 1 a 'stepped care' model is developed, which draws attention to the different needs that depressed individuals have – depending on the characteristics of their depression and their personal and social circumstances – and the responses that are required from services. Stepped care provides a framework in which to organise the provision of services supporting both patients and carers, and healthcare professionals in identifying and accessing the most effective interventions.

Figure 1: The stepped care model.

Who is responsible for care?	What is the focus?	What do they do?
Step 5: Inpatient care, crisis teams	Risk to life, severe self-neglect	Medication, combined treatments, ECT
Step 4: Mental health specialists, including crisis teams	Treatment-resistant, recurrent, atypical and psychotic depression, and those at significant risk	Medication, complex psychological interventions, combined treatments
Step 3: Primary care team, primary care mental health worker	Moderate or severe depression	Medication, psychological interventions, social support
Step 2: Primary care team, primary care mental health worker	Mild depression	Watchful waiting, guided self-help, computerised CBT, exercise, brief psychological interventions
Step 1: GP, practice nurse	Recognition	Assessment

Of those people whom primary healthcare professionals recognise as having depression, some prefer to avoid medical interventions, and others will improve in any case without them. Thus, in depressions of only mild severity, many GPs prefer a 'watchful waiting' approach, which can be accompanied by general advice on such matters as restoring natural sleep rhythms and getting more structure into the day. However, other people prefer to accept, or indeed require, medical, psychological or social interventions, and these patients are therefore offered more complex interventions. Various interventions are effective, delivered by a range of workers in primary care.

Treatment of depression in primary care, however, often falls short of optimal guideline recommended practice (Donoghue & Tylee, 1996a) and outcomes are correspondingly below what is possible (Rost *et al.*, 1995). As we have seen, only about one in five of the patients at this level will need referral to a mental healthcare professional, the main indications being failure of the depression to respond to treatment offered in primary care, incomplete response or frequent recurrences of depression. Those patients who are actively suicidal or whose depression has psychotic features may also benefit from specialist referral.

Finally, there are a few patients who will need admission to an inpatient psychiatric bed. Here they can receive round the clock nursing care and various special interventions.

- 2.6.7.1 For patients with mild depression who do not want an intervention or who, in the opinion of the healthcare professional, may recover with no intervention, a further assessment should be arranged, normally within two weeks ('watchful waiting'). (C)
- 2.6.7.2 Healthcare professionals should make contact with patients with depression who do not attend follow-up appointments. (C)
- 2.6.7.3 Patients with mild depression may benefit from advice on sleep hygiene and anxiety management. (C)

2.7 The experience of depression

For any guideline on the treatment of depression to be credible it has to be informed at every stage of its development by the perspective of patients. Intensive patient input has led to the development of the tiered and multifaceted management cascade described in this guideline ('stepped care'). Patients are keen to be given much more explanation and information about depression and to be offered a range of possible treatment choices. The patient view is that healthcare professionals have previously been over-reliant on the prescribing of antidepressant medications often without adequate psychological support (Smith, 1995; Singh, 1995). A patient narrative is described overleaf.

2.7.1 A personal perspective

The following is a personal account of an experience of long-term depression.

'Happily, my experience of taking antidepressants was not too unpleasant. I had been suffering from recurrent periodic bouts of depression for quite a long time without realising it. Various medications were prescribed for short-term use, which alleviated the condition for a while, although I was, and still am, averse to becoming dependent on them. Sometimes the side effects were extremely unpleasant – at times I felt almost suicidal and felt that the treatment was actually making me worse. I started to doubt my doctor's competence, feeling that he didn't understand or care.'

'The really effective treatment only began when I consulted a GP who knew my and my family history, not just my medical history. He took time to explain what was happening, described the possible side effects, the interaction with alcohol and other medications, but, most importantly, assured me that depression did not necessarily have to be a "life sentence".'

'After a short period on antidepressants we explored alternative therapies and identified practical steps that I could take in order to develop a coping strategy without recourse to antidepressants. This was done in a spirit of equal partnership between the GP and myself, with me being able to make informed choices.'

'By far the worst thing about my depression was not knowing what was happening to me, the feeling that life had nothing to offer me, the lack of interest and loss of motivation, in short, the feeling of helplessness and hopelessness.'

'I still suffer bouts of depression, but now understand what is happening, and know how to cope and seek help, as I know I can, and will, come out of it.'

'The provision of alternative therapies is paramount, instead of the reliance on medication as an ongoing first line defence. It is of extreme importance that patients feel that they will get well, and feel that they can contribute to the economy instead of feeling that they are a burden on it.'

'In summary, the main priorities should be the provision of understanding, time, choice and above all, hope. These are not as cost prohibitive as some of the alternatives.'

Patients have, through their involvement in the preparation of this guideline, made tangible changes to the suggested management of depression, particularly in primary care settings. They have endorsed the use of the term 'patient', where appropriate, to refer to people with depression.

2.8 Patient preference, information, consent and mutual support

There is now a wide range of different possible treatments, each with their own combination of general and specific effects, side effects and mechanisms of action, and variation in the NHS sites at which healthcare may be provided for people who are depressed and their carers. With this in mind, the provision of comprehensive information, using clear and understandable language, is increasingly necessary. Written material in the language of the patient, and access to interpreters for those whose first language is other than English, is essential in order for people to be able to express their preferences. This is especially the case when a range of broadly equivalent treatments is available for people with mild to moderate depression. Patients and carers need a good understanding of the treatment options and the risks involved before treatment is initiated.

The principle of informed consent should be followed even when a person has severe depression, or when a person is being treated under the Mental Health Act. When a person with recurrent depressive illness is sometimes unable to give consent, consideration should be given to the development and recording of advance directives.

In addition, given the emotional, social and economic cost that depression usually entails, patients and their families may need help in contacting support groups and self-help groups. This is also important to promote understanding and collaboration between patients, their carers and healthcare professionals at all levels of primary and secondary care.

- 2.8.1.1 A number of different treatment approaches may be equally effective for patients who are depressed, especially for those with mild and moderate depression who are not considered to be at substantial risk of self-harm. Patient preference and the experience and outcome of previous treatment(s) should be considered when deciding on treatment. (GPP)
- 2.8.1.2 Common concerns about taking medication should be addressed. For example, patients should be advised that craving and tolerance do not occur, and that taking medication should not be seen as a sign of weakness. (GPP)
- 2.8.1.3 Patients and, where appropriate, families and carers should be provided with information on the nature, course and treatment of depression including the use and likely side-effect profile of medication. (GPP)
- 2.8.1.4 When talking to patients and carers, healthcare professionals should use everyday, jargon-free language. If technical terms are used they should be explained to the patient. (GPP)
- 2.8.1.5 Where possible, all services should provide written material in the language of the patient, and independent interpreters should be sought for people whose preferred language is not English. (GPP)
- 2.8.1.6 Where available, consideration should be given to providing psychotherapies and information about medications in the patient's own language if this is not English. (GPP)

- 2.8.1.7 Healthcare professionals should make all efforts necessary to ensure that a patient can give meaningful and properly informed consent before treatment is initiated. This is especially important when a patient has a more severe depression or is subject to the Mental Health Act. (GPP)
 - 2.8.1.8 Although there are limitations with advance directives about the choice of treatment for people who are depressed, it is recommended that they are developed and documented in care plans, especially for people who have recurrent severe or psychotic depression, and for those who have been treated under the Mental Health Act. (GPP)
 - 2.8.1.9 Patients, families and carers should be informed of self-help groups and support groups and be encouraged to participate in such programmes where appropriate. (GPP)
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