Depression:

the management of depression in primary and secondary care

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National Clinical Practice Guideline Number ___

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TABLE OF CONTENTS: CHAPTERS 1-5

1 Introduction

This guideline has been developed to advise on the treatment and management of the depression and related conditions. The guideline recommendations have been developed by a multidisciplinary group of healthcare professionals, patients and their representatives, and researchers after careful consideration of the best available evidence. It is intended that the guideline will be useful to clinicians and service commissioners in providing and planning high quality care for those with depression while also emphasising the importance of the experience of care for patients and carers.

1.1 National guidelines

1.1.1 What are clinical practice guidelines?

Clinical practice guidelines are 'systematically developed statements that assist clinicians and patients in making decisions about appropriate treatment for specific conditions' (Department of Health, 1996). They are derived from the best available research evidence, using predetermined and systematic methods to identify and evaluate all the evidence relating to the specific condition in question. Where evidence is lacking, the guidelines will incorporate statements and recommendations based upon the consensus statements developed by the guideline development group.

Clinical guidelines are intended to improve the process and outcomes of health care in a number of different ways. Clinical guidelines can:

- provide up-to-date evidence-based recommendations for the management of conditions and disorders by healthcare professionals
- be used as the basis to set standards to assess the practice of healthcare professionals
- form the basis for education and training of healthcare professionals
- assist patients and carers in making informed decisions about their treatment and care
- improve communication between healthcare professionals, patients and carers
- help identify priority areas for further research.

1.1.2 Uses and limitations of clinical guidelines

Guidelines are not a substitute for professional knowledge and clinical judgment. Guidelines can be limited in their usefulness and applicability by a number of different factors: the availability of high quality research evidence, the quality of the methodology used in the development of the guideline, the generalisability of research findings and the uniqueness of individual patients.

Although the quality of research in depression is variable, the methodology used here reflects current international understanding on the appropriate practice for guideline development (AGREE: Appraisal of Guidelines for Research and Evaluation Instrument; www.agreecollaboration.org), ensuring the collection and selection of the best research evidence available, and the systematic generation of treatment recommendations applicable to the majority of patients and situations. However, there will always be some patients and situations for which clinical guideline recommendations are not readily applicable. This guideline does not, therefore, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or carer.

In addition to the clinical evidence, cost-effectiveness information, where available, is taken into account in the generation of statements and recommendations of the clinical guidelines. While national guidelines are concerned with clinical and cost effectiveness, issues of affordability and implementation costs are to be determined by the NHS.

In using guidelines, it is important to remember that the absence of empirical evidence for the effectiveness of a particular intervention is not the same as evidence for ineffectiveness. In addition, of particular relevance in mental health, evidence-based treatments are often delivered within the context of an overall treatment programme including a range of activities, the purpose of which may be to help engage the patient, and provide an appropriate context for the delivery of specific interventions. It is important to maintain and enhance the service context in which these interventions are delivered, otherwise the specific benefits of effective interventions will be lost. Indeed, the importance of organising care, so as to support and encourage a good therapeutic relationship, is at times more important than the specific treatments offered.

1.1.3 Why develop national guidelines?

The National Institute for Clinical Excellence (NICE) was established as a Special Health Authority for England and Wales in 1999, with a remit to provide a single source of authoritative and reliable guidance for patients, professionals and the public. NICE guidance aims to improve standards of care, to diminish unacceptable variations in the provision and quality of care

across the NHS and to ensure that the health service is patient-centred. All guidance is developed in a transparent and collaborative manner using the best available evidence and involving all relevant stakeholders.

NICE generates guidance in a number of different ways, two of which are relevant here. First, national guidance is produced by the Technology Appraisal Committee to give robust advice about a particular treatment, intervention, procedure or other health technology. Second, NICE commissions the production of national clinical practice guidelines focused upon the overall treatment and management of a specific condition. To enable this latter development, NICE established six National Collaborating Centres in conjunction with a range of professional organisations involved in healthcare.

1.1.4 The National Collaborating Centre for Mental Health

This guideline has been commissioned by NICE and developed within the National Collaborating Centre for Mental Health (NCCMH). The NCCMH is a collaboration of the professional organisations involved in the field of mental health, national service-user and carer organisations, a number of academic institutions and NICE. The NCCMH is funded by NICE and led by a partnership between the Royal College of Psychiatrists' research unit (College Research Unit – CRU) and the British Psychological Society's equivalent unit (Centre for Outcomes Research and Effectiveness – CORE). Members of the NCCMH reference group come from the following organisations:

- Royal College of Psychiatrists (RCPsych)
- British Psychological Society (BPS)
- Royal College of Nursing (RCN)
- National Institute for Social Work (NISW)
- College of Occupational Therapists (COT), now replaced by the Clinical Effectiveness Forum for the Allied Health Professions (CEFAHP)
- Royal College of General Practitioners (RCGP)
- Royal Pharmaceutical Society (RPS)
- Rethink Severe Mental Illness
- Manic Depression Fellowship (MDF)

- MIND
- Centre for Evidence Based Mental Health (CEBMH)
- Centre for Economics in Mental Health (CEMH)
- Institute of Psychiatry (IoP).

The NCCMH reference group provide advice on a full range of issues relating to the development of guidelines, including the membership of experts, professionals, patients and carers within guideline development groups.

1.1.5 From national guidelines to local protocols

Once a national guideline has been published and disseminated, local healthcare groups will be expected to produce a plan and identify resources for implementation, along with appropriate timetables. Subsequently, a multidisciplinary group involving commissioners of health care, primary care and specialist mental healthcare professionals, patients and carers should undertake the translation of the implementation plan into local protocols. The nature and pace of the local plan will reflect local health care needs and the nature of existing services; full implementation may take a considerable time, especially where substantial training needs are identified.

1.1.6 Auditing the implementation of guidelines

This guideline identifies key areas of clinical practice and service delivery for local and national audit. Although the generation of audit standards is an important and necessary step in the implementation of this guidance, a more broadly based implementation strategy will be developed. Nevertheless, it should be noted that the Commission for Health Care, Audit and Improvement (CHAI) will monitor the extent to which Primary Care Trusts (PCTs), trusts responsible for mental health and social care and Health Authorities have implemented these guidelines.

1.2 The national depression guideline

1.2.1 Who has developed this guideline?

The 'Guideline Development Group' (GDG) was convened by the NCCMH based upon advice from the Centre's reference group representatives, and supported by funding from NICE. The GDG included members from the following professional groups: psychiatry, clinical psychology, pharmacy, nursing, and general practice. In addition, the GDG included three patients.

Staff from the NCCMH provided leadership and support throughout the process of guideline development, undertaking systematic searches, information retrieval, appraisal and systematic review of the evidence.

Members of the GDG received training in the process of guideline development from the Centre for Evidence-Based Mental Health (CEBMH), and the National Guidelines and Audit Patient Involvement Unit, which has been established by NICE. The National Guidelines Support and Research Unit, also established by NICE, provided advice and assistance regarding all aspects of the guideline development process.

All members of the Group made formal declarations of interest at the outset, updated at every GDG meeting. GDG members met a total of twenty-six times throughout the process of guideline development. For ease of evidence identification and analysis, members of the GDG formed sub-groups, or 'Topic Groups", covering identifiable treatment approaches. Topic Groups were led by a national expert in the relevant field and supported by the NCCMH technical team, with additional expert advice from special advisors where necessary. Topic Groups oversaw the production and synthesis of research evidence before presentation to the wider GDG. All statements and recommendations in this guideline have been generated and agreed by the whole GDG.

1.2.2 For whom is this guideline intended?

This guideline will be of relevance to all people with a diagnosis of depression aged 18 years of age and over. This guideline will not explicitly provide guidance on the diagnosis or treatment of people with depression in the context of a separate physical or other primary mental disorder. These may also be dealt with in a future guideline.

Although this guideline will briefly address the issue of diagnosis, it will not make evidence-based recommendations or refer to evidence regarding diagnosis, primary prevention or assessment. In sum, this guideline is intended for use by:

- Individuals with a diagnosis of depression aged 18 years and over and their families/carers

- Professional groups who share in the treatment and care for people with a diagnosis of depression, including psychiatrists, clinical psychologists, mental health nurses, community psychiatric nurses, other community nurses, social workers, practice nurses, occupational therapists, pharmacists, general practitioners and others

- Professionals in other health and non-health sectors who may have direct contact with or are involved in the provision of health and other public services for those diagnosed with depression. These may include A&E staff, paramedical staff, prison doctors, the police and professionals who work in the criminal justice and education sectors

- Those with responsibility for planning services for people with a diagnosis of depression, and their carers, including directors of public health, NHS trust managers and managers in PCTs.

1.2.3 Specific aims of this guideline

The guideline makes recommendations and good practice points for pharmacological treatments and the use of psychological and service level interventions in combination with pharmacological treatments in the three phases of care. Specifically it aims to:

- Evaluate the role of specific pharmacological agents in the treatment and management of depression

- Evaluate the role of specific psychological interventions in the treatment and management of depression

- Evaluate the role of specific service delivery systems and service-level interventions in the management of depression

- Integrate the above to provide best practice advice on the care of individuals with a diagnosis of depression through the different phases of illness, including the initiation of treatment, the treatment of acute episodes and the promotion of recovery

- Consider economic aspects of various standard treatments for depression.

1.2.4 Other versions of this guideline

There are other versions of *Depression: the management of depression in primary and secondary care*, including:

- the NICE guideline, which is a shorter version of this guideline, containing the key recommendations and all other recommendations (see Chapter 4)

- the quick reference guide, which is a summary of the main recommendations in the NICE guideline

- the information for the public, which describes the guidance using non-technical language. It is written chiefly for patients, but may also be useful for family members, advocates, or those who care for people with depression.

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 only relates to those identified by the tenth edition of the *International Statistical Classification of Diseases and Related Health Problems* (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 sizable quantity of the research forming the evidence base from which much of this guideline is drawn has used a similar classificatory system – the 4th revision of the Diagnostic and Statistical Manual 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 postnatal 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 for 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 un-reactive 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 upon 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: depression, anxiety or mixed depression and anxiety, dependent upon which constellation of symptoms dominate the clinical picture. In addition, the presentation of depression varies with age: the young showing more behavioural symptoms and older adults more somatic symptoms while minimising complaints of low mood (Serby & Yu, 2003).

Major depression is generally diagnosed when a persistent and un-reactive 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 any case, the severity of depression varies considerably and is pragmatically classified as mild, moderate or severe. 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 6 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, Goldberg, Von Korff 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 illnesses at index consultation (Goldberg, Privett, Ustun 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 2 years, 20% had died and nearly 40% were still depressed (Cole et al., 1999).

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 (on or before 20 years) particularly associated with a significantly increased vulnerability to relapse (Giles, Jarrett, Biggs, 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 is guarded, 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.

'Patients with refractory depression' is a term used to describe those whose depression has failed to respond to two or more antidepressants at an adequate dose for an adequate duration given sequentially. The term is arguably not especially helpful in that it doesn't take into account depressive subtypes, makes no distinction between treatment resistance, chronicity, relapse or recurrence, and fails to take into account what psychosocial factors may be preventing recovery or indeed, whether the person as 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 commonest cause of loss of disability adjusted life years in the world, and by 2020, it is projected to become the second commonest 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, Lopez and Jamison, 1994). It is even more common in the developing world (for review, see Institute of Medicine 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 up 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 particular effects of 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 (op cit p338-40). 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 adversely affect outcomes from other illnesses, such as for people with myocardial infarction (MI), where 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 & Frasure-Smith, 2000). In one community study, patients with cardiac disease who were depressed had an increased risk of death from cardiac problems compared to 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 co-morbid depression is present (Cassano & Fava, 2002).

Suicides account for just under 1% of all deaths, of which nearly two-thirds occur in depressed people (Sartorius, 2001). Of all people who are diagnosed with major depressive disorder, a significant minority die by suicide.

Sometimes depression may also lead to acts of violence to others, including homicide. However, more commonly, and a greater cause of disability for people who are depressed, results from the impact depressive illnesses have upon 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 amongst 16 to 65 year olds in the UK was 21/1000 (males 17, females 25), but if the less specific, and broader category of "mixed depression & anxiety" (F41.2, ICD-10; WHO 1992) was included, these figures rose dramatically to 98/1000 (males 71, females 124). It can be seen that the gender ratio is more skewed to females with the broader concept (Meltzer et al 1995a & b; Gill et al 1996).

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 groupswere not greatly different from 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 were for West Indians or Africans (6/1000) (Meltzer et al 1995). However, these estimates are based on relatively small samples of people from minority ethnic groups.

Gender and a number of socioeconomic factors also significantly affect prevalence rates differentially: unemployed women have over twice the prevalence of depression than 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 & 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 & 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). In another study, the roofless homeless showed 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 attenders had a depressive disorder. Neighbourhood social deprivation accounted for 48.3% of the variance between 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 considered 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 and Christchurch, New Zealand (Jenkins, Lewis, Bebbington et al, 2003). Even higher rates are obtained for one-year prevalence using the International Composite Interview Schedule in the USA 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, Goldberg, Von Korff 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 (<4 symptoms), mild (4 symptoms), moderately depressed (5-6 symptoms), and severe (>7 symptoms, with or without various psychotic symptoms). Symptoms must be present for at least 2 weeks. These definitions have been used in the report

which follows. However, it is doubtful whether the severity of a depressive illness can realistically be captured in a single symptom count: clinicians will wish to consider family and previous history, as well as the degree of associated disability, in making this assessment.

Although reliability of diagnosis has improved, there has been no parallel improvement in the validity of diagnosis (Dohrenwend, B. P. (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 vs 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 co-morbid diagnosis, such as anxiety, social phobia, panic and various personality disorders (Brown, Campbell, Lehman, Grisham, & Mancill, 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, for which problem, for which person, and in which context, will be effective.

2.4 Aetiology

Unsurprisingly, 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 have 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 amenorrhea (Cassano & Fava, 2002).

Whatever theories of causation have gained credence none have 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, 2002). 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, 2002). It is worthy of mention that physical illness is 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, 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, C. 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 working class women 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, are all predictive factors for depression (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 many such events are not followed by a depressive disorder. Having said that, the presence of some factors protect 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 which 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 report, 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 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 the broader society. On average, depressed patients lose 11 days over a 6-month period, compared with 2 to 3 days for individuals without this condition (Lepine et al., 1997). It is also of interest that the cost of health and social service utilisation are 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 which investigated the economic burden of depression in the UK (Berto et al., 2000). One study (Jonsson & Bebbington, 1993) focused only on the direct costs of depression in the UK without giving detailed breakdown of their 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 £333M 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 & Sorensen (1993), using a different methodology, calculated the cost of depression for England and Wales in year 1990 from a broader societal perspective and. They estimated the direct care costs at £417 million, of which £47 million were drug treatment costs, £143 million were primary health care costs, £40 million were social services costs, £177 million were inpatient care costs and outpatient attendances account 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 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 6 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 11-19% of the direct costs and that the cost of lost productivity due to depression far overweighs 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 (OHS: Key Health Statistics from General Practice 1998) and that the number of GP consultations for depressive disorders more than doubled from 4 million to 9 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. Doctors' Independent Network database 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 major depression cases were diagnosed by general practitioners who issued 95% of all prescriptions for antidepressants (Henry, 1993). Freemantle et al. (1995, 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 annually on antidepressants. This figure has further increased as newer and more expensive antidepressants have become available (Eccles 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 (Kisley 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 1 in 4 or 5 are referred to secondary mental health services. There is considerable variation between individual GPs in their referral rates to the mental illness services, however, those seen by the mental illness service are a highly selected group - they are skewed towards those who do not respond to anti-depressants, more severe illnesses, single women and those below the age of 35 (Goldberg 1994).

General practitioners are immensely variable in their ability to recognize depressive illnesses, with some recognizing virtually all the patients found to be depressed at independent research interview, and others recognizing very few (Goldberg & Huxley, 1992; Ustun & 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 (Bridges & Goldberg, 1988; Goldberg et al., 1991).

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 contended. 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 & Ormel, 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, 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 95% of depressed people never entering secondary mental health services and nearly 50% of whom never consult a doctor, and for many more their depression goes unrecognised and untreated, this is clearly a problem for primary care.

2.6.2 Assessment and coordination of care

Given the low detection and recognition rates, especially in view of the fact that depression is associated with an increased suicide rate, a strong tendency for recurrence and the high personal and social costs of depression it is essential that primary care and mental health practitioners have the required skills to assess the depressed patient, their social circumstances and relationships and the risk they may pose to themselves and to others. The effective assessment of a patient, including risk assessment and the subsequent coordination of their care is highly likely to improve outcomes, and should therefore be comprehensive.

2.6.2.1 In older adults with depression, their nutritional state, living conditions, and social isolation should be assessed, and the involvement of more than one agency is recommended where appropriate.

2.6.2.2 When depressive symptoms are accompanied by anxious symptoms, it is important to usually first focus treatment on the depression as a priority. However, it should be noted that psychological treatment for depression often reduces anxiety, and many antidepressants also have sedative/anxiolytic effects. (GPP)

2.6.2.3 In deciding upon 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**)**

2.6.2.4 Healthcare professionals should always ask patients with depression directly about suicidal ideation and intent. (GPP)

2.6.2.5 Healthcare professionals should advise patients and carers to be vigilant for changes in mood, negativity and hopelessness, and suicidal ideation, particularly during high-risk periods. (GPP)

2.6.2.6 Healthcare professionals should assess whether patients with suicidal ideation have adequate social support and are aware of appropriate sources of help. They should advise them to seek appropriate help if the situation deteriorates. (GPP)

2.6.2.7 Where a patient presents considerable immediate risk to self or others urgent referral to a specialist mental health service should be arranged. (GPP)

2.6.2.8 Patients with severe depression referred directly to specialist care should be re-evaluated and their symptom profile and suicide risk re-assessed. The use of treatments recommended in Step 3 should be considered. (GPP)

2.6.2.9 For patients whose depression has failed to respond to various strategies for augmentation and combination treatments, consideration should be given to referral to a tertiary centre. (GPP)

2.6.2.10 Inpatient treatment should be considered for people with depression where the patient is at significant risk of suicide or self-harm. (C)

2.6.2.11 Where a 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.

2.6.2.12 When assessing a person with depression, healthcare professionals should consider the psychological, social and physical characteristics of the patient and the quality of interpersonal relationships and 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.

2.6.2.13 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.

2.6.2.14 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 between 4 and 8 weeks, and 50% improved in 6 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 6 months: the mean duration of episode was 6 months, with 50% remission in 25 weeks.

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 3 months, with 26% recovering by 1 month, 63% by 6 months; 85% by 1 year, and 88% by 2 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, 2002). Drug, and some other, treatments for depression, when compared to

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 to placebo for this diagnostic group, the clinical improvements resulting from antidepressants over and above that for placebo is not clinically significant (Kirsch et al, 2002). Given the recent focus upon publication bias, especially with regard to drug company funded trials (Lexchin et al, 2003; Melander et al 2003) 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 the 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-hydroxytryptymine (5HT) and dopamine. 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.

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 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). There 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 are 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 pharmocogenetic variations may effect the efficacy and tolerability of antidepressant drugs. It is likely that future research on this topic will lead to the development of clinically meaningful pharmocogenetic 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 properly 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 disorder have been elaborated and championed, although psychological treatments specifically for depression were only developed over the last 30 to 40 years, and research into their efficacy more recent still (Roth & Fonagy, 1996). Many, but not all, such therapies are derived from psychoanalysis, partly as a reaction to the difficulties of treating people with depression using psychoanalysis (Fonagy, 2003). In any event, the emergence of cognitive and behavioural approaches to the treatment of mental health problems have 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; behaviour therapy; interpersonal therapy; problem solving therapy; counselling; short-term psychodynamic therapy; and couple focussed 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 both with regard to policy (for example, see Department of Health, 1999), and research (e.g., evaluating day hospital treatment, Marshall et al., 2002). Research using RCT designs have 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: Managed Care, 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 the document that follows a "stepped care" model is developed (Figure 1), which draws attention to the different needs that depressed individuals have and the responses that are required from services, depending upon the characteristics of a persons depression and their personal and social circumstances. 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.

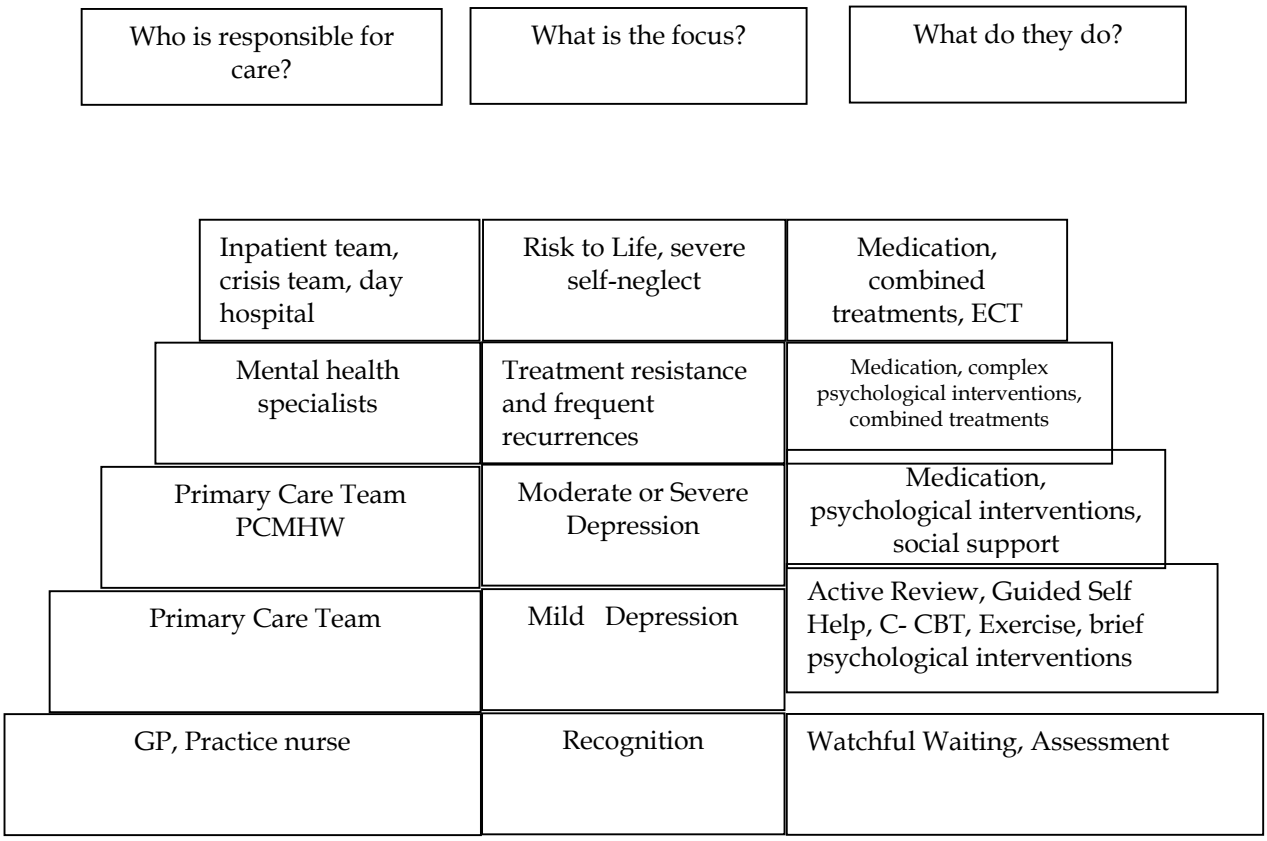


Figure 1. The stepped care model

Of those depressions that primary healthcare professionals recognise, 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, others 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, 1996) and outcomes are correspondingly below what is possible (Rost et al., 1995). As we have seen, only about 1 in 5 of the patients at this level will need referral to a mental healthcare professional, the main indications being failure to respond to treatment offered in primary care, incomplete response or frequent recurrences of depression. Those who are actively suicidal or who have psychotic features may also benefit from specialist referral.

Finally, at the top are those 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 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 2 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 advice about 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. Patients are keen on much more in the way of explanation and information about depression and to have a range of possible treatment choices. The patient view is that we have previously been over-reliant on the prescribing of antidepressant medications often without adequate psychological support. (Smith, 1995; Singh, 1995). A typical patient narrative is described below.

2.7.1 A Survivor's Perspective

"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 G.P. who knew my and my family history, not just my medical history. He took <u>time</u> to explain what was happening, described the possible side effects, the inter-action 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 G.P. 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

With a wide range of different possible treatments, each with their own combination of general and specific effects, side effects and mechanisms of action, and the variation in the NHS sites at which health care may be provided for people who are depressed and their carers, the provision of comprehensive information, using clear and understandable language, is increasingly necessary. To be able to express their preferences, especially for people with mild to moderate depression when a range of broadly equivalent treatments are available, written material in the language of the patient and access to interpreters for those whose first language is other than English, is essential. 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 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 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, a number of different treatment approaches may be equally effective. Patient preference and the experience and outcome of previous treatment(s) should be considered in determining the choice of treatment. (GPP)

2.8.1.2 Common concerns about taking medication, such as fears of addiction or of taking medication being seen as a weakness, should be addressed. (GPP)

2.8.1.3 Patients and carers should be provided with appropriate 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 language is used it should be explained to the patient. (GPP)

2.8.1.5 Where appropriate, all services should provide written material in the language of the patient, and independent interpreters should be sought for people whose first language is not English. (GPP)

2.8.1.6 Where available, consideration should be given to providing psychotherapies and information about medications in patients' own language where 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 regarding the choice of treatment for individuals who are depressed, it is recommended that they are developed and documented in individuals' care plans, especially for people who have recurrent severe or psychotic depressions, and for those who have been treated under the Mental Health Act. (GPP)

2.8.1.9 In addition to the provision of high quality information, patients, family and carers should be informed of self-help groups and support groups and be encouraged to participate in such programmes where appropriate. (GPP)

3 Methods used to develop this guideline

3.1 Overview

The development of this guideline drew upon methods outlined by NICE (NICE, 2002; Eccles & Mason, 2001). A team of experts, professionals and patients, known as the Guideline Development Group (GDG) with support from NCCMH staff undertook the development of a patient centred, evidence-based guideline. There are six basic steps in the process of developing a guideline:

- Define the scope, which sets the parameters of the guideline and provides a focus and steer for the development work
- Define clinical questions considered important for practitioners and patients
- Develop criteria for evidence searching and search for evidence
- Design validated protocols for systematic review and apply to evidence recovered by search
- Synthesise and (meta-) analyse data retrieved, guided by the clinical questions, and produce evidence statements
- Answer clinical questions with evidence-based recommendations for clinical practice.

The clinical practice recommendations made by the GDG are therefore derived from the most up-to-date and robust evidence base for the clinical and cost effectiveness of the treatments and services used in the management of depression. In addition, to ensure a patient and carer focus, the concerns of patients and carers regarding clinical practice have been highlighted and addressed by good practice points and recommendations agreed by the whole GDG. The evidence-based recommendations and good practice points are the core of this guideline.

3.2 The Guideline Development Group

The GDG consisted of patients, and professionals and academic experts in psychiatry, clinical psychology and general practice. NCCMH staff undertook the clinical and health economics literature searches, reviewed and presented the evidence to the GDG, managed the process and contributed to the drafting of the guideline.

3.2.1 Guideline Development Group meetings

Twenty-six GDG meetings were held between November 2001 and October 2003. During each day-long GDG meeting clinical evidence was reviewed and assessed to develop statements and recommendations. At each meeting all GDG members declared any potential conflict of interests. Patient and carer concerns were routinely discussed as part of a standing agenda.

3.2.2 Topic groups

The GDG divided its workload along clinically relevant lines in order to deal with the large volume of evidence efficiently. GDG members formed three topic groups: the Service topic group covered questions relating to the presentation of services to users, including screening, exercise and guided self-help; the Pharmacology topic group covered pharmacological treatments for depression; and the Psychology topic group covered psychotherapies. Each topic group was chaired by a GDG member with expert knowledge of the topic area. Topic groups refined the clinical definitions of treatment interventions, reviewed and prepared the evidence with the NCCMH review team. Topic group leaders reported the status of their group's work as part of the GDG standing agenda. They also assisted in drafting the section of the guideline relevant to the work of each topic group.

3.2.3 Patients and carers

Individuals with direct experience of services gave an integral patient focus to the GDG and the guideline. The GDG included three patients. They contributed as full GDG members to writing the clinical questions, helping to ensure that the evidence addressed their views and preferences, highlighting sensitive issues and terminology associated with depression, and bringing service-user research to the attention of the GDG. In drafting the guideline, they contributed to the editing of the first draft of the guideline's introduction and identified good practice points from the patient and carer perspective; their suggestions were incorporated before distributing the draft to the GDG for further review.

3.2.4 Special advisors

Special advisors who had specific expertise in one or more aspects of treatment and management relevant to the guideline, assisted the GDG, commenting on specific aspects of the developing guideline and making presentations to the GDG. Appendix 2 lists those who agreed to act as special advisors.

3.2.5 National and international experts

National and international experts in the area under review were identified through the literature search and through the experience of the GDG members. These experts were contacted to recommend unpublished or soon-to-be published studies in order to ensure up-to-date evidence was included

in the evidence base for the guideline. Appendix 5 lists researchers who were contacted.

3.3 Clinical questions

Clinical questions were used to guide the identification and interrogation of the evidence base. The questions were developed using a modified nominal group technique. The process began by asking each member of the GDG to submit as many questions as possible. The questions were then collated and refined by the review team. At a subsequent meeting, the guideline chair facilitated a discussion to further refine the questions. At this point, the GDG members were asked to rate each question for importance. The results of this process were then discussed and consensus reached about which questions would be of primary importance and which would be secondary. The GDG aimed to address all primary questions, while secondary questions would only be covered time permitting. Appendix 6 lists the clinical questions.

3.4 Systematic clinical literature review

The aim of the clinical literature review was to identify and synthesise systematically all relevant evidence in order to answer the clinical questions developed by the GDG. Thus, clinical practice recommendations are evidence-based as far as possible.

Where an existing NICE Technology Appraisal addressed one of the clinical questions, the GDG were obliged to adopt the relevant existing recommendations. If evidence was not available, then informal consensus methods were used (see section 3.4.4) and the need for future research was specified.

A stepwise, hierarchical approach was taken to locating and presenting evidence to the GDG. The NCCMH developed the methodology for this process with advice from the National Guidelines Support and Research Unit (NICE) and after considering recommendations from a range of other sources. These included:

- Centre for Clinical Policy and Practice of the New South Wales Health Department (Australia)
- Clinical Evidence Online
- Cochrane Collaboration
- New Zealand Guideline Group
- NHS Centre for Reviews and Dissemination
- Oxford Centre for Evidence-Based Medicine
- Scottish Intercollegiate Guidelines Network (SIGN)
- United States Agency for Health Research and Quality

- Oxford Systematic Review Development Programme.

3.4.1 The review process

Since most of the clinical questions for this guideline concerned interventions, much of the evidence base was formed from high quality randomised controlled trials (RCTs). Although there are a number of difficulties with the use of RCTs in the evaluation of interventions in mental health, this research design remains the most important method for establishing treatment efficacy (see introductions to later chapters for fuller discussions of this issue).

The review process involved:

- Developing search filters
- Searching for existing systematic reviews
- Searching for new RCTs
- Selecting studies
- Synthesising the evidence.

3.4.1.1Developing search filters

The review team developed search filters to search electronic databases that combined subject headings with free-text phrases. A filter was developed for the general topic 'depression', which was combined with specific filters for each clinical question. These were also combined with filters developed for 'systematic reviews' or 'RCTs' (or other research designs as appropriate) (Appendix 7)

1.1.1.1 3.4.1.2 Searching for existing systematic reviews

The NCCMH review team undertook searches for existing systematic reviews of RCTs published in English since 1995 (an arbitrary cut-off date to reduce the number of references found and to ensure recency), which would answer the clinical questions posed by the GDG. The initial searches were undertaken in December 2001 and January 2002, with update searches being carried out every two months until May 2002. A search of PubMed (MEDLINE) was also undertaken weekly beginning in April 2003 until the end of the guideline development process. The following databases were searched: EMBASE, MEDLINE, PsycINFO, Cochrane Library, CINAHL, Web of Science.

Systematic reviews were assessed for quality and eligibility (Appendices 8 and 9) before being assessed by the GDG for relevance to a clinical question. Searches were undertaken for RCTs published too late to be included in chosen systematic reviews beginning two years before the publication date of the review in question. Where authors stated the date searches had been undertaken, the NCCMH review team undertook new searches from the beginning of that year. Each study included in an existing review was

subjected to the same quality checks as those located through NCCMH searches, and the data were re-extracted according to NCCMH protocols (see below). Where existing reviews had been undertaken using Review Manager (any version) authors were approached for data sets, although any used were checked for accuracy. For clinical questions where no existing systematic review was identified, searches were undertaken for all relevant evidence.

3.4.1.3 Searching for RCTs

For clinical questions for the Service and Pharmacology topic areas searches of for RCTs were undertaken for each clinical question individually. However, RCTs to answer the clinical questions posed by the Psychology topic group were searched for together. For all questions the following electronic databases were searched: EMBASE, MEDLINE, PsycINFO, Cochrane Library, CINAHL. For the pharmacological review of St John's wort, AMED was also searched. In addition, hand searches were also made of the reference lists of all eligible RCTs, as well as of the list of evidence submitted by registered stakeholders (Appendix 3). Known experts in the field (see Appendix 5), based both on the references identified in earlier steps and on advice from GDG members, were approached for unpublished RCTs[1]. Studies were considered provided a full trial report was available. Studies published in languages other than English were used provided a native speaker was available.

If no RCTs were found to answer a clinical question the GDG adopted a consensus process (see Section 3.4.6). Future guidelines will be able to update and extend the usable evidence base starting from the evidence collected, synthesised and analysed for this guideline.

3.4.1.4 Study selection

All references located in searches of electronic databases were downloaded into Reference Manager and searched liberally to exclude irrelevant papers. The titles of excluded papers were double-checked by a second reviewer. All primary-level studies included after the first scan of citations were acquired in full and re-evaluated for eligibility. Appendix 8 lists the standard inclusion and exclusion criteria. Additional eligibility criteria were developed to assess trials of pharmacotherapy, and these are listed in chapter 7. All eligible papers were critically appraised for methodological quality (see Appendix 10). The eligibility of each study was confirmed by at least one member of the appropriate topic group.

For some clinical questions, it was necessary to prioritise the evidence with respect to the UK context. To make this process explicit, the topic group members took into account the following factors when assessing the evidence:

- Participant factors (e.g., gender, age, ethnicity)

[1] Unpublished full trial reports were accepted where sufficient information was available to judge eligibility and quality.

- Provider factors (e.g., model fidelity, the conditions under which the intervention was performed, the availability of experienced staff to undertake the procedure)
- Cultural factors (e.g., differences in standard care, differences in the welfare system).

It was the responsibility of each topic group to decide which prioritisation factors were relevant to each clinical question in light of the UK context, and then decide how they should modify their recommendations.

3.4.2 Synthesising the evidence

3.4.2.1 Outcomes

The vast majority of data extracted were scores on the Hamilton Rating Scale for Depression (HRSD), Montgomery Asberg Depression Scale (MADRS) and Beck Depression Inventory (BDI) at the end of treatment and, were available, at follow-up. Both mean endpoint scores and dichotomised data (number of people achieving below the cut-off for remission and/or the number of participant reducing their score by 50%) were extracted. In addition, where possible, sub-analyses were performed for severity of depression. Because no study gave information about participants' baseline severity of depression in terms of number of symptoms using the ICD classification (see Chapter 2), the mean depression score at baseline (most commonly an HRSD score) was used as a proxy measure. Scores were categorised mild, moderate, severe or very severe according to American Psychiatric Association criteria. The GDG used these categories with caution mindful of the problematic nature of this proxy measure, in particular the variation in the standard deviation around baseline mean scores. Details of the categories and further information about the depression rating scales are in Appendix 13. When drawing up recommendations the GDG related the APA categories to ICD categories. This method does not take account of the severity of individual symptoms but is nonetheless a rough approximation to clinical severity.

3.4.2.2 Data extraction

Where possible, outcome data from all eligible studies that met quality criteria were extracted using a data extraction form (Appendix 11) and input into Review Manager 4.2 (Cochrane Collaboration, 2003). Where trial reports contained incomplete data and it was possible to contact the original authors, additional information was sought. Where mean endpoint or change scores were extracted and trial reports did not provide standard deviations, standard conversion formulas were used (See Appendix 12).

Different versions of the HRSD were standardised using the method for prorating suggested by Walsh et al. (2002).

All dichotomous outcomes were calculated on an intention-to-treat basis (i.e., a 'once-randomised-always-analyse' basis). This assumes that those participants who ceased to engage in the study – from whatever group – had an unfavourable outcome. The effects of high attrition rates (defined as more than 50% of participants in a particular group leaving treatment early) were examined with sensitivity analyses, and studies were removed from efficacy outcomes if the possibility of bias was detected.

Consultation was used to overcome difficulties with coding. Data from studies included in existing systematic reviews were extracted independently by one reviewer directly into Review Manager and checked by a second reviewer. Where consensus could not be reached, a third reviewer was consulted. Masked assessment (i.e., blind to the journal from which the article comes, the authors, the institution, and the magnitude of the effect) was not used since it is unclear that doing so reduces bias (Jadad et al., 1996; Berlin, 2001).

Information describing each study was also extracted and input into Review Manager 4.2. This was used to generate evidence tables (see Appendix 18). Where meta-analysis was not appropriate and/or possible, the reported results from each primary-level study were also presented in the evidence tables.

3.4.2.3 Meta-analysis

Where possible, meta-analysis was used to synthesise data. If necessary, sub-analyses were used to answer clinical questions not addressed in the original studies or reviews.

The GDG were given a graphical presentation of the results using forest plots generated with Review Manager. Each forest plot displayed the effect size and 95% Confidence Interval (CI) for each study as well as the overall summary statistic with its 95% CI. The graphs were organised so that the display of data in the area to the left of the 'line of no effect' indicated a 'favourable' outcome for the treatment in question[2].

Dichotomous outcomes were presented as relative risks (RR) with the associated 95% CI (see Figure 1). A relative risk (or risk ratio) is the ratio of the treatment event rate to the control event rate. A RR of 1 indicates no difference between treatment and control. In Figure 1, the overall RR of 0.73 indicates that the event rate (i.e., non-remission rate) associated with intervention A is about ¾ of that with the control intervention, or in other words, intervention A reduces non-remission rates by 27%. In addition, the 95% CI around the RR does not cross the 'line of no effect' indicating that this

[2] The exception to this is the review of amitriptyline for which the GDG were provided with a data set for an existing systematic review (Barbui et al, 2001)

is a statistically significant effect. The CI shows with 95% certainty the range within which the true treatment effect should lie.

It had been planned to calculate the Number Needed to Treat (NNT) (or Number Needed to Harm (NNH)) for dichotomous outcomes with statistically significant effect sizes. However, when the baseline risk (i.e., control group event rate (CER)) or length of follow-up varies, NNT is a poor summary of the treatment effect, especially with low risk or where the CER is dissimilar across studies in a meta-analysis (Deeks, 2002). Since it was not possible to calculate the baseline risk for most outcomes NNT and NNH have not been calculated.

Continuous outcomes were analysed as weighted mean differences (WMD) or standardised mean differences (SMD) when different measures (or different versions of the same measure) were used in different studies to estimate the same underlying effect (see Figure 2).

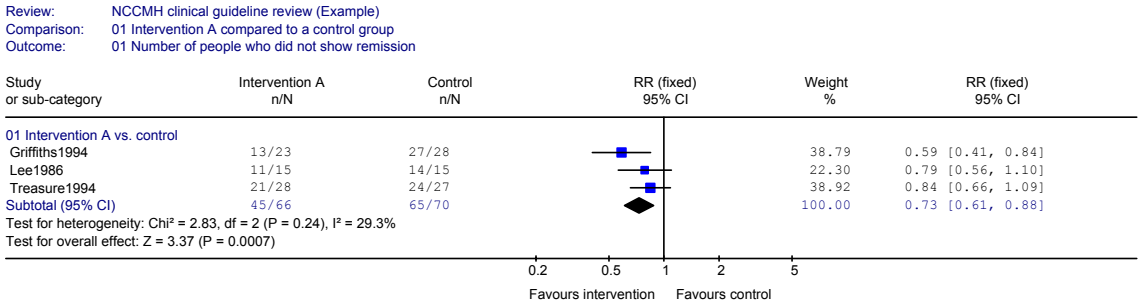


Figure 1. Example of a forest plot displaying dichotomous data

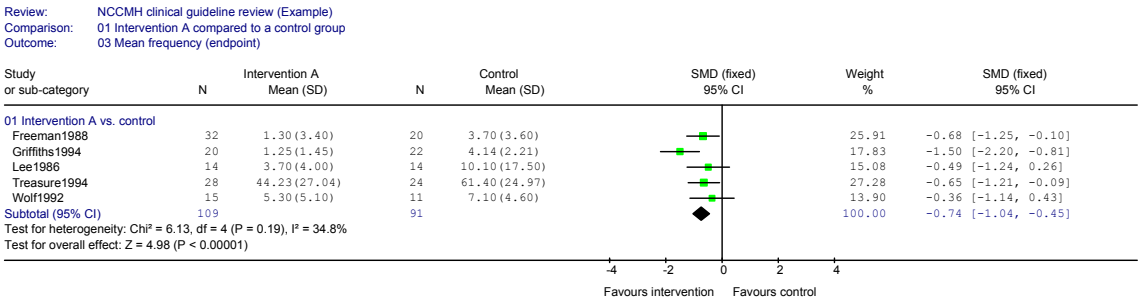


Figure 2. Example of a forest plot displaying continuous data

To check for heterogeneity between studies, both the I^2 test of heterogeneity and the chi-squared test of heterogeneity ($p < .10$), as well as visual inspection of the forest plots were used. The I^2 statistic describes the proportion of total variation in study estimates that is due to heterogeneity (Higgins & Thompson, 2002). An I^2 of less than 30% was taken to indicate mild heterogeneity and a fixed effects model was used to synthesise the results. This assumes that the underlying effect is the same (Egger et al., 2001). An I^2

of more than 50% was taken as notable heterogeneity. In this case, an attempt was made to explain the variation. If studies with heterogeneous results were found to be comparable, a random effects model was used to summarise the results (DerSimonian & Laird, 1986). In the random effects analysis, heterogeneity is accounted for both in the width of CIs and in the estimate of the treatment effect. With decreasing heterogeneity the random effects approach moves asymptotically towards a fixed effects model. An I^2 of 30% to 50% was taken to indicate moderate heterogeneity. In this case, both the chi-squared test of heterogeneity and a visual inspection of the forest plot were used to decide between a fixed and random effects model.

To explore the possibility that the results entered into each meta-analysis suffered from publication bias, data from included studies were entered, where there were sufficient data, into a funnel plot. Asymmetry of the plot was taken to indicate possible publication bias and investigated further.

3.4.3 Developing statements and graded recommendations

The summary statistics (effect sizes; ES) and evidence tables formed the basis for developing clinical statements and recommendations.

3.4.3.1 Developing statements

For each outcome a clinical statement describing the evidence found was developed. To do this both the statistical and clinical significance (i.e., the likely benefit to patients) of the summary statistic were taken into account.

Assessing statistically significant summary statistics

To assess clinical significance where a statistically significant summary was obtained (after controlling for heterogeneity) the GDG adopted the following 'rules of thumb', in addition to taking into account the trial population and nature of the outcome:

For dichotomous outcomes a RR of 0.80 or less was considered clinically significant (see section 3.4.2.3).

For continuous outcomes for which an SMD was calculated (for example, when data from different versions of a scale are combined), an effect size of ~0.5 (a 'medium' effect size, Cohen, 1988) or higher was considered clinically significant. Where a WMD was calculated, a between group difference of at least 3 points (2 points for refractory depression) was considered clinically significant for both BDI and HRSD.

Once clinical significance had been established the strength of the evidence was assessed by examining the 95% CIs surrounding the ES. For level I evidence, where the effect size was judged clinically important for the full range of plausible estimates, the result was characterised as 'strong evidence' (i.e., S1, Flowchart 1: Guideline Statement Decision Tree). For non-level I

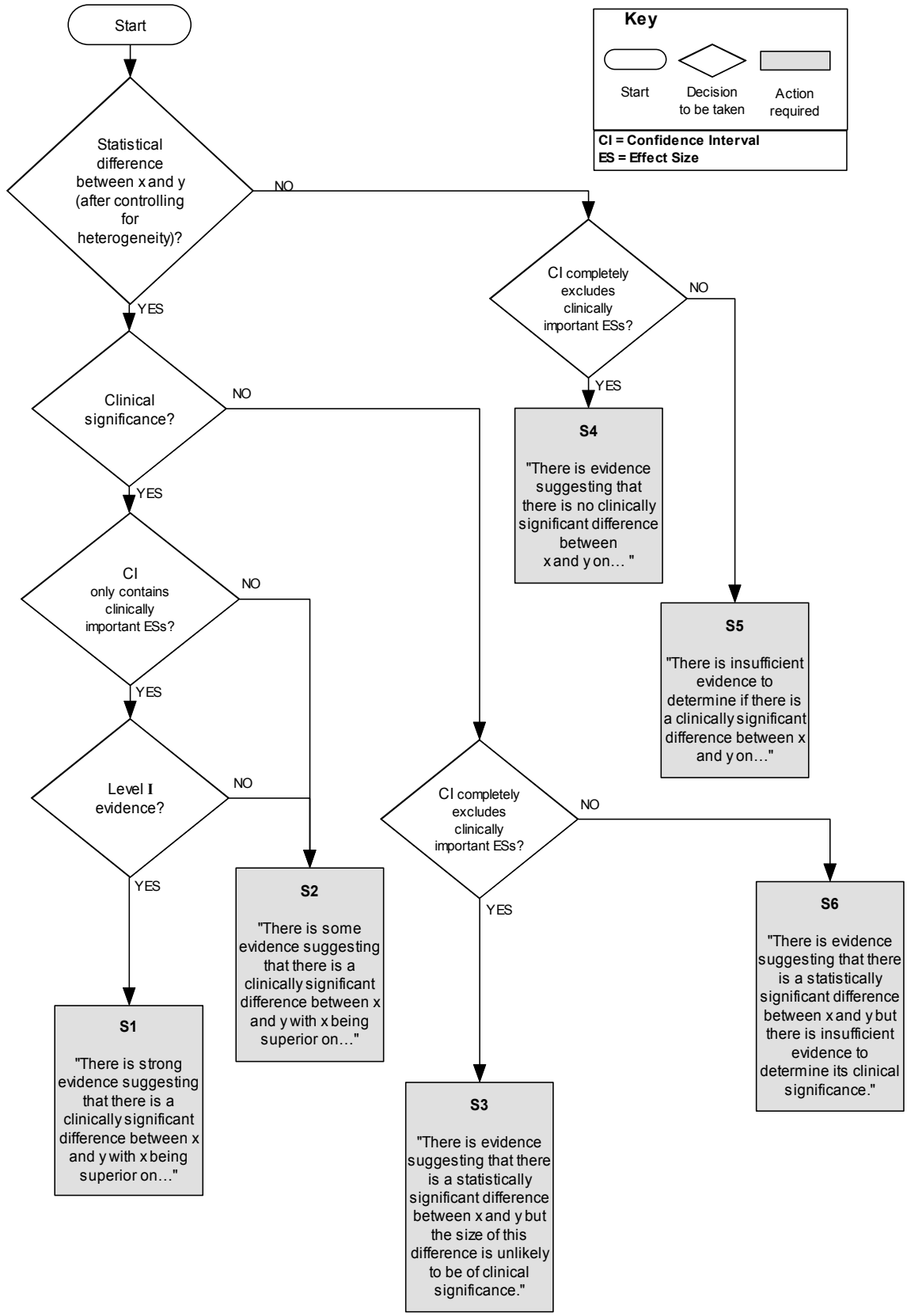
evidence or in situations where the CI also included clinically unimportant effects, the result was characterised as 'some evidence' (i.e., S2).

Where an ES was statistically significant, but *not* clinically significant and the CI excluded values judged clinically important, the result was characterised as 'unlikely to be clinically significant' (S3). Alternatively, if the CI included clinically important values, the result was characterised as 'insufficient to determine clinical significance' (S6).

Assessing non- statistically significant summary statistics
Where a non-statistically significant ES was obtained, the GDG reviewed the trial population, nature of the outcome, size of the effect and, in particular, the CI surrounding the result. If the CI was narrow and excluded a clinically significant ES, this was seen as indicating evidence of 'no clinically significant difference' (S4), but where the CI was wide this was seen as indicating 'insufficient evidence' to determine if there was a clinically significant difference or not (S5).

In order to facilitate consistency in generating and drafting the clinical statements the GDG utilised a statement decision tree (see flowchart 1). The flowchart was designed to assist with, but not replace clinical judgement.

Flowchart 1: Guideline Statement Decision Tree



3.4.3.2 Developing graded recommendations

Once all evidence statements relating to a particular clinical question were finalised and agreed by the GDG, the associated recommendations were produced and graded. Recommendations were graded A to C based on the level of associated evidence, or noted as coming from a previous NICE guideline or health technology appraisal (see text box 1).

Text Box 1: Hierarchy of evidence and recommendations grading scheme

Level	Type of evidence	Grade	Evidence
I	Evidence obtained from a single randomised controlled trial or a meta-analysis of randomised controlled trials	**A**	At least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence level-1) without extrapolation
IIa	Evidence obtained from at least one well-designed controlled study without randomisation	**B**	Well-conducted clinical studies but no randomised clinical trials on the topic of recommendation (evidence levels 2 or 3); or extrapolated from level-1 evidence
IIb	Evidence obtained from at least one other well-designed quasi-experimental study		
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies		
IV	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities	**C**	Expert committee reports or opinions and/or clinical experiences of respected authorities (evidence level IV). This grading indicates that directly applicable clinical studies of good quality are absent or not readily available
		GPP	Recommended good practice based on the clinical experience of the GDG
NICE	Evidence from NICE guideline or technology appraisal	**NICE**	Evidence from NICE guideline or Technology Appraisal

Adapted from Eccles, M. & Mason, J. (2001). How to develop cost-conscious guidelines. *Health Technology Assessment* 5: 8; NHS Executive. *Clinical Guidelines: Using Clinical Guidelines to Improve Patient Care Within the NHS*. London: 1996.

Grading allowed the GDG to distinguish between the level of evidence and the strength of the associated recommendation. It is possible that a statement

of evidence would cover only one part of an area in which a recommendation was to be made or would cover it in a way that would conflict with other evidence. In order to produce more comprehensive recommendations suitable for people in England and Wales, there were times when the GDG had to extrapolate from the available evidence based on their combined clinical experience. The resulting recommendations were then graded with a lower grade (e.g., a 'B' grade where data were based upon level I evidence). This allowed the GDG to moderate recommendations based on factors other than the strength of evidence. Such considerations include the applicability of the evidence to the people in question, economic considerations, values of the development group and society, or the group's awareness of practical issues (Eccles et al., 1998).

3.4.4 Method used to answer a clinical question in the absence of appropriately designed, high-quality research

In the absence of level I evidence (or a level that is appropriate to the question), or where the GDG were of the opinion (on the basis of previous searches or their knowledge of the literature) that there were unlikely to be such evidence, an informal consensus process was adopted. This process focused on those questions that the GDG considered a priority.

3.4.4.1 Informal consensus

The starting point for this process of informal consensus was that a member of the topic group identified, with help from the systematic reviewer, a narrative review that most directly addressed the clinical question. Where this was not possible, a brief review of the recent literature was initiated.

This existing narrative review or new review was used as a basis for beginning an iterative process to identify lower levels of evidence relevant to the clinical question and to lead to written statements for the guideline. The process involved a number of steps:

1. A description of what is known about the issues concerning the clinical question was written by one of the topic group members

2. Evidence from the existing review or new review was then presented in narrative form to the GDG and further comments were sought about the evidence and its perceived relevance to the clinical question

3. Based on the feedback from the GDG, additional information was sought and added to the information collected. This may include studies that did not directly address the clinical question but were thought to contain relevant data

4. If, during the course of preparing the report, a significant body of primary-level studies (of appropriate design to answer the question) were identified, a full systematic review was done

5. At this time, subject possibly to further reviews of the evidence, a series of statements that directly addressed the clinical question were developed

6. Following this, on occasions and as deemed appropriate by the development group, the report was then sent to appointed experts outside of the GDG for peer review and comment. The information from this process was then fed back to the GDG for further discussion of the statements

7. Recommendations were then developed and could also be sent for further external peer review

8. After this final stage of comment, the statements and recommendations were again reviewed and agreed upon by the GDG.

3.5 Health economics review strategies

The aim of the health economics review was to contribute to the guideline development process data on the economic burden of depression and evidence of cost-effectiveness of different treatment options for depression were collected and assessed in order to help the decision-making process. See Chapter 9, Health Economics Evidence, for the detailed review strategies.

3.6 Stakeholder contributions

Professionals, patients, and companies have contributed to and commented on the guideline at key stages in its development. Stakeholders for this guideline include:

- Patient/carer stakeholders: the national patient and carer organisations that represent people whose care is described in this guideline

- Professional stakeholders: the national organisations that represent health care professionals who are providing services to patients

- Commercial stakeholders: the companies that manufacture medicines used in the treatment of depression

- Primary Care Trusts

- Department of Health and Welsh Assembly Government.

Stakeholders have been involved in the guideline's development at the following points:

- Commenting on the initial scope of the guideline and attended a briefing meeting held by NICE
- Contributing lists of evidence to the GDG
- Commenting on the first and second drafts of the guideline.

3.7 Validation of this guideline

This guideline has been validated through two consultation exercises. The first consultation draft was submitted to the NICE Guidelines Advisory Committee Panel, and circulated to stakeholders and other reviewers nominated by GDG members.

The GDG reviewed comments from stakeholders, the NICE Guidelines Advisory Committee, a number of health authority and trust representatives and a wide range of national and international experts from the first round of consultation. The GDG then responded to all comments and prepared a final consultation draft which was submitted to NICE, circulated to all stakeholders for final comments and posted on the NICE website for public consultation. The final draft was then submitted to the NICE Guidelines Advisory Committee for review prior to publication.

4 Summary of recommendations

[The NICE guideline recommendations, without supporting text, will be inserted at a later stage.]

5 Service level and other interventions in the treatment and management of depression

5.1 Introduction

The large majority of people with depression are managed in primary care, but many cases are unrecognised (Del Piccolo *et al*, 1998; Raine *et al*, 2000). Where depression is recognised, care often falls short of optimal recommended practice (Donoghue & Tylee, 1996; Katon *et al*, 1992) and outcomes are correspondingly below what is possible (Rost *et al*, 1994). Given these problems of under recognition and sub-optimal treatment along with the considerable cost of care presented by depression in primary and secondary care, a number of responses have developed over the past twenty or so years. These methods have drawn from developments in the treatments of depression in primary and secondary care, the organisational and professional structures of primary and secondary care mental health services and the development and adaptation of models for the management of chronic medical conditions, for example diabetes (Von Korff *et al*, 1997; Von Korff & Goldberg, 2001). The focus of this section is primarily on those responses, which have been developed at a primary care level although some reference will be made to other approaches in secondary care.

The broad range of interventions that have emerged in recent years fall under a number of distinct headings that include:

- The development of staff roles in primary care and the development of new roles
- The introduction of secondary care mental health staff into primary care
- The use of computer based technologies
- The development of patients focused self-help and educational initiatives
- The use of the voluntary sector or informal support structures
- The introduction of interventions outside of those normally provided in mental health.

The framework of stepped care has often been proposed as the method by which these can be integrated. Stepped care seeks to identify the least restrictive and least costly intervention that will be effective for the problems with which an individual presents (Davison, 2000). In establishing a stepped care approach consideration should not only be given to the degree of restrictiveness associated with a treatment and its costs and effectiveness but the likelihood of its uptake by a patient and the likely impact that an unsuccessful intervention will have on the probability of other interventions being taken up.

For many staff based interventions, the focus has been the enhancement of the care provided. For example, improved outcomes have been found where the additional staff facilitate antidepressant uptake and adherence (Katon *et al*, 1995; Simon *et al*, 2000), provide or facilitate referral to psychological therapies (Schulberg *et al*, 1996; Ward *et al*, 2000), or both (Katon *et al*, 1996; Wells *et al*, 2000). More recently, the additional staff member has often taken the role of a care coordinator, liasing with the GP, providing educational materials to the patient, and providing informal support, as well as encouraging the patient to take up and adhere to treatment (Katon *et al*, 1995; Katon *et al*, 1996; Simon *et al*, 2000; Wells *et al*, 2000).

In many of the earlier studies, mental health professionals have provided the enhanced staff input and undertaken the care coordinator role (Katon *et al*, 1995; Katon *et al*, 1996; Unutzer *et al*, 2002). However, more recently, others including primary care nurses (Hunkeler *et al*, 2000; Mann *et al*, 1998; Rost *et al*, 2001) or graduates without a core mental health professional training (Katzelnick *et al*, 2000; Simon *et al*, 2000) have taken this role. Most studies have been from the USA. In the UK, one published study has used practice nurses in the care coordinator role, and this did not improve either patient antidepressant uptake or outcomes compared to usual GP care (Mann *et al*, 1998).

In the UK, there are not sufficient mental health professionals to provide enhanced input and care coordination for all primary care patients with depression. Primary care nurses also have multiple and increasing demands on their time and many are also uninterested in working with patients with psychological problems (Nolan *et al*, 1999), therefore, it is unlikely that practice nurses will take on a significant role in the routine care of patients with depression. A major NHS staffing initiative for primary care mental health is the new graduate primary care mental health workers (Department of Health, 2000; Department of Health, 2003) who may potentially and significantly affect this situation. The advent of these posts may also require further clarification of the role of all professionals working in primary care mental health.

There is an increasing focus in the NHS on the use of information technology to improve patient care, much of this work has centred on the use of such technology to support patient records. However, there has been a small but potentially valuable development in the use of information technology to directly impact on patient care. The most notable example of these is the use of computer technology to deliver direct patient care. This was recently the subject of a NICE Technology Appraisal (NICE 2002), which looked at Computerised CBT for anxiety and depression and made no specific recommendations.

There has been along tradition of self-help in mental services and a considerable publication industry rests on the production of such guidance. Recently the use of such approaches has been subjected to formal evaluation which looks both at the simple use of self-help guides by patients themselves and their use with limited but targeted support from professionals or others working in mental health services. A related area focuses on the provision of educational materials to patients, a tradition which is probably better developed in the area of schizophrenia than depression.

Depression, as seen in the introduction, has a strong social aspect to its development and maintenance and it is therefore not surprising that there have been a number of attempts to examine the role of interventions based on this in depression. Many such interventions though have not been subject to rigorous formal elevation (e.g., Cox et al, 1991) and where they have been on much broader diagnostic groups than the current focus of this guideline.

A novel intervention which has attracted considerable recent interest is the provision of exercise and this is an intervention which has broad application beyond just depression (Donaghy M & Durwood B, 2000)

We focussed on studies that included educational strategies for patients but not studies where the main focus was on educational strategies for primary care professionals. Although there have been several such studies concerning depression within a huge literature in this educational arena, this decision was taken because the guideline scope does not include educational strategies It is still noteworthy that most educational studies have obtained a negative result (e.g. Thompson et al.) in Europe except for the small Gotland study (Rutz et al., 1989) despite the success of studies in North America (e.g. Wells et al., 2000).

Although the large majority of people with depression are treated in primary care settings, a significant number do require the provision of specialist services. Inpatient services are used regularly by depressed patients although little is known about their effectiveness and considerable disquiet with their provision exists. In contrast, day hospitals have an uncertain role in the treatment of depression and may potentially be an underused resource. The

role of crisis teams in the treatment of depression has also been a particular concern for people who present at considerable risk.

The GDG discussed the priorities for review and settled on the following, screening, guided self-help, computerised CBT, exercise, organisational developments in the treatment of depression (and their various components), non-statutory support and key elements of the secondary care services including crisis resolution and home treatment teams, day hospitals and electroconvulsive therapy. In reaching this decision the GDG were assisted by access to the systematic reviews conducted by John Cape and Andrew Brown (unpublished).

5.2 Screening

5.2.1 Introduction

Screening has been advocated as a means of ensuring that depressed patients are identified and receive appropriate treatment. This, in part, stems from the fact that up to 50 percent of depressed patients are not recognised in primary care (Williams at al, 1995). Yet, recommendations for routine screening are frequently made without reference to empirical data demonstrating that it will have its intended effect. As a consequence screening remains controversial and considerable disagreement on it value remains (Gilbody et al 2001, Pignone et al, 2002, Palmer & Coyne, 2003).

The arguments in favor of routine screening for depression among general medical patients seem straightforward and may appear compelling, given the large number of undetected depression and the associated personal and social costs (Palmer & Coyne, 2003). However, relatively little is known of the impact of screening, particularly in primary care, on outcomes for those identified.

Many questionnaires for depression have been developed which have been used as screening instruments, such as the Beck Depression Inventory (BDI; Beck & Steer, 1987), the General Health Questionnaire (Goldberg &William, 1988), and the Zung Depression Scale (Zung, 1965), some of which have been validated for use in primary care. However, in most clinical situations these are not routinely used because they are time-consuming to administer, and may require training in their interpretation. In practice, primary care professionals tend to ask a couple of questions when they see a patient who they suspect may be depressed. There is also empirical support for this approach, with Whooley et al (1995) suggesting that two simple questions may be as effective as a longer questionnaire. Another important issue in the identification of depression is distinguishing current state from more enduring attitudes and feelings. This means effective screening is essentially a two-stage process with the initial brief assessment be followed by a more

detailed assessment of the individual's mental state, and related psychosocial circumstances.

Critics of routine screening have advanced a number of arguments against it. These include the low positive predictive value of the instruments, the lack of empirical evidence for benefit to patients, the expenditure of resources on patients who may gain little benefit (many patients who are detected by such an approach may be mildly depressed and recover with no formal intervention) and the diversion of resource away from more seriously depressed and known patients who may be inadequately treated as a result. These issues are well covered by Palmer and Coyne (2003) in their review of screening for depression. Palmer and Coyne also go on to make a number of suggestions for improving screening including ensuring effective interventions for those identified, focusing on patients with previous histories of depression and people known to have a high risk of developing depression such as those with a family history of depression or significant physical health problems, such as chronic pain.

The ability to interpret the findings of screening studies has been hindered by a number of factors, in addition to the standard issues of poor reporting. These include variation in the definition of screening and its implementation, variation in the population and setting in which the screening took place and very considerable variation in the outcomes reported. For the purpose of this review the definition of screening used in the National Screening Committee (NSC) first report was adopted and then further refined by the GDG; both definitions are set out below.

NSC Definition

The systematic application of a test or inquiry, to identify individuals at sufficient risk of a specific disorder to warrant further investigation or direct preventive action, amongst persons who have not sought medical attention on account of symptoms of that disorder.

5.2.2 Studies and reviews considered

In reviewing the effectiveness of screening the GDG took as its starting point the review by Pignone et al.(2002) supplementing this with further searches for other relevant studies and descriptive reviews, in particular those published subsequent to the studies covered by Pignone at al. A review of the available studies indicated that it would not be possible to perform a quantitative review using primarily meta-analytic techniques and therefore a predominately narrative review was undertaken.

Pignone et al, 2002, which summarises the work of a U.S Preventative Task Force working group on screening for depression, seemed an important starting point as it had recently led to a significant change in policy in the United States healthcare system with the recommendation that routine screening be adopted for the detection of depression. Specifically they recommended "screening adults for depression in clinical practices that have systems in place to assure diagnosis, effective treatment and follow-up". In recommending screening they were careful to emphasise the need for effective support following initial screening. This represented a significant change for the position in 1996, when a previous U. S. Preventive Services Task Force found insufficient evidence to recommend for or against routine screening for depression with standardised questionnaires (U. S. Preventive Services Task Force, 1996).

The Pignone et al (2002) review identified 14 RCTs (which included trials where patients or services were the unit of randomisation) conducted in primary care settings evaluating the effect of routine screening of adult patients for depression. In 8 of the studies reviewed, the only intervention was feedback of screening results to clinicians, the remaining studies combined feedback with other interventions for patients or clinicians. Outcomes varied across the trials including recognition of depression, rates of treatment, and clinical improvement among patients with depression. In 50 per cent of studies screening with feedback of results resulted in an increased recognition of depression, especially major depression but this did not generally result in increased uptake of treatment compared to usual care unless feedback was combined with treatment advice or other system supports. The majority of trials reported significant improvements in the clinical outcomes of depressed patients; in 5 cases this was significant but the period of follow up varied considerably from 1 month to two years.

Screening was most effective where it was combined with an integrated approach to the subsequent management of depression, often involving complex systemic intervenions in primary care (see section 5.6 Organisational Developments).

Pignone et al. (2002) also provide helpful indications of the likely benefits in primary care. For example, 11 patients identified as depressed as a result of screening would need to be treated to produce one additional remission and assumming depression (which includes here not only major depression, but also dysthymia, and minor depression) is present in 10 per cent of primary care patients, then 110 patients would need to be screened to produce one additional remission after 6 to 12 months of treatment.

Gilbody et al (2001) report a less positive picture and after reviewing a similar but not identical group of studies conclude that routine administration and feedback of scores for all patients did not increase the overall rate of

recognition of mental disorders and that this increased recognition, however, did not translate into an increased rate of intervention.

The studies reviewed by Pignone et al. (2002) and Gilbody et al. (2001) were re-assessed and no additional screening studies were identified by further electronic or hand searches. The re-assessment revealed considerable differences in the populations, setting and design of the trials, which led to a number being excluded from consideration by the GDG. The criteria on which trials were excluded were first, population characteristics (specifically those which included significant proportions of non-depressed patients) and secondly those that did not report any usable data on outcomes in relation to depression.

Five studies (CALLAHAN1994, KATZELNICK2000, WELLS2000, WHOOLEY2000, ZUNG1983) met the GDG's inclusion criteria providing data on 5,302 participants. Of these 4 were cluster randomised (CALLAHAN1994, KATZELNICK2000, WELLS2000, WHOOLEY2000) and 1 patient randomised (ZUNG1983) and as result were analysed separately. The primary outcome was not identification of depression but was the number of identified patients with persisting depression.

CALLAHAN1994, KATZELNICK2000 andWELLS2000 involved complex organisational interventions. For example KATZELNICK2000 provided not only screening but patient and professional educational programmes and coordination of treatment programmes by telephone contact. WHOOLEY2000 offered a more limited intervention and ZUNG1983 essentially offered only feedback.

Limited analysis of the data obtained from the studies produced the following results for the cluster-randomised trials.

There is evidence that there is a significant difference between screening and associated interventions and usual care on decreasing the likelihood of persistent depression but the difference is unlikely to be of clinical significance (N=3; n=1862; RR = 0.93; 95% C.I.0.87 to 0.99)

For patient randomised trials, the following statement was produced.

There is some evidence of a clinically significant difference favouring screening and associated interventions over usual care on decreasing the likelihood of persistent depression (N=1; n=49; RR= 0.54; 95% CI, 0.31 to 0.94).

5.2.3 Clinical Summary

Routine screening for depression may be effective in identifying an increased number of cases but there is only limited evidence that screening alone may have any beneficial effect on depressive symptomatology, even when

integrated into an accessible treatment programme in which a range of appropriate interventions is available for the identified patient routine screening. Studies do indicate that two brief focused questions that address mood and interest are likely to be as effective as more elaborate methods and are more compatible with routine use in settings such as primary care (Whooley *et al*, 1997). However, although none of the studies reviewed have directly addressed the question there is considerable concern that particular populations known to be at high risk of developing depression including individuals with chronic physical health problems (e.g., heart disease, cerebrovascular disease, arthritic conditions, chronic pain, cancer), women around the time of child birth, personal of family histories of depression, and chronic drug or alcohol abuse may also benefit from a more targeted approach to screening.

5.2.4 Clinical practice recommendations

5.2.4.1 Screening in primary care and general hospital settings should be undertaken in high-risk groups for example those with significant physical illnesses, other mental health problems such as dementia, recent unemployment, childbirth, bereavement, and other psychosocial stressors, such as past physical or sexual abuse. (C)

5.2.4.2 Potential physical causes of depression and the possibility that it may be caused by medication should be born in mind, and screening should be considered if appropriate. (C)

5.2.4.3 Screening for depression should include the use of at least two questions concerning mood and interest: "During the last month, have you often been bothered by feeling down, depressed or hopeless?" and "During the last month, have you often been bothered by having little interest or pleasure in doing things?". (B)

5.2.5 Future research recommendations

5.2.5.1 Research into the cost effectiveness of routine screening of populations known to be at high risk of depression is needed.

5.3 Guided Self-help

5.3.1 Introduction

Guided self-help is generally accepted as being more than simply giving patients literature to read (this simpler alternative is usually referred to as Pure Self-Help), and often is based on a cognitive or behavioural psychological approach. Contact with professionals is limited and only of a supportive or facilitative nature. It is potentially more cost-effective, and could lead to a wider and more effective use of professional resources.

Most of the literature on guided self-help emanates from the USA. In the USA, there are over 2,000 self-help manuals of different sorts published each year, and it is not within the scope of these guidelines to make specific recommendations of self-help manuals, but the principle and practice of directed guided self-help for motivated patients appears to be one that can easily transpose to the UK.

Guided self-help has obvious limitations such as a requirement of a certain reading ability, and understanding of the language used, for example, 22% of the USA population is functionally illiterate, and 44% will not read a book in any year.

Many patients are not keen on using medication, because of antidepressants intolerance, drug interactions, pregnancy, breast feeding, or personal preference, and many patients are understandably worried about having a formal diagnosis of depression recorded in their medical records, and for those people, guided self-help can be a more accessible and acceptable form of therapy. Carers and family members can also be involved in understanding the nature and course of depression through the material made available..

In a meta-analysis of seven studies of guided self-help in unipolar depression (Cuijpers, 1997), guided self-help was found to be no less effective than individual or group therapy, although the numbers involved in the studies were small. Benefit appears to be sustained at 6 months follow-up. In a review of guided self-help across a number of disorders including depression, commissioned by the Department of Health, Lewis et al. (2003) concluded that there was evidence to recommend guided self-help, provided this was CBT-based and that its use was monitored by a healthcare professional.

There is also some evidence (Munoz, 1994) that guided self-help can have preventative implications, helping to forestall an episode of major depression in individuals with sub-syndromal depression.

Tha majority of guided self-help programmes are in book form and this review is limited to these studies However, a number of computer-based approaches are emerging. For example, Osgood-Hynes (1998) describes a system comprising a computer-aided telephone system and a series of booklets was used successfully by people with mild to moderate depression An interactive voice response system was used, with free phone calls. It was often accessed out-of-hours, and obviously enhances patient flexibility and choice.

5.3.2 Definition

Guided self-help may be defined as a self-administered intervention designed to treat depression, which makes use of a range of books or a self-help manual

that is based on an evidence-based intervention and designed specifically for the purpose. A healthcare professional (or paraprofessional) would facilitate the use of this material by introducing monitoring and reviewing the outcome of such treatment. This intervention would have no other therapeutic goal, and would be limited in nature, usually no more than three contacts.

5.3.3 Studies considered

The review team conducted a new systematic search for RCTs of different types of guided self-help interventions used in the treatment and management of depression. Nine RCTs (BEUTLER1991, BOWMAN1995, BROWN1984, JAMISON1995, LANDREVILLE1997, , SCHMIDT1983, SCOGIN1987, SCOGIN1989, , WOLLERSHEIM1991) were included, providing data on 631 participants. Seven studies (BLENKIRON2001, DONNAN1990, HANNAY1999, HOLDSWORTH1996, KIELY1986, ROBINSON1997, SORBY1991) were excluded.

Data were available to compare guided self-help with delayed guided self-help, individual and group CBT, group guided self-help, telephone contact, individual or group psychotherapy and wait list control. Guided self-help materials used were either based on CBT or behaviour principles.

5.3.4 Clinical evidence statements

1.1.1.2 Guided self-help versus wait list control

Effect of treatment on remission

There is strong evidence suggesting that there is a clinically significant difference favouring guided self-help over wait list control on increasing the likelihood of patients achieving remission (defined as BDI<=11) at the end of treatment (N= 2; n= 96; RR= 0.60; 95% C.I., 0.44 to 0.80).

Effect of treatment on symptom levels

There is strong evidence suggesting that there is a clinically significant difference favouring guided self-help over wait list control on reducing depression symptoms by the end of treatment as measured by the BDI (N= 7; n= 194; WMD= -7.70; 95% C.I., -9.84 to –5.56)..

There is strong evidence suggesting that there is a clinically significant difference favouring guided self-help over wait list control on reducing depression symptoms by the end of treatment as measured by the HRSD (N= 4; n= 151; WMD= -8.91; 95% C.I., -10.62 to -7.20).

Effect of treatment on acceptability

There is insufficient evidence to determine if there is a clinically significant difference between guided self-help and wait list control on reducing the likelihood of patients leaving the study early (N = 5; n = 189; RR = 2.01; 95% C.I., 0.80 to 5.03).

1.1.1.3 Guided self-help versus group CBT

Effect of treatment on remission

There is insufficient evidence to determine if there is a clinically significant difference between guided self-help and group CBT on increasing the likelihood of achieving remission(defined as BDI <= 11) by the end of treatment. (N= 1; *n*= 16; RR= 0.80; 95% C.I., 0.33 to 1.92).

Effect of treatment on symptom levels

There is insufficient evidence to determine if there is a clinically significant difference between guided self-help and group CBT on reducing depressions symptoms by the end of treatment as measured by the BDI (N = 2; n = 57; WMD = 3.24; 95% C.I., -3.14 to 9.62).

There is insufficient evidence to determine if there is a clinically significant difference between guided self-help and group CBT on reducing depressions symptoms by the end of treatment as measured by the HRSD (N = 1; n = 41; WMD = -1.02; 95% C.I., -4.83 to 2.79).

There is insufficient evidence to determine if there is a clinically significant difference between guided self-help and group CBT on reducing depressions symptoms as measured by the BDI at 3-months follow-up (N = 1; n = 41; WMD = 0.03; 95% C.I., -6.8 to 6.86) or at 6-months follow-up (N = 1; n = 11; WMD = 0.07; 95% C.I., -12.64 to 12.78).

There is insufficient evidence to determine if there is a clinically significant difference between guided self-help and group CBT on reducing depressions symptoms at 3-month follow-up as measured by the HRSD (N = 1; n = 41; WMD = -0.59; 95% C.I., -4.01 to 2.83).

1.1.1.4 Individual guided self-help versus group guided self-help versus telephone contact

Effect of treatment on remission

There is insufficient evidence to determine if there is a clinically significant difference between individual guided self-help and group guided self-help on increasing the likelihood of achieving remission as measured by the Schedule for Affective Disorders and Schizophrenia - Change at 6 months post-treatment (N = 1; n = 38; RR = 0.96; 95% C.I., 0.36 to 2.6).

There is insufficient evidence to determine if there is a clinically significant difference between individual guided self-help and telephone contact on increasing the likelihood of achieving remission as measured by the Schedule for Affective Disorders and Schizophrenia - Change at 6 months post-treatment (N = 1; n = 39; RR = 4.48; 95% C.I., 0.62 to 32.23).

Effect of treatment on symptom levels

There is insufficient evidence to determine if there is a clinically significant difference between individual guided self-help and group guided self-help on reducing depressions symptoms by the end of treatment as measured by the BDI (N = 1; n = 38; WMD = -0.40; 95% C.I., -7.84 to 7.04).

There is some evidence suggesting that there is a clinically significant difference favouring group guided self-help over individual guided self-help on reducing depressions symptoms at one month follow-up as measured by the BDI (N = 1; n = 38; WMD = 5.84; 95% C.I., 0.3 to 11.38).

There is insufficient evidence to determine if there is a clinically significant difference between individual guided self-help and group guided self-help on reducing depressions symptoms at six months follow-up as measured by the BDI (N = 1; n = 38; WMD = 2.34; 95% C.I., -2.47 to 7.15)

There is insufficient evidence to determine if there is a clinically significant difference between individual guided self-help and telephone contact on reducing depressions symptoms as measured by the BDI:

- by the end of treatment (N = 1; n = 27; WMD = 2.01; 95% C.I., -6.03 to 10.05)
- at one month follow-up (N = 1; n = 27; WMD = 3.1; 95% C.I., -3.77 to 9.97)
- at six months follow-up (N = 1; n = 27; WMD = -0.33; 95% C.I., -5.2 to 4.54).

There is insufficient evidence to determine if there is a clinically significant difference between group guided self-help and telephone contact on reducing depressions symptoms as measured by the BDI:

- by the end of treatment (N = 1; n = 39; WMD = 2.41; 95% C.I., -5.05 to 9.87)
- at one month follow-up (N = 1; n = 39; WMD = -2.74; 95% C.I., -7.82 to 2.34)
- at six months follow-up (N = 1; n = 39; WMD = -2.67; 95% C.I., -6.34 to 1).

1.1.1.5 Guided self-help versus individual or group psychotherapies

Effect of treatment on symptom levels

There is insufficient evidence to determine if there is a clinically significant difference between guided self-help and individual psychological therapies

on reducing depression symptoms by the end of treatment as measured by the BDI (N =2; n = 44; WMD = 1.45; 95% C.I., -2.69 to 5.60) or at 10-month follow-up (N = 2; n = 39; WMD = -1.02; 95% C.I., -5.07 to 3.03).

There is insufficient evidence to determine if there is a clinically significant difference between guided self-help and group psychotherapy on reducing depressions symptoms by the end of treatment as measured by the BDI (N = 3[3]; n = 81; WMD = 0.92; 95% C.I., -3.40 to 5.24) or at follow-up (N = 2; n = 63; WMD = 0.64; 95% C.I., -3.86 to 5.13).
There is some evidence suggesting that there is a clinically significant difference favouring guided self-help over large group psychotherapy on reducing depressions symptoms by the end of treatment as measured by the BDI (N = 1; n = 23; WMD = -7.5; 95% C.I., -12.92 to -2.08).

There is insufficient evidence to determine if there is a clinically significant difference between guided self-help and large group psychotherapy on reducing depressions symptoms at 10 months follow-up as measured by the BDI (N = 1; n = 21; WMD = -4.10; 95% C.I., -10.56 to 2.36).

Effect of treatment on acceptability

There is insufficient evidence to determine if there is a clinically significant difference between guided self-help and individual psychological therapies on reducing the likelihood of patients leaving treatment early (N = 2; n = 44; RR = 1.50; 95% C.I., 0.28 to 8.09).

There is insufficient evidence to determine if there is a clinically significant difference between guided self-help and large group psychotherapy on reducing the likelihood of patients leaving treatment early (N = 1; n = 23; RR = 2.77; 95% C.I., 0.12 to 61.66).

5.3.5 Clinical summary

Guided self-help produces a clinically significant reduction in depressive symptoms when compared to no intervention and, in patients with mild to moderate depression, may be as effective as some forms of individual therapy and more effective than group psychotherapy on reducing depression symptoms, although there is insufficient evidence that this benefit is retained at follow-up. There is insufficient evidence of its efficacy and acceptability to patients compared with other treatments. It potentially provides a cost-effective and acceptable intervention with potential for widespread use in the treatment of mild to moderate depression, in particular as part of a stepped care programme.

[3] Data from the small group therapy arm of SCHMIDT1983 was used since using the large group therapy arm introduced heterogeneity to the data set. This did not effect the overall result.

5.3.6 Clinical practice recommendations

5.3.6.1 For patients with mild depression healthcare professionals should consider recommending a CBT-based guided self-help programme. (B)

5.3.6.2 An adequate programme of guided self-help should consist of the provision of appropriate written materials and limited support from a healthcare professional who typically introduces the self-help programme and reviews progress and outcome. Such an intervention usually takes place over 6 to 8 weeks. (B)

5.3.6.3 All individuals in receipt of guided self-help should be offered a follow-up appointment/contact with an appropriate member of the care team to monitor the impact of the intervention. (C)

5.3.7 Research recommendations

5.3.7.1 Efficacy studies of the role of guided self-help in a stepped care programme are required. The focus of such studies should be on both the role of GSH in early intervention and maintenance.

5.4 Computerised Cognitive Behavioural Therapy

5.4.1 Introduction

Whilst many patients generally prefer psychological therapies over other interventions for depression (Angermeyer & Matschinger, 1996; Tylee, 2001) and the National Service Framework for Mental Health (Department of Health, 1999) has called for increased availability of such treatments for common mental health problems such treatments are often not available. This limited access arises from the shortage of trained therapists, expense, waiting lists, (Goldberg & Gournay, 1997) and some patients may also be reluctant to enter therapy. A number of authors have called for alternative methods for delivering psychological therapies (Lovell & Richards, 2000).

In addition to the self-help methods discussed elsewhere in this chapter, the use of information technology to deliver psychological treatments has also been explored, for example self-help delivered by phone (Osgood-Hynes et al., 1998) over the internet (Mental gym) or by computer (Selmi et al., 1990). Cognitive behavioural therapy (CBT) may lend itself readily to computerisation and to date CBT is the main psychological treatment approach which has been developed in this manner. Previous studies have shown that patients find computer-based treatment acceptable and they manifest degrees of clinical recovery similar to those after face-to-face therapy (Selmi et al. 1990). However, these studies were carried out with relatively

small samples and the majority of programs consisted largely of text, multiple choice questions and cartoons, without the advantage provided by the full multimedia interactive capability of contemporary computers to address important non-specific aspects of therapy.

The technology more recently available has led to the development of a number of more sophisticated and interactive computer-based or internet-based CBT programmes, for example, *Beating the Blues* (Gray et al., 2000) and *Fear Fighter* (Marks et al., 2002). These have recently been the subject of a rigorous evaluation by NICE (NICE 2002). Essentially these programmes engage the patient in a structured programme of care, which replicates the care provided by a therapist following a standard CBT programme. They require little direct staff input, which is often limited to the introduction to the programme, brief monitoring and being available for consultation. It has been suggested that this can be done by paraprofessional or administrative staff. Most of these technologies have been developed to treat a range of depressive and anxiety disorders, often explicitly as part of a stepped care programme. Since the completion of the NICE HTA further work, particularly in the area of depression and CCBT has emerged and so a separate review from the NICE HTA focusing only on depression was conducted. In view of the fact that most programmes so far developed and that the NICE HTA focused solely on computerised cognitive behavioural therapy (CCBT), this was taken as the sole focus for this review.

5.4.2 Definition

Computerised cognitive behaviour therapy (CCBT) is a form of CBT, which is delivered using a computer (including CD-ROM and the internet). It can be used as the primary treatment intervention, with minimal therapist involvement or as augmentation to a therapist delivered programme where the introduction of CCBT supplements the work of the therapist.

5.4.3 Studies considered

The review team conducted a new systematic search for RCTs evaluating the use of CCBT in the treatment and management of depression. Four RCTs (BOWERS1993, PROUDFOOT2003, PROUDFOOT2003A, SELMI1990) were included, providing data on 499 participants. One study was excluded (WRIGHT2002).

Data were available to compare CCBT with CBT and treatment as usual.

5.4.4 Clinical evidence statements

1.1.1.6 Computerised cognitive behavioural therapy versus treatment as usual

Effect of treatment on remission

There is insufficient evidence to determine if there is a clinically significant difference between CCBT and treatment as usual on increasing the likelihood of achieving remission by the end of treatment as measured by a BDI score of less than or equal to 8 and a HRSD score of less than or equal to 7 (N = 1; n = 14; RR = 1.14; 95% C.I., 0.88 to 1.49).

Effect of treatment on symptom levels

There is strong evidence suggesting that there is a clinically significant difference favouring CCBT over treatment as usual on reducing depression symptoms by the end of treatment as measured by BDI (N = 2; n = 273; WMD = -5.95; 95% C.I., -8.50 to -3.40)[4].

There is some evidence suggesting that there is a clinically significant difference favouring CCBT over treatment as usual on reducing depression symptoms at 1 month follow-up as measured by BDI (N = 2; n = 244; WMD = -3.74; 95% C.I., -6.62 to -0.86).

There is some evidence suggesting that there is a clinically significant difference favouring CCBT over treatment as usual on reducing depression symptoms at 3 months follow-up as measured by BDI (N = 1; n = 147; WMD = -3.47; 95% C.I., -6.55 to -0.39).

There is some evidence suggesting that there is a clinically significant difference favouring CCBT over treatment as usual on reducing depression symptoms at 6 months follow-up as measured by BDI (N = 1; n = 166; WMD = -5.1; 95% C.I., -8.22 to -1.98).

Effect of treatment on acceptability

There is some evidence suggesting that there is a clinically significant difference favouring treatment as usual over CCBT with fewer patients receiving treatment as usual leaving the study early for any reason (N = 3; n = 455; RR = 1.38; 95% C.I., 1.07 to 1.77).

1.1.1.7 Computerised cognitive behavioural therapy versus traditional cognitive behavioural therapy

Effect of treatment on remission

There is insufficient evidence to determine if there is a clinically significant difference between CCBT and treatment as usual on increasing the likelihood of achieving remission by the end of treatment as defined by the study (N = 2; n = 38; RR = 1.23; 95% C.I., 0.74 to 2.05).

There is insufficient evidence to determine if there is a clinically significant difference between CCBT and treatment as usual on increasing the likelihood

[4] BOWERS1993 was removed from the analysis due to heterogeneity.

of achieving remission at 2-months follow-up as defined by the study (N = 1; n = 24; RR = 1.33; 95% C.I., 0.38 to 4.72).

Effect of treatment on symptom levels

There is insufficient evidence to determine if there is a clinically significant difference between CCBT and traditional CBT on reducing depression symptoms by the end of treatment as measured by BDI (N = 2; n = 38; WMD = 3.48; 95% C.I., -0.29 to 7.26).

There is insufficient evidence to determine if there is a clinically significant difference between CCBT and traditional CBT on reducing depression symptoms at 2-months follow-up as measured by BDI (N = 1; n = 24; WMD = -2.1; 95% C.I., -8.01 to 3.81).

There is insufficient evidence to determine if there is a clinically significant difference between CCBT and traditional CBT on reducing depression symptoms by the end of treatment as measured by HRSD (N = 2; n = 38; WMD = 1.64; 95% C.I., -0.68 to 3.96).

There is insufficient evidence to determine if there is a clinically significant difference between CCBT and traditional CBT on reducing depression symptoms at 2-months follow-up as measured by HRSD (N = 1; n = 24; WMD = 0.38; 95% C.I., -1.61 to 2.37).

5.4.5 Computerised cognitive behavioural therapy versus wait-list control

Effect of treatment on remission

There is insufficient evidence to determine if there is a clinically significant difference between CCBT and waiting-list controls on increasing the likelihood of achieving remission by the end of treatment as defined by the study (N = 1; n = 24; RR = 0.60; 95% C.I., 0.32 to 1.12).

There is some evidence suggesting that there is a clinically significant difference favouring CCBT over waiting-list controls on increasing the likelihood of achieving remission at 2-months follow-up as measured by a BDI score of less than or equal to 9 (N = 1; n = 24; RR = 0.36; 95% C.I., 0.16 to 0.82).

Effect of treatment on symptom levels

There is some evidence suggesting that there is a clinically significant difference favouring CCBT over waiting-list controls on reducing depression symptoms by the end of treatment as measured by BDI (N = 1; n = 24; WMD = -8.17; 95% C.I., -14.2 to -2.14).

There is some evidence suggesting that there is a clinically significant difference favouring CCBT over waiting-list controls on reducing depression

symptoms at 2-months follow-up as measured by BDI (N = 1; n = 24; WMD = -14.5; 95% C.I., -20.92 to -8.08).

There is some evidence suggesting that there is a clinically significant difference favouring CCBT over waiting-list controls on reducing depression symptoms by the end of treatment as measured by HRSD (N = 1; n = 24; WMD = -8; 95% C.I., -11.06 to -4.94).

There is some evidence suggesting that there is a clinically significant difference favouring CCBT over waiting-list controls on reducing depression symptoms at 2-months follow-up as measured by HRSD (N = 1; n = 24; WMD = -9.58; 95% C.I., -13.62 to -5.54).

5.4.6 Clinical summary

Computerised cognitive behavioural therapy (CCBT) can have a positive impact on depressive symptoms compared to treatment as usual and there is also evidence from a few small studies of similar benefits when compared with wait list controls but no evidence of superiority or inferiority compared to standard CBT in two small studies. The more recent, larger studies, which focus primarily on depression or mixed anxiety and depression, show some encouraging results. CCBT may therefore have value with mild and moderate depression as part of a stepped care programme. Its potential as an augmenter of therapist delivered treatment is unknown. Other developments such as internet delivered treatments may further increase the accessibility of such treatments and further reduce the costs.

5.4.7 Clinical practice recommendation

5.4.7.1 Computerised cognitive behavioural therapy programmes may have specific benefits for patients with mild and moderate depression and should be considered as part of a stepped care framework for the treatment of depression. (C)

5.5 Exercise

5.5.1 Introduction

The effect of exercise on mental health has been the subject of research for several decades. There is a growing body of literature primarily from North America examining the effects of exercise in the management of depression. In the past decade "exercise on prescription" schemes have become popular in primary care in the United Kingdom (Biddle et al., 1994), many of which include depression as a referral criterion. Guidelines for exercise referral schemes have been laid down by the Department of Health (2002).

Several plausible mechanisms for how exercise affects depression have been proposed. In the developed world, taking regular exercise is seen as a virtue;

the depressed patient who takes regular exercise may, as a result, get positive feedback from other people and an increased sense of self worth. Exercise may act as a diversion from negative thoughts, and the mastery of a new skill may be important (Lepore, 1997; Mynors-Wallis et al., 2000). Social contact may be an important mechanism, and physical activity may have physiological effects such as changes in endorphin and monoamine concentrations (Leith, 1994; Thornen et al., 1990).

This research has raised some interesting points in terms of the type of exercise, frequency, intensity and duration of exercise programmes impact of "dose" response of exercise a means of managing depression.

5.5.2 Definition

For the purposes of the guideline, exercise was defined as a structured, achievable physical activity characterised by frequency, intensity and duration and used as a treatment for depression. It can be undertaken individually or in a group.

Exercise may be divided into aerobic forms (training of cardio-respiratory capacity) and anaerobic forms (training of muscular strength/endurance and flexibility/ co-ordination/ relaxation) (American College of Sports Medicine, 1980).

The aerobic forms of exercise, especially jogging or running, have been most frequently investigated. In addition to the type of exercise, the frequency, duration and intensity should be described.

5.5.3 Studies considered

The review team conducted a new systematic search for RCTs of different types of exercise interventions used in the treatment and management of depression. Nine RCTs (BOSSCHER1993, FREMONT1987, GREIST1979, HERMAN2002, KLEIN1985, MCCANN1984, MCNEIL1991, SINGH1997, VEALE1992) were included, providing data on 523 participants. Six studies (BLAIR1998, DOYNE1987, KRITZ-SILVERSTEIN2001, LABBE1988, MARTINSEN1989, MARTINSEN1993) were excluded.

Data were available to compare exercise (general, mixed and running therapy) with no exercise, antidepressants, cognitive therapy, group psychotherapy, social contact, meditation and time-limited psychotherapy.

5.5.4 Clinical evidence statements

1.1.1.8 Exercise versus no exercise

Effect of treatment on remission

There is some evidence suggesting that there is a clinically significant difference favouring exercise over no exercise on increasing the likelihood of achieving remission by the end of treatment as measured by DSM-IV criteria for depression or dysthymia (N = 1; n = 32; RR = 0.29; 95% C.I., 0.10 to 0.89).

There is insufficient evidence to determine if there is a clinically significant difference favouring exercise over no exercise on achieving remission at 20 weeks follow up as measured by BDI<9 (N = 1; n = 32; RR = 0.53; 95% C.I., 0.25 to 1.11).

Effect of treatment on symptom levels

There is strong evidence suggesting that there is a clinically significant difference favouring exercise over no exercise on depression symptoms as measured by the Beck Depression Inventory by the end of treatment (N = 4; n = 146; SMD = -0.84; 95% C.I., -1.18 to -0.49).

There is insufficient evidence to determine if there is a clinically significant difference between exercise and no exercise on BDI scores at 26 weeks follow-up (N = 1; n = 29; SMD = -0.62; 95% C.I., -1.37 to 0.13).

There is some evidence suggesting that there is a clinically significant difference favouring exercise over no exercise on depression symptoms as measured by the HDRS by the end of treatment (N = 1; n = 32; WMD = -3.6; 95% C.I., -4.50 to -2.70).

Response to treatment

There is some evidence suggesting that there is a clinically significant difference favouring exercise over no exercise on achieving a 50% reduction in depression symptoms by the end of treatment as measured by the Hamilton Depression Rating Scale (N = 1; n = 32; RR = 0.51; 95% C.I., 0.28 to 0.96).

Effect of treatment on acceptability

There is insufficient evidence to determine if there is a clinically significant difference between exercise and no exercise on patients leaving the study early for any reason (N = 2; n = 115; RR = 1.24; 95% C.I., 0.56 to 2.79).

1.1.1.9 Running therapy versus time-limited psychotherapy

Effect of treatment on acceptability

There is insufficient evidence to determine if there is a clinically significant difference between running therapy and time-limited psychotherapy on reducing the likelihood of patients leaving treatment early (N = 1; n = 16; RR = 1.2; 95% C.I., 0.14 to 10.58).

1.1.1.10 Running therapy versus mixed exercise

Effect of treatment on symptom levels

There is some evidence suggesting there is a clinically significant difference favouring running therapy over mixed exercise on the Self-rating depression scale at the end of treatment (N = 1; n = 18; WMD = -11.9; 95% C.I., -20.48 to -3.32).

There is some evidence suggesting there is a clinically significant difference favouring running therapy over mixed exercise on the Hopkins Symptom Checklist at the end of treatment (N = 1; n = 18; WMD = -32.7; 95% C.I., -57.89 to -7.51).

Effect of treatment on acceptability

There is insufficient evidence to determine if there is a clinically significant difference between running therapy and mixed exercise on reducing the likelihood of patients leaving treatment early (N = 1; n = 24; RR = 1.00; 95% C.I., 0.25 to 4.00).

1.1.1.11 Exercise versus cognitive therapy

Effect of treatment on symptom levels

There is insufficient evidence to determine if there is a clinically significant difference between exercise and cognitive therapy in individuals experiencing problems with negative moods on reducing depressions symptoms (BDI) by the end of treatment (N = 1; n = 31; WMD = -1.90; 95% C.I., -6.72 to 2.92) or at 2 month follow-up (N = 1; n = 31; WMD = -0.60; 95% C.I., -5.40 to 4.20) or at 4 month follow-up (N = 1; n = 26; WMD = -3.10; 95% C.I., -8.79 to 2.59).

Effect of treatment on acceptability

There is insufficient evidence to determine if there is a clinically significant difference between exercise and cognitive therapy in individuals experiencing problems with negative moods on leaving the study early (N = 1; n = 40; RR = 1.81; 95% C.I., 0.52 to 6.25).

1.1.1.12 Exercise versus social contact

Effect of treatment on symptom levels

There is insufficient evidence to determine if there is a clinically significant difference between exercise and social contact in community-dwelling depressed older individuals on reducing depressions symptoms by the end of treatment as measured by the Beck Depression Inventory (N = 1; n = 20; WMD = -0.70; 95% C.I., -3.80 to 2.40).

1.1.1.13 Exercise versus meditation

Effect of treatment on symptom levels

There is insufficient evidence to determine if there is a clinically significant difference between running and meditation on reducing depressions

symptoms by the end of treatment as measured by the Depression Symptom Checklist (N = 1; n = 22; WMD = 0.20; 95% C.I., -0.41 to 0.81).

There is insufficient evidence to determine if there is a clinically significant difference between running and meditation on reducing depressions symptoms at 9 months follow-up as measured by the Depression Symptom Checklist (N = 1; n = 16; WMD = 0.04; 95% C.I., -0.72 to 0.80).

Effect of treatment on acceptability

There is insufficient evidence to determine if there is a clinically significant difference between running and meditation on leaving the study early (N = 1; n = 50; RR = 0.85; 95% C.I., 0.48 to 1.51).

1.1.1.14 Exercise versus group psychotherapy

Effect of treatment on symptom levels

There is insufficient evidence to determine if there is a clinically significant difference between running and group psychotherapy on reducing depressions symptoms by the end of treatment as measured by the Depression Symptom Checklist (N = 1; n = 28; WMD = -0.20; 95% C.I., -0.86 to 0.46).

There is insufficient evidence to determine if there is a clinically significant difference between running and group psychotherapy on reducing depressions symptoms at 9 months follow-up as measured by the Depression Symptom Checklist (N = 1; n = 18; WMD = -0.45; 95% C.I., -1.13 to 0.23).

Effect of treatment on acceptability

There is insufficient evidence to determine if there is a clinically significant difference between running and group psychotherapy on leaving the study early (N = 1; n = 51; RR = 1.33; 95% C.I., 0.66 to 2.70).

1.1.1.15 Exercise versus antidepressant drugs

Effect of treatment on remission

There is insufficient evidence to determine if there is a clinically significant difference between exercise and antidepressants on increasing the likelihood of achieving remission by the end of treatment as measured by DSM-IV criteria for depression and a score of less than 6 on the Hamilton Depression Rating Scale (N = 1; n = 101; RR = 1.21; 95% C.I., 0.80 to 1.82).

Effect of treatment on symptom levels

There is insufficient evidence to determine if there is a clinically significant difference between exercise and antidepressants on reducing depression symptoms by the end of treatment as measured by the Beck Depression Inventory (N = 1; n = 101; WMD = 1.06; 95% C.I., -1.55 to 3.67).

There is insufficient evidence to determine if there is a clinically significant difference between exercise and antidepressants on reducing depressions symptoms by the end of treatment as measured by the Hamilton Depression Rating Scale (N = 1; n = 101; WMD = 0.40; 95% C.I., -1.82 to 2.62).

Effect of treatment on acceptability

There is insufficient evidence to determine if there is a clinically significant difference between exercise and antidepressants on leaving the study early (N = 1; n = 101; RR = 1.81; 95% C.I., 0.80 to 4.11).

1.1.1.16 Exercise versus exercise plus antidepressant drugs

Effect of treatment on remission

There is insufficient evidence to determine if there is a clinically significant difference between exercise and exercise + antidepressants on increasing the likelihood of achieving remission by the end of treatment as measured by DSM-IV criteria for depression and a score of less than 6 on the Hamilton Depression Rating Scale (N = 1; n = 108; RR = 1; 95% C.I., 0.70 to 1.43).

Effect of treatment on symptom levels

There is insufficient evidence to determine if there is a clinically significant difference between exercise and exercise + antidepressants on reducing depressions symptoms by the end of treatment as measured by the Beck Depression Inventory (N = 1; n = 108; WMD = -1.4; 95% C.I., -3.98 to 1.18).

There is insufficient evidence to determine if there is a clinically significant difference between exercise and exercise + antidepressants on reducing depressions symptoms by the end of treatment as measured by the Hamilton Depression Rating Scale (N = 1; n = 108; WMD = -1.15; 95% C.I., -3.44 to 1.14).

Effect of treatment on acceptability

There is insufficient evidence to determine if there is a clinically significant difference between exercise and exercise + antidepressants on leaving the study early (N = 1; n = 108; RR = 1.32; 95% C.I., 0.66 to 2.64).

1.1.1.17 Exercise plus antidepressant drugs versus antidepressant drugs alone

Effect of treatment on remission

There is insufficient evidence to determine if there is a clinically significant difference between exercise and exercise + antidepressants on increasing the likelihood of achieving remission by the end of treatment as measured by DSM-IV criteria for depression and a score of less than 6 on the Hamilton Depression Rating Scale (N = 1; n = 103; RR = 1.21; 95% C.I., 0.80 to 1.81).

Effect of treatment on symptom levels

There is insufficient evidence to determine if there is a clinically significant difference between exercise + antidepressants and antidepressants on reducing depressions symptoms by the end of treatment as measured by the Beck Depression Inventory (N = 1; n = 103; WMD = 2.40; 95% C.I., -0.09 to 4.89).

There is insufficient evidence to determine if there is a clinically significant difference between exercise + antidepressants and antidepressants on reducing depressions symptoms by the end of treatment as measured by the Hamilton Depression Rating Scale (N = 1; n = 103; WMD = 1.60; 95% C.I., -0.48 to 3.68).

Effect of treatment on acceptability

There is insufficient evidence to determine if there is a clinically significant difference between exercise + antidepressants and antidepressants on leaving the study early (N = 1; n = 103; RR = 1.37; 95% C.I., 0.58 to 3.26).

Effect of treatment on tolerability

There is insufficient evidence to determine if there is a clinically significant difference between exercise + antidepressants and antidepressants on leaving the study early due to side-effects (N = 1; n = 103; RR = 0.87; 95% C.I., 0.27 to 2.83).

5.5.5 Clinical summary

For patients with depression, in particular those with mild or moderate depressive disorder, structured and supervised exercise can be an effective intervention that has a clinically significant impact on depressive symptoms. There is also evidence to suggest that individuals with low mood may also benefit from structured and supervised exercise. There is no evidence to indicate any differential advantage to the type of exercise. Generally, exercise programmes are of relatively high frequency (up to 3 times a week) and of moderate duration (45 min–1 hr) and are typically provided for 10 – 12 weeks. Older individuals and those suffering from physical health problems may also to benefit from such programmes. There is no evidence on the long term benefits of such exercise in preventing relapse, nor is there any evidence on the provision of 'maintenance' exercise programmes.

5.5.6 Clinical practice recommendations

5.5.6.1 Patients of all ages with mild depression should be advised of the benefits of following a structured and supervised exercise programme of, typically up to 3 sessions per week of moderate duration (45 minutes to 1 hour) for between 10 and 12 weeks. (C)

5.5.7 Future research recommendations

5.5.7.1 Efficacy trials of the long-term effectiveness of exercise in improving outcomes in depression, including maintenance interventions and intensity of exercise should be undertaken.

5.6 Organisational developments in the treatment of depression

5.6.1 Introduction

Over the past 15 years, there has been a growing interest in the development, primarily from North America, looking at systems of care for managing depression. This work has been influenced by organisational developments in health care in the United States, such as managed care and Health Maintenance Organisations, (Katon et al) developments in the treatment of depression, the development of stepped care (Davison, 2000) and influences from physical health care, for example, chronic disease management. A significant factor in driving these developments has been the recognition that for many people depression is a chronic and disabling disorder.

A similar process in now taking place in the UK, fuelled in part by the advent of Primary Care Organisations in the NHS A key challenge in reviewing this literature is the translation of findings from non-UK setting in the NHS in England and Wales.

Other international developments, for example the development of Crisis Intervention Teams have also been lead by non-UK base services (for example, in the United States (Stein & Test, 1980) and Australia (Hoult et al, 1983), although their place in the UK health care system is more well developed (see the role of crisis services in the National Service Framework, Department of Health, 1999) that managed care systems for the treatment of depression.

5.6.2 Definitions

There are many terms used to describe the interventions covered in this section and they are often used inter-changeably in this area. For the purposes of the guideline, we identified a series of interventions, which we consider to be of most relevance to the NHS. They included telephone support, guideline implementation, development in the roles of mental health specialists and primary care staff, and multifaceted care (where a number of different models are delivered concurrently).

These approaches may or may not be provided within the context of a fixed budget (e.g., the Health Maintenance Organisation (HMO) in the USA). Primary Care Trusts are required to develop protocols for the treatment of

depression in primary care within the National Service Framework for Mental Health.

Other terms subsumed within the definition are: collaborative care, stepped care, enhanced care and integrated care.

5.6.3 Interventions included

The following interventions were considered:

- Organisational developments - this is used as an 'umbrella' term to cover all interventions considered in this section.

- Multifaceted care – this was defined as any systematic approach to the treatment of depression which combined any standard treatment approach with any of the following approaches to the management of depression (telephone contact, specialist assessment or consultation, professional or paraprofessional role development and guideline implementation)

- Telephone support (protocol and non-protocol driven) – this was defined an augmentation of a therapeutic intervention designed to improve the effectiveness of the intervention; it usually consisted of a limited number of telephone contacts which had a facilitative and monitoring function

- Guideline implementation – this was defined as any intervention designed to support the implementation of guideline recommendations

- Nurse-led care (either primary care or specialist nurses) – this was defined as any intervention which placed a specific role or responsibility on a nurse (either a practice or specialist nurse) for the implementation of whole or part of a intervention

Psychoeducation was considered for inclusion in this section, but the searches revealed no separate and appropriate trials in this area specifically for depression.

5.6.4 Studies considered

The review team conducted a new systematic search for RCTs of different types of managed care interventions used in the treatment and management of depression. Twenty-one RCTS were considered, with 15 meeting the inclusion criteria set by the GDG (ARAYA2003, BAKER2001, BLANCHARD1995, HUNKELER2000, KATON1995, KATON1996, KATON1999, KATON2001, KATZELNICK2000, MANN1998STUDY2, ROLLMAN2002, ROST2002, SIMON2000, UNUTZER2002, WELLS2000). Five of these were cluster randomised (BAKER2001, KATZELNICK2000, ROLLMAN2002, ROST2002, WELLS2002) so were not included in the main

analyses. However, BAKER2001 and ROLLMAN2002 were included in the analysis of guideline implementation since they were the only studies in this comparison (see below). Overall there were data from 5163 participants (4234 in 'organisational developments' plus 929 in 'guideline approach'). Four studies were excluded (ARTHUR2002, COLEMAN1999, LLEWELYN-JONES1999, PEVELER1999).

Apart from ARAYA2003 which was undertaken in Chile with low-income women, and BAKER2001, BLANCHARD2001 and MANN1998 (study 1 and study2) which were UK-based, all studies were carried out in the US. Since all interventions were compared with usual care, it should be noted that the usual care received by those in the ARAYA2003 study was of poorer quality than that in studies based in more developed countries because of deficiencies in primary health care.

All participants in BLANCHARD1995 and UNUTZER2002 were older adults (aged at least 60). At least 65% of those in UNUTZER2002 are described as having significant chronic pain, and 35% had cognitive impairment.

Apart from those, which were cluster randomised, all studies were included in more than one comparison as follows:

Organisational development: ARAYA2003, BLANCHARD1995, HUNKELER2000, KATON1995, KATON1996, KATON1999, KATON2001, MANN1998 STUDY2, SIMON2000, UNUTZER2002.

Multi-faceted care: ARAYA 2003, HUNKELER2000, KATON1995, KATON1996, KATON1999, KATON2001, SIMON2000, UNUTZER2002.

Nurse-led care: (primary-care nurse) HUNKELER2000, MANN1998 STUDY2; (specialist nurse) BLANCHARD1995

Guideline approach: BAKER2001, ROLLMAN2002

Telephone support: (protocol-driven telephone support) KATON2001, KATZELNICK2000, SIMON2000; (non-protocol driven telephone support) HUNKELER2000)

Comparisons are all with usual care.

5.6.5 Clinical evidence statements

1.1.1.18 Organisational developments **versus usual care**

Effect of treatment on remission

There is evidence suggesting that there is a statistically significant difference favouring organisational developments over usual care on increasing the likelihood of patients achieving remission (as defined by the study) 3 or 4 months after the start of treatment but the size of this difference is unlikely to be of clinical significance (N = 5[5]; n = 2925; RR = 0.88; 95% CI, 0.84 to 0.91).

There is some evidence suggesting that there is a clinically significant difference favouring organisational developments over usual care on increasing the likelihood of patients achieving remission (as defined by the study) :

- 6 months after the start of treatment (N = 3[6]; n = 2398; RR = 0.83; 95% CI, 0.79 to 0.87)

- 12 months after the start of treatment (N = 1; n = 1759; RR = 0.82; 95% CI, 0.78 to 0.85).

Effect of treatment on achieving a response

There is evidence to suggest that there is no clinically significant difference between organisational developments and usual care on increasing the likelihood of patients achieving a response 6 weeks after the start of treatment (N = 1; n = 302; RR = 1; 95% CI, 0.85 to 1.17).

There is strong evidence suggesting that there is a clinically significant difference favouring organisational developments over usual care on increasing the likelihood of patients achieving a response:

- 3 or 4 months after the start of treatment (N = 4[7]; n = 2552; RR = 0.8; 95% CI, 0.76 to 0.84)

- 6 months after the start of treatment (N = 3[8]; n = 2472; RR = 0.74; 95% CI, 0.69 to 0.79)

- 12 months after the start of treatment (N = 1; n = 1759; RR = 0.68; 95% CI, 0.64 to 0.73).

Effect of treatment on relapse

There is insufficient evidence to determine if there is a clinically significant difference between organisational developments and usual care on reducing the likelihood of patients experiencing a relapse (N = 1; n = 386; RR = 0.95; 95% CI, 0.55 to 1.64).

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[5] ARAYA2003 was removed from the analysis to reduce heterogeneity.
[6] ARAYA2003 was removed from the analysis to reduce heterogeneity.
[7] ARAYA2003 was removed from the analysis to reduce heterogeneity.
[8] ARAYA2003 was removed from the analysis to reduce heterogeneity.

Effect of treatment on reducing depression symptoms

There is evidence to suggest that there is no clinically significant difference between organisational developments and usual care on reducing depression symptoms 1 month after the start of treatment as measured by the HRSD and the SCL-20 (N = 3; n = 381; SMD = -0.08; 95% CI, -0.29 to 0.12).

There is some evidence suggesting that there is a clinically significant difference favouring organisational developments over usual care on reducing depression symptoms 3 or 4 months after the start of treatment as measured by the HRSD and the SCL-20 (N = 4[9]; n = 2171; SMD = -0.44; 95% CI, -0.53 to -0.36).

There is evidence suggesting that there is a statistically significant difference favouring organisational developments over usual care on reducing depression symptoms 6 or 7 months after the start of treatment as measured by the HRSD and the SCL-20 but the size of this difference is unlikely to be of clinical significance (N = 4[10]; n = 2159; SMD = -0.39; 95% CI, -0.48 to -0.31).

There is strong evidence suggesting that there is a clinically significant difference favouring organisational developments over usual care on reducing depression symptoms 12 months after the start of treatment as measured by the HRSD and the SCL-20 (N = 1; n = 1759; SMD = -0.6; 95% CI, -0.69 to -0.5).

There is evidence to suggest that there is no clinically significant difference between organisational developments and usual care on reducing symptoms 19 months after the start of treatment as measured by the SCL-90 (N = 1; n = 116; SMD = 0.01; 95% CI, -0.36 to 0.37).

Acceptability of treatment

There is insufficient evidence to determine whether there is a clinically significant difference between organisational developments and usual care on reducing the likelihood of patients leaving treatment early (N = 511; n = 2906; RR = 1.15; 95% CI, 0.90 to 1.46).

1.1.1.19 Multifaceted care versus usual care

Effect of treatment on remission (as defined by the study)

There is strong evidence suggesting that there is a clinically significant difference favouring multifaceted care over usual care on increasing the likelihood of patients achieving remission (as defined by the study) 3 or 4

[9] ARAYA2003 was removed from the analysis to reduce heterogeneity.
[10] ARAYA2003 was removed from the analysis to reduce heterogeneity.
[11] KATON2001 was removed from the analysis in order to reduce heterogeneity. This study does not contribute data to any efficacy outcome. However, some heterogeneity remains which could not be removed systematically.

months after the start of treatment (N = 3[12]; n = 860; RR = 0.71; 95% CI, 0.63 to 0.81).

There is some evidence suggesting that there is a clinically significant difference favouring multifaceted care over usual care on increasing the likelihood of patients achieving remission (as defined by the study) 6 months after the start of treatment (N = 3[13]; n = 2398; RR = 0.83; 95% CI, 0.79 to 0.87).

There is some evidence suggesting that there is a clinically significant difference favouring multifaceted care over usual care on increasing the likelihood of patients achieving remission (as defined by the study) 12 months after the start of treatment (N = 1; n = 1759; RR = 0.82; 95% CI, 0.78 to 0.85).

Effect of treatment on achieving a response

There is evidence to suggest that there is no clinically significant difference between multifaceted care and usual care on increasing the likelihood of patients achieving a response 6 weeks after the start of treatment (N = 1; n = 302; RR = 1; 95% CI, 0.85 to 1.17).

There is strong evidence suggesting that there is a clinically significant difference favouring multifaceted care over usual care on increasing the likelihood of patients achieving a response:

- 3 or 4 months after the start of treatment (N = 4[14]; n = 2552; RR = 0.8; 95% CI, 0.76 to 0.84)

- 6 months after the start of treatment (N = 3[15]; n = 2472; RR = 0.74; 95% CI, 0.69 to 0.79)

- 12 months after the start of treatment (N = 1; n = 1759; RR = 0.68; 95% CI, 0.64 to 0.74).

Effect of treatment on relapse

There is insufficient evidence to determine if there is a clinically significant difference between multifaceted care and usual care on reducing the likelihood of patients experiencing a relapse (N = 1; n = 386; RR = 0.95; 95% CI, 0.55 to 1.64).

Effect of treatment on depression symptoms

There is evidence to suggest that there is no clinically significant difference between multifaceted care and usual care on reducing depression symptoms

[12] UNITZER2002 was removed from the analysis to reduce heterogeneity.
[13] ARAYA2003 was removed from the analysis to reduce heterogeneity.
[14] ARAYA2003 was removed from the analysis to reduce heterogeneity.
[15] ARAYA2003 was removed from the analysis to reduce heterogeneity

1month after the start of treatment as measured by the HRSD and the SCL-20 (N = 3; n = 381; SMD = -0.08; 95% CI, -0.29 to 0.12).

There is evidence suggesting that there is a statistically significant difference favouring multifaceted care over usual care on reducing depression symptoms 3 or 4 months after the start of treatment as measured by the HRSD and the SCL-20 but the size of this difference is unlikely to be of clinical significance (N = 4[16]; n = 2171; SMD = -0.44; 95% CI, -0.53 to -0.36).

There is evidence suggesting that there is a statistically significant difference favouring multifaceted care over usual care on reducing depression symptoms 6 or 7 months after the start of treatment as measured by the HRSD and the SCL-20 but the size of this difference is unlikely to be of clinical significance (N = 4[17]; n = 2159; SMD = -0.39; 95% CI, -0.48 to -0.31).

There is strong evidence suggesting that there is a clinically significant difference favouring multifaceted care over usual care on reducing depression symptoms 12 months after the start of treatment as measured by the HRSD and the SCL-20 (N = 1; n = 1759; SMD = -0.6; 95% CI, -0.69 to -0.5).

Acceptability of treatment

There is insufficient evidence to determine if there is a clinically significant difference between multifaceted care and usual care on reducing the likelihood of patients leaving treatment early (N = 3[18]; n = 2433; RR = 1.17; 95% CI,0.92 to 1.49).

1.1.1.20 Nurse-led care versus usual care

Effect of treatment on remission (as defined by the study)

There is insufficient evidence to determine if there is a clinically significant difference between nurse led care and usual care on increasing the likelihood of patients achieving remission (as defined by the study) 3 or 4 months after the start of treatment (N = 2; n = 515; Random effects RR = 0.94; 95% CI, 0.63 to 1.4).

There is some evidence suggesting that there is a clinically significant difference favouring nurse led care over usual care on increasing the likelihood of patients achieving remission (as defined by the study) 24 months after the start of treatment (N = 1; n = 211; RR = 0.81; 95% CI, 0.66 to 1).

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[16] ARAYA2003 was removed from the analysis to reduce heterogeneity.
[17] ARAYA2003 was removed from the analysis to reduce heterogeneity.
[18] KATON2001 was removed from the analysis in order to reduce heterogeneity. This study does not contribute data to any efficacy outcome. However, some heterogeneity remains which could not be removed systematically.

There is evidence to suggest that there is no clinically significant difference between nurse led care and usual care on increasing the likelihood of patients achieving a response 6 weeks after the start of treatment (N = 1; n = 302; RR = 1; 95% CI, 0.85 to 1.17).

Effect of treatment on response

There is some evidence suggesting that there is a clinically significant difference favouring nurse led care over usual care on increasing the likelihood of patients achieving a response 6 months after the start of treatment (N = 1; n = 302; RR = 0.76; 95% CI, 0.63 to 0.92).

There is insufficient evidence to determine if there is a clinically significant difference between nurse led care and usual care on reducing the likelihood of patients leaving treatment early (N = 2; n = 515; RR = 0.65; 95% CI, 0.37 to 1.14).

Results are similar when the data set is divided by type of nurse (primary care or specialist nurse).

Acceptability of treatment

There is insufficient evidence to determine if there is a clinically significant difference between nurse led care and usual care on reducing the likelihood of patients leaving treatment early (N = 3; n = 726; Random effects RR = 0.92; 95% CI, 0.42 to 1.98).

1.1.1.21 Telephone versus usual care

Effect of treatment on remission (as defined by the study)

There is some evidence suggesting that there is a clinically significant difference favouring telephone support over usual care on increasing the likelihood of patients achieving remission (as defined by the study) 3 or 4 months after the start of treatment (N = 1; n = 392; RR = 0.65; 95% CI, 0.42 to 1).

There is insufficient evidence to determine if there is a clinically significant difference between telephone support and usual care on increasing the likelihood of patients achieving remission (as defined by the study) 6 months after the start of treatment (N = 1; n = 392; RR = 0.57; 95% CI, 0.32 to 1.02).

Effect of treatment on response

There is evidence to suggest that there is no clinically significant difference between telephone support and usual care on increasing the likelihood of patients achieving a response 6 weeks after the start of treatment (N = 1; n = 302; RR = 1; 95% CI, 0.85 to 1.17).

There is some evidence suggesting that there is a clinically significant difference favouring telephone support over usual care on increasing the likelihood of patients achieving a response:

- 3 or 4 months after the start of treatment (N = 1; n = 392; RR = 0.83; 95% CI, 0.72 to 0.95)

- 6 months after the start of treatment (N = 2; n = 694; RR = 0.74; 95% CI, 0.65 to 0.85).

Effect of treatment on relapse

There is insufficient evidence to determine if there is a clinically significant difference between telephone support and usual care on reducing the likelihood of patients experiencing a relapse (N = 1; n = 386; RR = 0.95; 95% CI, 0.55 to 1.64).

Acceptability of treatment

There is insufficient evidence to determine if there is a clinically significant difference between telephone support and usual care on reducing the likelihood of patients leaving treatment early (N = 2; n = 778; Random effects RR = 0.96; 95% CI, 0.24 to 3.76).

Results are similar when the data set is divided by protocol- and non-protocol-driven interventions.

1.1.1.22 Guideline approach versus usual care

Effect of treatment on remission (as defined by the study)

There is evidence to suggest that there is no clinically significant difference between guideline approach and usual care on increasing the likelihood of patients achieving remission (as defined by the study) 3 or 4 months after the start of treatment (N = 2; n = 929; RR = 1.07; 95% CI, 0.93 to 1.23).

Acceptability of treatment

There is evidence to suggest that there is no clinically significant difference between guideline approach and usual care on reducing the likelihood of patients leaving treatment early (N = 2; n = 929; RR = 1.01; 95% CI, 0.85 to 1.19).

5.6.6 Clinical summary

The complex nature of many of the interventions covered in this section make for difficult interpretation; this is exacerbated by the fact that the majority of the large well-conducted studies have been undertaken almost exclusively in the United States and this leads inevitably to considerable caution in their extrapolation to the UK.

Four key findings emerge from the review. First, that multifaceted care has a number of significant benefits on the treatment and care of depression. Although there was considerable variation in both the nature of the populations covered and in the complexity of the interventions these programme shave a number of shared characteristics that common to most if not all of the studies. These include a system-based approach to the delivery of care focusing on all levels of the primary care organisation, the use of clear protocols to guide professional practice (for example, medication protocols) and facilitate inter-professional communication, a stepped approach to care, and the development of specific staff roles (for example, depression care managers). There has also been an increasing trend in these studies towards the use of para-professional or non-specialist mental health staff.

Secondly, and in contrast to the work on multi-faceted care, there appears to be no support for guideline implementation programmes as single interventions for improving outcomes for people with depression. This finding is consistent with other reviews (von Korff & Goldberg, 2001), which recommends a multi-modal (or multifaceted) approach to guideline implementation.

Thirdly, the evidence for an enhanced role for nurses working in primary care in the care of depression in interventions is equivocal. It is possible that this reflect difference between health care systems, the results in the United States looked better but it could reflect some other difference than just the characteristics of the health care system. One such possibility is that the enhanced nurse in the United States appeared to have a more system based approach and were supported by the protocols that may well play an important part in the success of multifaceted care. Cleary this area need further research.

Fourthly, there is some limited evidence that telephone contact (particularly in supporting patient adherence to medication) may be of value in promoting better outcomes in depression.

5.6.7 Clinical practice recommendations

5.6.7.1 The provision of telephone support by appropriately trained members of the primary care team, informed by clear treatment protocols, should be considered for all patients, in particular for the monitoring of antidepressant medication regimes. (B)

5.6.7.2 Primary care organisations should consider establishing multi-faceted care programmes, that integrate - through clearly specified protocols - the delivery and monitoring of appropriate psychological and pharmacological interventions for the care of people with depression. (C)

5.7 Non-statutory support

5.7.1 Introduction

It is widely accepted that social support can play in important part in an individual's propensity to develop depression and their ability to recover from it. Despite this and the considerable amount of work that has described the importance of social support, few formal studies of the potential therapeutic benefits of different forms of social support have been undertaken.

There is evidence from a series of studies that providing social support in the sense of befriending (women with depression) confers benefits (Brown & Harris, 1978). There is also evidence to suggest that supported engagement with a range of non-statutory sector services, but this study was not limited to patients with depression and so was excluded from the review (Grant et al. (2000)). Given that social isolation is associated with poor outcome and chronicity in depression, this is regrettable. Several descriptive reports suggest that the provision of social support (e.g., Newpin, (Mills and Pound (1996)) in a variety of non-health care settings may confer some benefit and it is hoped that such protects are the subject of more formal evaluation.

There are many organisations offering local group peer support to people with depression, including Depression Alliance and MIND [check]. Although such self-help groups are likely to be beneficial, we were unable to find any research evidence for their effectiveness.

5.7.2 Definition

A range of community-based interventions often not provided by health care professionals, which provide support, activities and social contact in order to improve the outcome of depression.

5.7.3 Studies considered

The review team found one RCT (HARRIS1999) of befriending compared to wait-list control in people with depression.

5.7.4 Clinical evidence statements

1.1.1.23 Befriending versus wait-list control

One RCT of befriending (HARRIS1999) was identified, so a descriptive review of the data is presented here. In this trial befriending was defined as 'meeting and talking with a depressed woman for a minimum of one hour each week and acting as a friend to her, listening and "being there for her"'. The trained volunteer female befrienders were also encouraged to accompany their 'befriendee' on trips, to broaden their range of activities, to offer practical support with ongoing difficulties and to help create 'fresh-start' experiences often found to precede remission in previous work. 'Befriendees' were

women with chronic depression in inner London who were interested in being befriended. Women were allowed to be on other treatments such as antidepressants and contact with other health professionals. On an intention to-treat-analysis a clinically significant effect upon remission was found at one year with an association with initial PSE score:

There is some evidence suggesting that there is a clinically significant difference favouring befriending over wait list control on increasing the likelihood of patients achieving remission (defined as patients not meeting 'caseness' for depression[19]) (N=1, n=86, RR=0.58; 95% CI 0.36 to 0.93).

Other treatments monitored naturalistically did not relate to remission nor did initial duration of chronic episode or comorbidity. Although remission tended to be higher among those completing the full twelve months befriending as opposed to two to six months this did not reach statistical significance. This suggests that the benefits of befriending may be obtained by a shorter intervention.

Additional trials with less restricted intake conditions and in more naturalistic general practice settings might confirm volunteer befriending as a useful adjunct to current treatments.

5.7.5 Clinical summary

There is some evidence that befriending given to women with chronic depression as an adjunct to drug or psychological treatment may reduce the likelihood of remission.

5.7.6 Clinical practice recommendations

5.7.6.1 For patients with chronic depression who would benefit from additional social support, befriending should be considered as an adjunct to pharmacological or psychological treatments . Befriending should be by trained volunteers providing, typically, at least weekly contact for between 2 and 6 months. (C)

5.7.6.2 Primary care trusts and mental health communities should collate information on local self-help groups for practitioners. (GPP)

5.7.7 Future research recommendations

5.7.7.1 Further trials of the efficacy of a range of social support interventions for social isolated and vulnerable groups of people with depression should be undertaken.

[19] Depressed mood at 4 out of 10 symptoms on the Present State Examination (PSE-10).

5.8 Crisis resolution and home treatment teams

5.8.1 Introduction

Traditionally, a depressive episode marked by serious risk to self (most often suicidal ideation and intent) or very severe deterioration to care for the self is managed by admission to an acute inpatient unit. However, in recent years there has been growing interest in attempting to manage such episodes in the community. If this could be done safely, it might avoid the stigma and costs associated with hospital admission, thus providing benefits to both patients and service providers. Crisis resolution and home treatment teams (CRHTTs) are a form of service that aims to offer intensive home-based support in order to provide the best care for someone with depression where this is the most appropriate setting.

5.8.2 Definition

The GDG adopted the definition of crisis resolution developed by the Cochrane Review of crisis intervention for people with serious mental health problems (Joy *et al*, 2002). Crisis intervention and the comparator treatment were defined as follows:

- Crisis resolution is any type of crisis-oriented treatment of an acute psychiatric episode by staff with a specific remit to deal with such situations, in and beyond 'office hours'

- 'Standard care' is the normal care given to those suffering from acute psychiatric episodes in the area concerned; this involved hospital-based treatment for all studies included.

For the purposes of the guideline, the focus of this section is to examine the effects of CRHTT care for people with serious mental illness (where the majority of the sample were diagnosed with non-psychotic disorders) experiencing an acute episode, compared with the standard care they would normally receive. Studies were excluded if they were largely restricted to people who were under 18 years or over 65 years old, or to those with a primary diagnosis of substance misuse or organic brain disorder.

5.8.3 Studies considered

The GDG chose to use the Cochrane Review of CRHTTs (Joy *et al*, 2002), which included five RCTs (PASAMANICK1964, FENTON1979, HOULT1981, MUIJEN21992, STEIN1975), as the starting point for this section. A further search identified no new RCTs suitable for inclusion. Of the five RCTs included in the Cochrane review, only STEIN1975 met the inclusion criteria set by the GDG (all the other studies had a very significant or exclusive focus on schizophrenia), providing data for 130 participants.

5.8.4 Clinical evidence statements

1.1.1.24 Crisis resolution and home treatment teams versus standard care

Effect of treatment on death (suicide or death in suspicious circumstances)

There is insufficient evidence to determine whether there is a clinically significant difference between CRHTTs and 'standard care' on death during the study (N= 1; *n*= 130; RR= 1.00; 95% CI, 0.06 to 15.65).

Effect of treatment on acceptability

There is insufficient evidence to determine whether there is a clinically significant difference between CRHTTs and 'standard care' on the number of people leaving the study early by 6 or 12 months (N= 1; *n*= 130; RR= 0.60; 95% CI, 0.15 to 2.41) or by 20 months (N= 1; *n*= 130; RR= 1.17; 95% CI, 0.41 to 3.28).

Effect of treatment on burden to family

There is insufficient evidence to determine whether there is a clinically significant difference between CRHTTs and 'standard care' on the burden to family in terms of disruption to daily routine (N= 1; *n*= 100; RR= 0.82; 95% CI, 0.60 to 1.12).

There is insufficient evidence to determine whether there is a clinically significant difference between CRHTTs and 'standard care' on the burden to family in terms of disruption to social life (N= 1; *n*= 100; RR= 0.76; 95% CI, 0.56 to 1.02).

There is some evidence suggesting a clinically significant difference favouring CRHTTs over 'standard care' on the burden to family in terms of physical illness due to patient's illness by three months (N= 1; *n*= 100; RR= 0.78; 95% CI, 0.65 to 0.95) and by six months (N= 1; *n*= 100; RR= 0.71; 95% CI, 0.55 to 0.92).

Effect of treatment on burden to community

There is insufficient evidence to determine whether there is a clinically significant difference between CRHTTs and 'standard care' on the burden to community in terms of patient being arrested (N= 1; *n*= 120; RR= 0.71; 95% CI, 0.46 to 1.12).

There is insufficient evidence to determine whether there is a clinically significant difference between CRHTTs and 'standard care' on the burden to community in terms of patient using emergency services (N= 1; *n*= 120; RR= 0.81; 95% CI, 0.43 to 1.54).

5.8.5 Clinical summary

The very large majority of patients with depression are never admitted to hospital (in contrast to schizophrenia where 60% to 70% are admitted to hospital at first presentation, McGorry et al, 2000). Therefore, it is unsurprising that much of the evidence base is drawn fro the treatment of schizophrenia and means that there is currently insufficient evidence from RCTs to determine the value of CRHTTs for people with depression. Nevertheless, CRHTTs may have value for that small group of patients with depression that require a higher level of care than can be provided by standard community services.

5.8.6 Clinical practice recommendations

5.8.6.1 Crisis resolution and home treatment teams should be used as a means of managing crises for patients with severe depression who are assessed as presenting significant risk, and as a means of delivering high quality acute care. In this context, teams should pay particular attention to risk monitoring as a high priority routine activity in a way that allows people to continue their normal lives with minimal disruption. (C)

5.8.6.2 Crisis resolution and home treatment teams should be considered for patients with depression who might benefit from an early discharge from hospital following a period of inpatient care. (C)

5.9 Day hospitals

5.9.1 Acute day hospital care

5.9.1.1 Introduction

Given the substantial costs and high level of use of inpatient care, the possibility of day hospital treatment programmes acting as an alternative to acute admission gained credence in the early 1960s, initially in the USA (Kris, 1965; Herz *et al*, 1971) and later in Europe (Wiersma *et al*, 1989) and the UK (Dick *et al*, 1985; Creed *et al*, 1990).

5.9.1.2 Definition

Acute psychiatric day hospitals were defined for the purposes of the guideline as units that provided 'diagnostic and treatment services for acutely ill individuals who would otherwise be treated in traditional psychiatric inpatient units'. Thus, trials would only be eligible for inclusion if they compared admission to an acute day hospital with admission to an inpatient unit. Participants were people with acute psychiatric disorders (where the majority of the sample were diagnosed with non-psychotic disorders) who would have been admitted to inpatient care had the acute day hospital not been available. Studies were excluded if they were largely restricted to people

who were under 18 years or over 65 years old, or to those with a primary diagnosis of substance misuse or organic brain disorder.

5.9.1.3 Studies considered

The GDG selected a Health Technology Assessment (Marshall *et al*, 2001) as the basis for this section. Marshall *et al* (2001) reviewed nine trials of acute day hospital treatment published between 1966 and 2000. A further search identified no new RCTs suitable for inclusion. Of the nine studies included in the existing review, only three (DICK1985, SCHENE1993, SLEDGE1996) met the inclusion criteria set the GDG, providing data for 510 participants.

5.9.1.4 Clinical evidence statements

The studies included in this review examined the use of acute day hospitals as an alternative to acute admission to an inpatient unit. The individuals involved in the studies were a diagnostically mixed group, including between 50 and 62% of people with a diagnosis of mood or anxiety disorder. Moreover, acute day hospitals are not suitable for people subject to compulsory treatment, and some studies explicitly excluded people with families unable to provide effective support at home. Clearly, the findings from this review, and the recommendations based upon them, cannot be generalised to all people with depression who present for acute admission.

Effect of treatment on efficacy

There is insufficient evidence to determine whether there is a clinically significant difference between acute day hospitals and inpatient care on reducing the likelihood of readmission to hospital after discharge from treatment (N= 2; *n*= 288; RR= 1.02; 95% CI, 0.74 to 1.43).

Effect of treatment on inpatient days per month

There is some evidence suggesting that there is a clinically significant difference favouring acute day hospitals over inpatient care on inpatient days per month (N= 1; *n*= 197; WMD= -2.11; 95% CI, -3.46 to -0.76).

Effect of treatment on acceptability

There is insufficient evidence to determine whether there is a clinically significant difference between acute day hospitals and inpatient care on the number of people leaving the study early for any reason (N= 2; *n*= 288; RR= 0.67; 95% CI, 0.43 to 1.04).

5.9.2 Non-acute day hospital care

5.9.2.1 Introduction

Although the earliest use of day hospitals in mental health care was to provide an alternative to inpatient care (Cameron, 1947), non-acute day hospitals have also been used for people with refractory mental health problems unresponsive to treatment in outpatient clinics. Two broad groups of people have been referred for non-acute day hospital care: those with

anxiety and depressive disorders who have residual or persistent symptoms, and those with more severe and enduring mental disorders such as schizophrenia.

Given the need for services for people with severe and enduring mental health problems who are refractory to other forms of treatment, the review team undertook a review of the evidence comparing the efficacy of non-acute day hospitals with that of traditional outpatient treatment programmes.

5.9.2.2 Definition

For this section, the GDG agreed the following definition for non-acute day hospitals, in so far as they apply to people with serious mental health problems:

- Psychiatric day hospitals offering continuing care to people with severe mental disorders.

Studies were excluded if the participants were predominantly either over 65 years or under 18 years of age.

5.9.2.3 Studies considered

The GDG chose to use the Cochrane systematic review (Marshall *et al*, 2003) that compared day treatment programmes with outpatient care for people with non-psychotic disorders, as the starting point for the present section. Of the four studies included in the Cochrane review (BATEMAN1999, DICK1991, PIPER1993TYRER1979), BATEMAN1999 was excluded from the current section because the sample were patients diagnosed with borderline personality disorder.

Therefore, three studies (DICK1991, PIPER1993, TYRER1979) were included involving 426 participants.

5.9.2.4 Clinical evidence statements

Effect of treatment on death (all causes)

There is insufficient evidence to determine whether there is a clinically significant difference between non-acute day hospitals and outpatient care on death during the study (N= 1; *n*= 106; RR= 2.42; 95% CI, 0.23 to 25.85).

Effect of treatment on efficacy

There is insufficient evidence to determine whether there is a clinically significant difference between non-acute day hospitals and outpatient care on reducing the likelihood of admission to hospital during the study at 6-8 months (N= 2; *n*= 202; RR= 1.48; 95% CI, 0.38 to 5.76) and at 24 months (N= 1; *n*= 106; RR= 1.81; 95% CI, 0.54 to 6.05).

There is insufficient evidence to determine whether there is a clinically significant difference between non-acute day hospitals and outpatient care on mental state (change from baseline on the PSE) at four months (N= 1; *n*= 89; WMD= -3.72; 95% CI, -8.69 to 1.25) and at eight months (N= 1; *n*= 88; WMD= -3.39; 95% CI, -8.96 to 2.18).

Effect of treatment on social functioning

There is insufficient evidence to determine whether there is a clinically significant difference between non-acute day hospitals and outpatient care on social functioning (change from baseline on the SFS) at four months (N= 1; *n*= 89; WMD= -3.24; 95% CI, -8.07 to 1.59) and at eight months (N= 1; *n*= 89; WMD= -4.38; 95% CI, -9.95 to 1.19).

Effect of treatment on acceptability

There is insufficient evidence to determine whether there is a clinically significant difference between non-acute day hospitals and outpatient care on the number of people saying they were not satisfied with care (assuming that people who left early were dissatisfied; N= 2; *n*= 200; RR= 0.97; 95% CI, 0.68 to 1.39).

There is insufficient evidence to determine whether there is a clinically significant difference between non-acute day hospitals and outpatient care on the number of people lost to follow-up at 6-8 months (N= 2; *n*= 202; RR= 1.08; 95% CI, 0.49 to 2.38), at about 12 months (N= 1; *n*= 226; RR= 1.35; 95% CI, 0.94 to 1.94) and at 24 months (N= 1; *n*= 106; RR= 1.61; 95% CI, 0.85 to 3.07).

5.9.3 Clinical summary

There is currently insufficient evidence to determine whether acute day hospital care differs from inpatient care in terms of readmission to hospital after discharge. With regard to treatment acceptability, the evidence is inconclusive although there is a trend favouring day hospitals.

There is currently insufficient evidence to determine whether non-acute day hospital care differs from outpatient care in terms of admission to hospital, mental state, death, social functioning or acceptability of treatment.

5.10 Electroconvulsive Therapy

5.10.1 Introduction

Electroconvulsive therapy (ECT), as a treatment for depression has been used since the 1930s. In its modern form ECT is perceived by many, in particular healthcare professionals, to be a safe and effective treatment for severe depression which has not respond to other standard treatments (Geddes et al, 2003) but many others consider, including may patient groups, consider it to be a out-dated and potentially damaging treatment (Rose et al, 2003). During ECT, an electric current is passed briefly through the brain, via electrodes

applied to the scalp, to induce generalised seizure activity. The individual receiving treatment is placed under general anesthetic and muscle relaxants are given to prevent body spasms. The ECT electrodes can be placed on both sides of the head (bilateral placement) or on one side of the head (unilateral placement). Unilateral placement is usually to the non-dominant side of the brain, with the aim of reducing cognitive side effects. The number of sessions undertaken during a course of ECT usually ranges from 6 to 12, although a substantial minority of patients respond to fewer than 6 sessions. ECT is usually given twice a week; less commonly it is given once a fortnight or once a month as continuation or maintenance therapy to prevent the relapse of symptoms. It can be given on either an inpatient or day patient basis.

ECT may cause short- or long-term memory impairment for past events (retrograde amnesia) and current events (anterograde amnesia), this has been highlighted as a particular concern by many patients (Rose et al, 2003).

In line with NICE policy regarding the relationship of Technology Appraisal to clinical practice guidelines, the clinical practice recommendations in this guideline are taken directly from the Technology Appraisal (NICE, 2003), which itself drew on other recent reviews of ECT. The TA covered the use of ECT in the treatment of mania and schizophrenia as well as depression in children and adolescents. Only the recommendations on the use of ECT for adults with depression are reproduced here.

Key points to emerge from the review, which conclude that ECT is an effective treatment, include:

- Real ECT had greater benefit than sham ECT
- ECT had greater benefit than the use of certain antidepressants
- Bilateral ECT was reported to be more effective than unilateral ECT
- The combination of ECT with pharmacotherapy was not shown to be superior to ECT alone
- Cognitive impairment does occur but may well only be short term
- Compared with placebo, continuation pharmacotherapy with tricyclic antidepressants and/or lithium reduced the rate of relapses in people who had responded to ECT
- Preliminary studies indicate that ECT is more effective than repetitive transcranial magnetic stimulation.

5.10.2 Clinical practice recommendations

5.10.2.1 It is recommended that electroconvulsive therapy (ECT) is used only to achieve rapid and short-term improvement of severe symptoms after an adequate trial of other treatment options has proven ineffective, and/or when the condition is considered to be potentially life-threatening, in individuals with a severe depressive illness. (NICE 2003)

5.10.2.2 The decision as to whether ECT is clinically indicated should be based on a documented assessment of the risks and potential benefits to the individual, including: the risks associated with the anaesthetic; current comorbidities; anticipated adverse events, particularly cognitive impairment; and the risks of not having treatment. (NICE 2003)

5.10.2.3 The risks associated with ECT may be enhanced during pregnancy, in older people, and in children and young people, and therefore clinicians should exercise particular caution when considering ECT treatment in these groups. (NICE 2003)

5.10.2.4 Valid consent should be obtained in all cases where the individual has the ability to grant or refuse consent. The decision to use ECT should be made jointly by the individual and the clinician(s) responsible for treatment, on the basis of an informed discussion. This discussion should be enabled by the provision of full and appropriate information about the general risks associated with ECT and about the risks and potential benefits specific to that individual. Consent should be obtained without pressure or coercion, which may occur as a result of the circumstances and clinical setting, and the individual should be reminded of their right to withdraw consent at any point. There should be strict adherence to recognised guidelines about consent and the involvement of patient advocates and/or carers to facilitate informed discussion is strongly encouraged. (NICE 2003)

5.10.2.5 In all situations where informed discussion and consent is not possible advance directives should be taken fully into account and the individual's advocate and/or carer should be consulted. (NICE 2003)

5.10.2.6 Clinical status should be assessed following each ECT session and treatment should be stopped when a response has been achieved, or sooner if there is evidence of adverse effects. Cognitive function should be monitored on an ongoing basis, and at a minimum at the end of each course of treatment. (NICE 2003)

5.10.2.7 It is recommended that a repeat course of ECT should be considered under the circumstances indicated in 5.10.2.1 only for individuals who have severe depressive illness, and who have previously responded well to ECT. In patients who are experiencing an acute episode but have not previously responded, a repeat trial of ECT should be undertaken only after all other options have been considered and following discussion of the risks and benefits with the individual and/or where appropriate their carer/advocate. (NICE 2003)

5.10.2.8 Because the longer-term benefits and risks of ECT have not been clearly established, it is not recommended as a maintenance therapy in depressive illness. (NICE 2003)

[NB Chapter 6 to 10, and the appendices are in separate documents]