

SAMPLE CHAPTER FROM:

Depression in Adults with a Chronic Physical Health Problem

The NICE Guideline on Treatment and Management

By the National Collaborating Centre for Mental Health (NCCMH)

ISBN: 978-1-904671-86-2

Year: 2010

(one of a series of full guidelines on mental health from NICE)

Co-published by the Royal College of Psychiatrists
and the British Psychological Society

Distributed by RCPsych Publications (via Turpin Distribution for the trade)

www.rcpsych.ac.uk/nice



2 DEPRESSION IN ADULTS WITH A CHRONIC PHYSICAL HEALTH PROBLEM

2.1 INTRODUCTION

The management of depression for people with a chronic physical health problem was not specifically addressed in the 2004 NICE guideline on depression (NICE, 2004a; NCCMH, 2004). Given the size and the scope of that guideline, a decision was made that as part of the updating of the 2004 guideline a separate guideline on depression in adults with a chronic physical health problem should be developed. However, it is not the intention in developing this guideline to argue that depression in adults with a chronic physical health problem is a separate disorder requiring novel and different forms of treatment; rather, it is as much a recognition of the context (both in terms of the illness and the service settings) and the breadth of the field. Some of the work undertaken in this guideline (for example, on case identification) was carried out jointly with the depression guideline update (NCCMH, 2010), and in developing recommendations for depression in people with a chronic physical health problem the GDG both explicitly drew on this evidence and extrapolated from it where this was considered appropriate.

In this guideline, particular attention is paid to the following as chronic physical health problems: cancer, heart disease, musculoskeletal disorders, respiratory disorders, neurological disorders and diabetes. However, it must be appreciated that people with any chronic physical health problem have higher rates of depression and anxiety than physically healthy controls – depression is approximately two to three times more common in people with a chronic physical health problem than in people who are in good physical health. But it must also be emphasised that the majority of those with a chronic physical health problem do not have depressive or anxiety disorders (depression occurs in about 20% of those with a chronic physical health problem).

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2.2.1 Depressive disorders

The terminology and diagnostic criteria used for this heterogeneous group of related disorders has changed over the years, and previous guidance (NICE, 2004a) related only to those identified by the *International Classification of Diseases, 10th edition* (ICD-10) *Classification of Mental and Behavioural Disorders* (WHO, 1992) as

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having a depressive episode (classification category F32), recurrent depressive episode (F33) or mixed anxiety and depressive disorder (F41.2). In this guideline and in the depression guideline update (NICE, 2009; NCCMH, 2010) the scope has been widened to cover dysthymia (F34.1) and depression falling below the threshold for depression in recognition of the fact that a substantial proportion of people present with less severe forms of depression. Subthreshold depression does not have a coding in ICD-10, but is included in other mood (affective) disorders (F38).

It should, however, be noted that much of the research forming the evidence base from which this guideline is drawn has used a different classificatory system – the *Diagnostic and Statistical Manual of Mental Disorders* of the American Psychiatric Association, currently in its fourth edition (DSM-IV) (APA, 2000a). The two classificatory systems, while similar, are not identical especially with regard to definitions of severity. After considerable discussion, the GDG took the decision to base the guidelines on the DSM-IV and this covers major depressive disorder single episode (296.2) and recurrent (296.3), and also dysthymic disorder (300.4) and subthreshold depressive disorder (included in 311, depressive disorder not otherwise specified) (APA, 2000a). The guideline does not address the management of depression in bipolar disorder, postnatal depression or depression in children and adolescents, all of which are covered by separate guidelines.

Depression refers to a wide range of mental health problems characterised by the absence of a positive affect (a loss of interest and enjoyment in ordinary things and experiences), low mood and a range of associated emotional, cognitive, physical and behavioural symptoms. Distinguishing the mood changes between clinically significant degrees of depression (for example, major depression) and those occurring ‘normally’ remains problematic and it is preferable to consider the symptoms of depression as occurring on a continuum of severity (Lewinsohn *et al.*, 2000). The identification of major depression is based not only on its severity but also on persistence, the presence of other symptoms and the degree of functional and social impairment. However there appears no hard-and-fast ‘cut-off’ between ‘clinically significant’ and ‘normal’ degrees of depression; the greater the severity of depression the greater the morbidity and adverse consequences (Lewinsohn *et al.*, 2000; Kessing, 2007). In addition to assessing severity, considerable problems remain when attempting to classify depression into categories, such as duration, stage of illness and treatment history. Behavioural and physical symptoms often include tearfulness, irritability, social withdrawal, reduced sleep, an exacerbation of pre-existing pains, 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).

Although it is generally thought that depression is usually a time-limited disorder lasting up to 6 months with complete recovery afterwards, in the World Health Organization's (WHO) study of mental disorders in 14 centres across the world, 66% of those with depression were still found to meet criteria for a mental disorder 1 year later and for 50% the diagnosis was depression (Simon *et al.*, 2002). In the case of depression accompanying a chronic physical health problem the prognosis is likely to be substantially worse because the physical health problem will still be present, but objective evidence on this point is not available.

Major depression is generally diagnosed when a persistent and unreactive low mood and an absence of positive affect are accompanied by a range of symptoms, the number and combination needed to make a diagnosis being operationally defined (ICD-10, WHO, 1992; DSM-IV, APA, 1994). Depression occurring in the absence of a chronic physical health problem is commonly accompanied by various somatic symptoms; when it accompanies a chronic physical health problem the difficulty of distinguishing the somatic symptoms of the physical health problem from those associated with the depression can be particularly challenging.

2.2.2 Presentations of depression in adults with a chronic physical health problem

People with depression and a chronic physical health problem are especially common in primary and general hospital care. But only a minority of patients attending primary care mention psychological problems as their presenting complaint. In WHO's Psychological Problems in Primary Care study (Ustun & Sartorius, 1995), only 9.4% did so in the UK centre, compared with just 5% from all the other 15 centres combined. The majority complained of pain and other somatic complaints (63% in the UK, 62.1% across the world), with the remainder mentioning sleep problems and fatigue. This study showed that 26.2% of attendees in the UK had a diagnosable mental disorder, of which depression, at 16.9%, was the most common disorder. It follows that people with depression usually present with non-psychological symptoms, and the healthcare professional's first task is to investigate the possible causes of these symptoms. When a chronic physical health problem is either found or is known to be present, attention may shift to it and the depression may then be overlooked (Thompson *et al.*, 2000; Tiemens *et al.*, 1999; Ustun & Sartorius, 1995).

2.2.3 Impairment and disability

Mental disorders account for as much of the total disability in the general population as physical disorders (Ormel *et al.*, 1995), and there is a clear dose-response relationship between illness severity and the extent of disability (Ormel *et al.*, 1995). 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

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of both social and occupational disability (Ormel *et al.*, 1999). When both depression and physical health problems are present, disability is likely to be correspondingly greater.

Depression can also exacerbate the pain and distress associated with physical health problems, as well as adversely affecting outcomes. For example, death rates are significantly greater for those who are depressed following a myocardial infarction, not only in the immediate post-myocardial infarction period but also for the subsequent year (Lesperance *et al.*, 2000). In one community study, patients with cardiac disease who were depressed had an increased risk of death from cardiac problems compared with those without depression, and depressed people without cardiac disease also had a significantly increased risk of cardiac mortality (Penninx *et al.*, 2001). Similar findings for a range of physical illnesses also suggest an increased risk of death when comorbid depression is present (Cassano & Fava, 2002). Von Korff and colleagues (2005) also showed that depression predicts functional disability in diabetes better than the number of physical complications of diabetes, glycaemic control or the extent of chronic disease comorbidity.

An important distinction is that between social disability, which has a linear relationship with the number of depressive symptoms, and any functional disability due to physical health problems (for example, impaired mobility because of arthritis, or limitation of movements because of stroke). It is likely that such functional impairments or disabilities greatly increase the risk of depression among those with a chronic physical health problem.

2.2.4 Suicide risk in people with a chronic physical health problem

Large population-based epidemiological studies have reported higher suicide risk linked with various major physical health problems including cancer (Allebeck *et al.*, 1989), diabetes (Tsang, 2004), end-stage renal disease (Kurella *et al.*, 2005), epilepsy (Christensen *et al.*, 2007), multiple sclerosis (Brønnum-Hansen *et al.*, 2005), stroke (Teasdale & Engberg, 2001a) and traumatic brain injury (Teasdale & Engberg, 2001b). These findings indicate the importance of detecting and treating depression in people with a chronic physical health problem.

2.2.5 Diagnosis of depression in people with a chronic physical health problem

Although the advent of operational diagnostic criteria has improved the reliability of diagnosis, this does not circumvent the fundamental problem of attempting to classify a disorder that is heterogeneous and best considered on a number of dimensions. This is further complicated in patients with a chronic physical health problem because somatic criteria such as fatigue, appetite disturbance and sleep disturbance may be sequelae of physical health problems rather than depression. Zimmerman and

colleagues (2006) have suggested a simplified method of diagnosis using five non-somatic criteria as a response to the problems of overlapping symptoms. For a fuller discussion, see Appendix 12.

DSM-IV and ICD-10 have virtually the same diagnostic features for a 'clinically significant' severity of depression (termed a major depressive episode in DSM-IV or a depressive episode in ICD-10). Nevertheless their thresholds differ, with DSM-IV requiring a minimum of five out of nine symptoms (which must include depressed mood and/or anhedonia) and ICD-10 requiring four out of ten symptoms (including at least two of depressed mood, anhedonia and loss of energy). This may mean that more people may be identified as depressed using ICD-10 criteria compared with DSM-IV (Wittchen *et al.*, 2001a), or at least that somewhat different populations are identified (Andrews *et al.*, 2008), related to the need for only one of two core symptoms for DSM-IV but two out of three for ICD-10. These studies emphasise that, although similar, the two systems are not identical and that this is particularly apparent at the threshold taken to indicate clinical significance. In the depression guideline update (NICE, 2009; NCCMH, 2010) the GDG widened the range of depressive disorders to be considered and emphasised that the diagnostic 'groupings' it used should be viewed as pragmatic subdivisions of dimensions in the form of vignettes or exemplars rather than firm categories. The GDG considered it important to acknowledge the uncertainty inherent in our current understanding of depression and its classification, and that assuming a false categorical certainty is likely to be unhelpful and, even worst, damaging.

In contrast with the 2004 guideline, the GDG for both the depression guideline update and this guideline used DSM-IV rather than ICD-10 to define the diagnosis of depression because the evidence base for treatments nearly always uses DSM-IV. In addition, both GDGs have attempted to move away from focusing on one aspect such as severity, which can have the unwanted effect of leading to the categorisation of depression and influencing treatment choice based on a single factor such as symptom count.

The implication of the change in diagnostic system used in the depression guideline update and this guideline, combined with redefining the severity ranges, is that it is likely to raise the thresholds for some specific treatments such as antidepressants. An important motivation has been to provide a strong steer away from only using symptom counting to make the diagnosis of depression and, by extension, to emphasise that symptom severity rating scales should not be used by themselves to make the diagnosis, although they can be an aid in assessing severity and response to treatment.

It is important to emphasise that making a diagnosis of depression does not automatically imply a specific treatment. A diagnosis is a starting point in considering the most appropriate way of helping that individual in their particular circumstances. The evidence base for treatments considered in this guideline are based primarily on randomised controlled trials (RCTs), in which standardised criteria have been used to determine entry into the trial. Patients seen clinically are rarely assessed using standardised criteria, reinforcing the need to be circumspect about an over-rigid extrapolation from RCTs to clinical practice.

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To make a diagnosis of a depression requires assessment of three linked but separate factors, (a) severity, (b) duration and (c) course, with four severity groupings:

- subthreshold depressive symptoms: fewer than five symptoms of depression
- mild depression: few, if any, symptoms in excess of the five required to make the diagnosis, and symptoms result in only minor functional impairment
- moderate depression: symptoms or functional impairment are between ‘mild’ and ‘severe’
- severe depression: most symptoms, and the symptoms markedly interfere with functioning; can occur with or without psychotic symptoms.

However, diagnosis using the three factors listed above (severity, duration, course) only provides a partial description of the individual experience of depression. People with depression vary in the pattern of symptoms they experience, their family history, personalities, premorbid difficulties (for example, sexual abuse), psychological mindedness and current relational and social problems – all of which may significantly affect outcomes. It is also common for depressed people to have a comorbid psychiatric diagnosis, such as anxiety, social phobia, panic and various personality disorders (Brown *et al.*, 2001), and physical comorbidity (the specific concern of this guideline). Gender and socioeconomic factors account for large variations in the population rates of depression, and few studies of pharmacological, psychological or indeed other treatments for depression either control for or examine these variations. This serves to emphasise that choice of treatment is a complex process and involves negotiation and discussion with patients, and, given the current limited knowledge about which factors are associated with better antidepressant or psychotherapy response, most decisions will rely upon clinical judgement and patient preference until there is further research evidence. Trials of treatment in unclear cases may be warranted, but the uncertainty needs to be discussed with the patient and benefits from treatment carefully monitored.

2.2.6 Incidence and prevalence

Egede (2007) studied the 1-year prevalence of depression in 10,500 patients with chronic disease with 19,460 age-matched healthy controls in the US and found that as a group they were almost three times more likely to be depressed (odds ratio [OR] was 2.6, confidence intervals [CIs] 2.31–2.94). Rates for depression were double in diabetes, hypertension, coronary artery disease and heart failure, and three times in end-stage renal failure, chronic obstructive pulmonary disease (COPD) and cerebrovascular disease compared with healthy controls. Broadly similar results are reported by Moussavi and colleagues (2007) in a WHO study of the 1-year prevalence of depression among 245,400 patients in 60 countries: in this study, those with two or more chronic physical health problems experienced a prevalence of depression of 23%, whereas healthy controls only reported depression in 3.2%. Similar findings are reported in the WHO World Mental Health Survey where data is now complete in 29 countries (both developing and developed) (Von Korff *et al.*, 2009).

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Patients with comorbid depression and anxiety disorders – who by definition have a greater number of symptoms than either depression or anxiety disorders on their own – have a stronger relationship with chronic physical health problems than people with either depression or anxiety (Scott *et al.*, 2007). Studies conducted in single countries are shown in Table 2.

Table 2: Difference in prevalence of depression in a range of physical health problems compared with controls

Physical health problem	Main findings
<p>Diabetes Egede (2007), US</p> <p>Das-Munshi and colleagues (2007), UK</p>	<p>Diabetes mellitus (n = 1794) versus no health problem (n = 19, 462) OR = 1.96 (1.59, 2.42)</p> <p>Diabetes mellitus versus no diabetes: adjusted OR = 1.50 (0.60, 4.10)</p> <p>Adjusted for demographic and comorbid health problems</p>
<p>Hypertension Egede (2007), US</p> <p>Kessler and colleagues (2003), US</p>	<p>Hypertension (n = 7371) versus no health problem (n = 19, 462) OR = 2.00 (1.74, 2.31)</p> <p>Hypertension versus no health problem OR = 1.80 (1.20, 2.90)</p>
<p>Heart problems Egede (2007), US</p> <p>Wilhelm and colleagues (2003), Australia</p> <p>Hebst and colleagues (2007), US</p>	<p>Coronary artery disease (n = 3491) versus no health problem (n = 19, 462) OR = 2.30 (1.94, 2.63)</p> <p>Coronary heart failure (n = 391) versus no health problem (n = 19, 462) OR = 1.96 (1.23, 3.11)</p> <p>Heart disease: present versus absent OR = 1.94 (1.13, 3.33)</p> <p><i>Past year:</i> Adjusted OR = 2.49 (1.81, 3.43)</p> <p>Adjusted for demographic, health and substance misuse</p>
<p>Stroke Egede (2007), US</p>	<p>Stroke (n = 710) versus no health problem (n = 19, 462) OR = 3.15 (2.33, 4.35)</p>
<p>Cancer Wilhelm and colleagues (2003), Australia</p>	<p>Cancer: present versus absent OR = 2.19 (1.05, 4.56)</p>

Continued

Table 2: (Continued)

Physical health problem	Main findings
Arthritis Wilhelm and colleagues (2003), Australia Kessler and colleagues (2003), US	Arthritis: present versus absent OR = 1.58 (1.12, 2.22) Arthritis: present versus no physical health problem OR = 2.50 (1.80, 3.40)
COPD/bronchitis/emphysema Egede (2007), US Wilhelm and colleagues (2003), Australia Wagena and colleagues (2005), Netherlands	COPD (n = 1681) versus no health problem (n = 19, 462) OR = 3.21 (2.72, 3.79) Bronchitis: present versus absent OR = 4.26 (2.47, 7.34) COPD (n = 93) versus no COPD (n = 4427) OR = 4.38 (2.35, 8.16) Adjusted for age, sex, smoking status, education
Asthma Wilhelm and colleagues (2003), Australia Katon and colleagues (2007), US Kessler and colleagues (2003), US	Asthma: present versus absent OR = 1.70 (1.17, 2.47) Asthma versus no asthma OR = 1.89 (1.15, 3.11) Asthma versus no asthma OR = 2.5 (1.80, 3.50)
Kidney disease Wilhelm and colleagues (2003), Australia	Kidney disease: present versus absent OR = 4.32 (2.06, 9.05)
Liver disease Wilhelm and colleagues (2003), Australia	Liver disease: present versus absent OR = 5.43 (2.74, 10.76)
End stage renal disease Egede (2007), US	End stage renal disease (n = 431) versus no health problem (n = 19, 462) OR = 3.56 (2.61, 4.87)
Multiple sclerosis Patten and colleagues (2003), US	Multiple sclerosis versus no multiple sclerosis OR = 2.3 (1.6, 3.3)

2.3 THE RECIPROCAL RELATIONSHIP BETWEEN DEPRESSION AND CHRONIC PHYSICAL HEALTH PROBLEMS

Not only can chronic physical health problems both cause and exacerbate depression, but the reverse also occurs with depression antedating the onset of physical health problems that go on to become chronic. In a model of the relationship between major depression and chronic physical health problems, Katon (2003) points out a number of ways that major depression and physical health problems interact with one another. For example, major depression and childhood adversity are associated with risk factors such as obesity, sedentary lifestyle and smoking, which are also risk factors for physical health problems. In addition, major depression is linked with poorer self-management of chronic physical health problems, which increases the burden of the disease. Moreover, the functional impairment associated with physical illness, as well as indirect pathophysiological factors (for example, increased cytokine levels or other inflammatory factors) may increase the risk of developing and worsening depression. These interactions between mental and physical health disorders will be discussed in further detail below.

2.3.1 Chronic physical health problems causing depression

Two population-based prospective cohort studies found that physical illness was a risk factor for the later development of depression. Patten (2001) studied people who were free of depression at baseline in a large population-based cohort ($n = 11,859$). After 2 years 3.5% of this group had developed major depressive disorder, and physical illness was a risk factor (OR = 2.5, [95% CI: 1.3-4.6]). The risk was similar for a wide range of physical health problems, namely hypertension, asthma, arthritis and rheumatism, back pain, diabetes, heart disease and chronic bronchitis. In a Dutch cohort study of 4,664 participants who had never had depressive disorder, the presence of two out of three illnesses (migraine, respiratory problems or abdominal problems) predicted the later development of depressive disorder (incident relative risk [RR] 2.85) after adjusting for confounders. In this study, 2.7% of the population developed depression after 1 year (Smit *et al.*, 2004).

In clinical populations, the year after the diagnosis of cancer and after first hospitalisation with a heart attack are associated with a particularly high rate of new onset of depression or anxiety – approximately 20% (Burgess *et al.*, 2005; Dickens *et al.*, 2004). Prince and colleagues (2007) also argue that there is consistent evidence for depression being a consequence of coronary heart disease, stroke and human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS).

Causal pathways

There are at least three distinct ways in which a chronic physical health problem causes depression.

First, the number of different pains a person experiences is directly proportional to the prevalence of depression: Dworkin and colleagues (1990) showed that primary care patients with a single pain had no increased risk of depression, those with two pains had double the risk, but those with three or more had five times the risk. Pain,

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in turn, causes emotional distress and poor sleep irrespective of whether pain has a known cause (Von Korff & Simon, 1996).

Second, chronic physical health problems carry the risk of disability and this can be very depressing for a person who has previously been healthy. For example, Prince and colleagues (1998) showed that the attributable fraction of disability or handicap for the prediction of onset of depression among the elderly was no less than 0.69, and Ormel and colleagues (1997) showed similar findings in Holland.

Third, there are physical changes in some diseases that may underlie the development of depression, such as changes in the allostatic load. Allostasis refers to the ability of the body to adapt to stressful conditions. It is a dynamic, adaptive process. Tissue damage, degenerative disease (like arthritis) and life stress all increase allostatic load and can induce inflammatory changes which produce substances such as bradykinin, prostaglandins, cytokines and chemokines. These substances mediate tissue repair and healing, but also act as irritants that result in peripheral sensitisation of sensory neurons, which in turn activate central pain pathways (Rittner *et al.*, 2003). In stroke (especially left-sided), cerebral ischaemia may favour development of depression, and in degenerative dementias the same processes may account for increased rates of depression. Other features of chronic physical health problems that may lead to depression include disfigurement, the necessity for undergoing stressful investigations and the fear of impending death.

2.3.2 Depression causing chronic physical health problems

A depressive illness can also precede a new episode of a physical health problem. Systematic reviews of 11 prospective cohort studies in healthy populations show that depression predicts later development of coronary heart disease in all of them (OR 1.18 to 5.4 median = 2.05, and for new coronary heart disease events after adjustment for traditional risk factors: OR = 1.90 [95% CI: 1.48–2.42]) (Hemingway & Marmot, 1999; Nicholson *et al.*, 2006). The occurrence of a depressive episode before an episode of myocardial infarction has been reported by Nielsen and colleagues (1989). Three prospective studies have also shown that depression is an independent risk factor in stroke (Everson *et al.*, 1998; Larson *et al.*, 2001; Ohira *et al.*, 2001). In prospective population-based cohort studies, depression has been shown to predict the later development of colorectal cancer (Kroenke *et al.*, 2005), back pain (Larson *et al.*, 2004), irritable bowel syndrome (Ruigómez *et al.*, 2007) and multiple sclerosis (Grant *et al.*, 1989), and there is some (inconsistent) evidence that depression may precede the onset of type 2 diabetes (Prince *et al.*, 2007). Prince and colleagues (2007) argue that there is consistent evidence for depression leading to the development of chronic physical health problems such as coronary heart disease and stroke, and depression in pregnancy potentially leading to infant stunting and mortality.

Causal pathways

It has been hypothesised that increases in proinflammatory cytokines in depression and increased adrenocortical reactivity may also lead to atherosclerosis, and with it

increased risk for both stroke and coronary artery disease (Wichers & Maes, 2002). In the latter, autonomic changes in depression may also cause electrocardiogram (ECG) changes, which favour the development of coronary disease. Another suggested way in which depression may increase the likelihood of a person developing a physical disease is by the immune changes that occur during depression: changes in immune cell classes with an increase in white cell counts and a relative increase in neutrophils, increases in measures of immune activation, and a suppression of mitogen-induced lymphocyte proliferation with a reduction in natural killer cells (Irwin, 1999). Changes in natural killer cells and T-lymphocytes in depression may also lead to lowered resistance to AIDS in HIV infections. Menkes and McDonald (2000) have argued that exogenous interferons may cause both depression and increased pain sensitivity in susceptible people, by suppressing tryptophan availability and therefore serotonin synthesis. More prosaic explanations include reduced physical activity in people with depression (Whooley *et al.*, 2008).

2.4 CONSEQUENCES OF DEPRESSION IN ADULTS WITH A CHRONIC PHYSICAL HEALTH PROBLEM

Prince and colleagues (2007) argue that there is consistent evidence for depression affecting the outcome of coronary heart disease, stroke and diabetes. The evidence in support of this is reviewed below.

2.4.1 Effects on length of survival

Depression may lead to a shorter life expectancy (Evans *et al.*, 2005), and therefore treatment might be expected to prolong life. However, the studies required to demonstrate this have not been carried out because they would require long follow-up periods accompanied by prolonged treatment of depression with a control group denied, or at least not in receipt of, such treatment. DiMatteo and colleagues (2000), in a meta-analysis of factors related to non-compliance, found that depressed patients were three times more likely to be non-compliant with treatment recommendations than non-depressed patients, suggesting that there may be real advantages to treating depression among the physically ill. In people with heart disease, Van Melle and colleagues (2004) report a more than double greater risk of death with comorbid depression.

2.4.2 Effects on quality of life

As the severity of depression increases, the subjective quality of life decreases. One of the reasons for persevering with active treatment for depression is that even if the outlook for survival is not improved, the quality of survival may be greatly enhanced. In the large study by Moussavi and colleagues (2007), particularly low health-status scores were found in those with depression comorbid with a chronic physical health problem.

2.4.3 Advantages of treating depression in adults with a chronic physical health problem

Effects on length of survival

Depressive disorder predicts increased mortality after a heart attack, but the risk may be confined to people who develop depression after their heart attack (Frasure-Smith *et al.*, 1993). Others such as Prince and colleagues (2007) argue that there is consistent evidence for depression being a consequence of coronary heart disease, stroke and HIV/AIDS and while Bogner and colleagues (2007) claim that effective treatment of depression may decrease mortality in diabetes.

Effects on disease management of the chronic physical health problem

While randomised trials on the treatment of depression often report beneficial effects on outcome measures of depression, they often fail to show much effect on heart disease (Berkmann *et al.*, 2003; Glassman *et al.*, 2002) or diabetes (Katon *et al.*, 2006; Williams *et al.*, 2004). More recently, trials of collaborative care for depression (which has its origins in the management of chronic disease) have focused on people with depression and a chronic physical health problem (for example, Katon *et al.*, 2004). However, Gilbody and colleagues (2008a) conclude on the basis of a meta-analysis that depression can be treated effectively by collaborative care, but there does not appear to be consistent evidence that such treatment improves physical outcomes.

Effects on quality of life and related measures

Treatment for depression does have other beneficial effects on outcomes other than measures of depression. Simon and colleagues (2005) showed improvements in social and emotional functioning, and disability, in a mixed group of people with chronic physical health problems in primary care; Mohr and colleagues (2007) demonstrated improvements in both disability and fatigue with cognitive behavioural therapy (CBT) for depression in patients with multiple sclerosis; Lin and colleagues (2003) showed that treatment of depression in patients with arthritis resulted in improved arthritis-related pain, functional outcomes, and better general health status and overall quality of life, in addition to having fewer depressive symptoms. Based on studies in this area, von Korff and colleagues (2009) argue that the weight of the evidence suggests that, in addition to reducing depressive symptoms, the treatment of depression is effective in reducing functional disability. Treatment for depression, as one might expect, is associated with a smaller beneficial effect for severe pain (Kroenke *et al.*, 2008; Mavandadi *et al.*, 2007; Thielke *et al.*, 2007).

2.4.4 Disadvantages of treating depression in adults with a chronic physical health problem

The possibility of the iatrogenic effects of treatment, especially with reference to interactions and side effects of antidepressant medication, needs to be noted. Side

effects may add to a patient's discomfort from the physical health problem, while others may deleteriously affect the disease process; for example Broadley and colleagues (2002) argue that selective serotonin reuptake inhibitors (SSRIs) such as paroxetine can inhibit the function of vascular endothelial cells in arteries: these cells are crucial to the maintenance of arterial integrity and hence to the prevention of atherosclerosis.

2.5 THE ECONOMIC COST OF DEPRESSION IN ADULTS WITH A CHRONIC PHYSICAL HEALTH PROBLEM

There is widespread recognition of the significant burden that depression alone imposes on individuals, their carers, health services and communities, around the world. Within the UK, it is estimated that there are 1.24 million people with depression in England, and this is projected to rise by 17% to 1.45 million by 2026. Overall, the total cost of services for depression in England in 2007 was estimated to be £1.7 billion while lost employment increased this total to £7.5 billion. By 2026, these figures are projected to be £3 billion and £12.2 billion respectively (McCrone *et al.*, 2008). However, while there is plenty of published evidence on the economic burden of depression alone, there is less evidence on the combined economic impact of depression in patients with a chronic physical health problem, especially within the UK setting.

Two US studies assessed healthcare costs in relation to patients with a diagnosis of diabetes and depressive symptoms (Ciechanowski *et al.*, 2000, Egede *et al.*, 2002). The study by Ciechanowski and colleagues (2000) assessed direct healthcare costs over 6 months including primary care, specialty care, emergency department, inpatient services, mental healthcare and prescription medications. Overall, the results showed higher healthcare utilisation and costs among diabetic patients with severe comorbid depression. These increased healthcare costs were largely explained by increased medical, rather than mental health, utilisation. The study by Egede and colleagues (2002) compared depressed and non-depressed individuals from the 1996 Medical Expenditure Panel Survey to identify differences in healthcare use and expenditures in patients with diabetes (Egede *et al.*, 2002). Healthcare resource-use categories included hospital inpatient days, outpatient visits, emergency department visits and medications. Overall, diabetic patients with depression had significantly higher total healthcare expenditures than non-depressed diabetic patients. These differences were largely due to higher numbers of outpatient visits and prescription medications among diabetic individuals with depression.

A Canadian-based study evaluated healthcare costs over 1 year among post-myocardial infarction patients with depressive symptoms (Beck Depression Inventory [BDI] scores of ≥ 10) (Frasure-Smith *et al.*, 2000). Medicare billing records were used to collect resource-use data including: physician costs, inpatient stay, revascularisation procedures, re-admissions, emergency visits and outpatient visits. Overall, during the first year post-discharge, estimated costs were significantly higher for depressed patients than for non-depressed patients. Depressed post-myocardial

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infarction patients were more likely to be re-admitted and spent more days in hospital than non-depressed patients. The major reasons for the depression-related increase in costs were greater use of emergency rooms and outpatient visits to physicians, although psychiatric contacts were rare. Another Canadian-based study evaluated healthcare costs over 3 years in a retrospective cohort of patients with heart failure who were diagnosed with depression or receiving antidepressant medication (Sullivan *et al.*, 2002). After adjusting for confounding variables, in comparison with patients with heart failure and no depression, costs were 26% higher in the antidepressant prescription group and 29% higher in patients diagnosed with depression.

The limited non-UK based evidence presented here suggests that depression imposes a significant additional burden on patients with a chronic physical health problem and society in general, in terms of healthcare costs and lost productivity. It is also likely that these costs will continue to rise significantly in future years. Therefore, efficient use of available healthcare resources is necessary to treat depression in adults with a chronic physical health problem.