



The epidemiology of depression in diabetes

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Introduction

Diabetes health professionals are increasingly aware of the adverse outcomes associated with depression in people with diabetes, namely: increased morbidity and mortality; loss of economic and social roles; and poor quality of life. However, clinicians often feel ill-equipped – through lack of time and resources – to assess and treat this common condition. There is awareness that diabetes is psychologically stressful^{1–3} and that the patient's ability to manage the condition may determine the course of the illness. So, is depression in people with diabetes the proverbial elephant in the corner? Can we afford to ignore it?

Diagnostic criteria for depression

Depression is arguably the most common psychological problem affecting people with diabetes. The main characteristics of depression, according to the International Classification of Diseases 10 (ICD-10)⁴ and Diagnostic and Statistical Manual-4 (DSM-IV),⁵

Summary

Depression is characterised by a period of low mood and loss of interest in everyday activities, and its prevalence in people with diabetes is thought to be twice as high as for those without the condition. Depression in diabetes is associated with a number of adverse outcomes such as increased morbidity, mortality and poor quality of life. As diabetes is increasingly common amongst the economically active, this has serious implications for health services and in the UK, the National Health Service (NHS) has recognised that depression in people with diabetes is a significant problem and recommends screening for depression in this group. Risk factors for depression in diabetes are almost identical to those in people without diabetes, but less is known about its course when people have diabetes, although the available evidence suggests it is more chronic. Research into the mechanisms by which depression is bad for people with diabetes suggests that biological, psychological and social factors play a part but the inter-relationships between these factors are likely to be complex and are not yet fully understood. Depression in people with diabetes can be treated successfully with pharmacological and psychological treatments at least in the short-term, but we do not yet know which treatments are successful in the long-term. Further research into the pathological mechanisms of depression and its treatment are needed if we are to continue to improve the health and lives of people with diabetes.

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Key Words

Diabetes; depression

are a period of low mood, loss of pleasure or interest in everyday activities, and fatigue. In addition, there are a number of symptoms, which vary according to the severity of depression and may include: sleep/appetite disturbance; loss of concentration; feelings of guilt or worthlessness; loss of self-confidence; pessimistic views about the future; and suicidal ideation or self-harm.

Both the ICD-10 and DSM-IV criteria allow us to categorise depression as mild, moderate or severe, and these categories may direct the type of treatment provided. As a rule of thumb, a depressive episode is distinguishable from a period of sadness, in that the symptoms of depression are present for at least two weeks, most of the days of the week and most of the day, and there is a distinct loss of functioning. Assessment of depression can be carried out in three ways: using

self-report questionnaires such as the Patient Health Questionnaire (PHQ-9),⁶ which are quick to administer while patients are waiting for consultations; talking to patients in the context of therapeutic relationships, asking them the core questions regarding their mood and ability to enjoy everyday activities; or performing diagnostic interviews such as the World Health Organization (WHO) Schedules of Clinical Assessment in Neuropsychiatry (SCAN 2.1),^{1,7} Structured Clinical Interview for DSM-IV (SCID),⁸ or the WHO Composite International Diagnostic Interview (CIDI).⁹ However, the latter option would involve a degree of training for professionals who are not psychologists or psychiatrists.

Prevalence of depression

Depression is thought to be around twice as common in people with

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diabetes compared with the general population. A meta-analysis of 42 studies by Anderson *et al*¹⁰ found the prevalence to be 26% in people with diabetes versus 14% in those without when assessed by self-report questionnaire, and 9% versus 5% respectively, when assessed by diagnostic interview. A recent US population-based postal survey (the Pathways study) involving 4385 people with diabetes used the PHQ-9 to determine depression, and demonstrated that 8.5% of those surveyed met the DSM-IV diagnostic criteria for minor depression and 12% met criteria for major depression.¹¹

There is no simple explanation as to why depression is so common in people with diabetes, but it is an important question to ask if we want to understand and treat depression in this group. Diabetes is not necessarily uniquely stressful, as we know from other chronic conditions (such as cardiovascular disease and chronic obstructive pulmonary disease) that the prevalence of depression is at least as high or higher.^{12,13} So could it be that depression and diabetes have the same developmental origins? Early life experiences of trauma or adversity may impact on self esteem. For example, it is well known that maltreatment in childhood is a major risk factor for depression in adulthood^{14,15} and is associated with unhealthy lifestyles,¹⁶ with comfort eating perhaps occurring secondary to low self-esteem. Chronic stressors such as these may be on the causal pathway to chronic diseases, including type 2 diabetes.^{17,18}

Risk factors for depression

Depression in people with diabetes is associated with a number of demographic factors such as female gender, younger age, lower educational level and socio-economic status, ethnic minorities, being unmarried and unhealthy lifestyles,^{19,20} which are the same risk factors for depression in the general population. However, in people with diabetes, depression is also

more common when there is obesity²¹ or diabetes complications,²² and is cross-sectionally associated with poorer glycaemic control.¹¹

Course of depression

Few studies have examined the course of depression in people with diabetes. Still, available evidence suggests that depression is more chronic in people with diabetes than in general population samples.^{23,24} For example, 64% of people with diabetes have depression with a relapsing-remitting course (relapse is defined as a worsening of mood within a nine-month period), 15% never recover from their depression and only around 20% recover fully.^{25,26}

Common psychological problems associated with depression in diabetes

Other psychological problems such as anxiety can be linked to depression. People who are depressed often have symptoms of anxiety, including excessive rumination or worrying, but usually depression is the primary problem. Research into anxiety in diabetes populations has focused on generalised anxiety disorder and symptoms rather than anxiety disorders *per se*.²⁷ A systematic review found that around 14% of people with diabetes had generalised anxiety disorder, but subclinical anxiety and symptoms were more common, affecting 27% and 40% of these people, respectively.²⁷ Diabetes-specific psychological problems such as fear of self-injecting insulin, self-testing blood glucose (which may or may not be full-blown needle phobia) and fear of complications are associated with anxiety and depression.^{28–30} Fears regarding hypoglycaemia, complications and psychological insulin resistance are also common, but their relationship with depression is less clear.^{31,32}

People who are depressed often have very negative views regarding their diabetes and these may

perpetuate adverse coping behaviours and increase the likelihood of poor outcome. For example, having positive beliefs about controlling diabetes is associated with better insulin and dietary adherence, blood glucose monitoring and exercise, and lower glycosylated haemoglobin (HbA_{1c}) levels and care seeking.^{33–40} Conversely, negative beliefs about controlling diabetes are associated with depression and anxiety.⁴¹ Reporting a greater impact of diabetes on daily life is also associated with poorer physical and psychological functioning.^{35,39–42} Prospective studies of diabetes-specific illness beliefs demonstrate that reporting greater perceived control of diabetes was associated with better glycaemic control (as measured by HbA_{1c} levels), and believing diabetes to be more serious was associated with poorer physical functioning and worse mental health at 12-month follow-up.⁴³

Adverse consequences of depression

Depression has been identified as a potential risk factor for the onset of type 2 diabetes. Knol *et al*⁴⁴ performed a systematic review of cohort studies to determine whether depression increases the risk of developing type 2 diabetes. They identified nine studies that could be entered into a meta-analysis and found a 37% increased risk of developing type 2 diabetes in those who were depressed. This study did not identify the direction of causality, because depression may occur as a consequence of having diabetes and patients with diabetes (prior to diagnosis) may not have symptoms, but it does suggest that there is a possibility in terms of the origin of onset, as previously suggested. Since the publication of this review, a large Swedish cohort study of more than 5000 men and women with normal glycaemia at baseline, confirmed that psychological distress (including symptoms of depression, anxiety, apathy, insomnia and fatigue)



is associated with type 2 diabetes and pre-diabetes at 8–10 year follow-up, even after controlling for other potential risk factors, but interestingly only in men.⁴⁵

The biopsychosocial costs of depression in people with established diabetes have been studied both cross-sectionally and prospectively. Depressive symptoms are cross-sectionally associated with less dietary adherence, poorer physical and mental functioning and people who use health service resources more heavily.⁴⁶ There is also evidence of reduced physical activity and non-adherence to oral medication (including hypoglycaemic, antihypertensive and lipid-lowering medication) in people with type 2 diabetes.⁴⁷ A meta-analysis of 27 studies examining the association between depression and diabetes complications demonstrated a significant overall (moderate) effect size of 0.25 across studies, with the largest effects in men with sexual dysfunction (0.32).²² Another meta-analysis of 24 studies demonstrated a small but significant association with poor glycaemic control (effect size of 0.17) in people with diabetes who are depressed,⁴⁸ although at present there is no evidence to suggest that this relationship exists prospectively.^{49–51} Therefore, it appears that depression is more likely when diabetes is perceived as severe and its complications are apparent.

Prospective evidence which demonstrates that the human cost of depression in diabetes is substantial and cannot be ignored is accumulating. Depression is associated with a three-fold increased risk of mortality in people with diabetes and their first foot ulcer at 18 months.⁵⁰ In a large US cohort study of 4385 people with type 2 diabetes followed up for three years, there was a 1.67 fold increase in mortality in people with minor depression and a 2.30 fold increase in those with major depression.⁴⁹ In the US National Health

and Nutrition Examination Survey, where patients with diabetes and depression were compared with patients with diabetes and no depression and other non-diabetes groups, at eight years' follow-up those in the depressed diabetes group were 2.50 times more likely to die from all-cause mortality and 2.43 times more likely to die from coronary heart disease mortality.⁵² Furthermore, a prospective study of 2830 Mexican Americans with type 2 diabetes aged over 65 years, followed up over seven years, demonstrated that depressed individuals were almost five times more likely to die and were significantly more likely to develop early-onset diabetes complications than non-depressed individuals.⁵³

Mechanisms

Why is depression so bad for people with diabetes? It is likely that there is a complex interaction between psychological, biological and social factors, but the relationship between the three is poorly understood.

If we look to a psychological explanation, it is probable that people who are depressed neglect themselves and fail to adjust their lifestyles or manage their diabetes, as has been demonstrated by the cross-sectional evidence.⁴⁶ We also know that some beliefs about diabetes might perpetuate maladaptive diabetes coping behaviours, which in turn may accelerate the onset of complications and worsening of diabetes control. However, prospective evidence confirming this theory is not yet available and a longitudinal study of unhealthy lifestyles suggested that this was not enough to explain the association between depressive symptoms and cardiac mortality,⁵⁴ so it seems unlikely to be the complete story.

From a biological perspective, an alternative explanation of the interactive effect of depression on increased mortality could be that depression negatively influences

cardiovascular health and macrovascular complications, through activation of the hypothalamic pituitary adrenal axis, or immune system dysfunction.⁵⁵ In depression there is an over-stimulation of the hypothalamic pituitary axis and associated sympathetic response. These factors may affect cardiovascular risk by: increasing the release of counter-regulatory stress hormones that raise blood glucose levels and increase insulin resistance;⁵⁶ accelerating the atherosclerotic process by increasing platelet activity;⁵⁷ and decreasing heart rate variability due to altered autonomic tone.^{58,59} Like-wise, gene-environment interactions may be important, as there is evidence to suggest a clustering of factors such as obesity, insulin-resistance and hypertension with depression, in other conditions.⁶⁰

People with diabetes may also be socially disadvantaged. Ethnic minorities, lower socio-economic status and obesity are factors that are also associated with more mental health disease.^{61–63} Social factors like these may exert their influence on diabetes outcomes directly or indirectly through their influence on depression.⁶⁴ We know that diabetes affects people who are economically active and if diabetes leads to a loss of economic or social roles, causing marital and family discord, this may lead to isolation and stigmatisation, which may perpetuate depressive symptoms. However, there has been little quantitative research into the social aspects of diabetes or depression and diabetes.

Treatment for depression in diabetes

In the UK, depression in people with diabetes has been recognised by the NHS as a priority, and depression screening is now included within the UK diabetes annual review. National Institute for health and Clinical Excellence (NICE) guidelines suggest that general practitioners and



practice nurses should each play an active role in assessment.⁶⁵ NICE recommends that the treatment of mild depression may include watchful waiting by the primary care health team, guided self-help, computerised cognitive-behavioural therapy (CBT), brief psychological interventions and exercise; moderate to severe depression may be treated with more complex psychological interventions and pharmacotherapy.⁶⁶

If adverse outcomes in people with diabetes and depression are mediated by self-neglect, we would expect that treating depression would result in improvements in mood and diabetes. However, while pharmacological and psychological treatments for depression improve depression,⁶⁷⁻⁷⁴ the evidence that they also improve glycaemic control is inconsistent and unproven.⁶⁷⁻⁷⁴ A randomised controlled trial (RCT) of relapse prevention of depression in diabetes (performed after a period of open-label sertraline to treat the current episode of depression) found that when patients were randomised to prophylactic sertraline there was no further improvement in glycaemic control, following an initial improvement in the open-label stage.⁶⁹

Studies utilising psychological therapy for the treatment of depression have demonstrated more success, in as much as they appear to improve both the diabetes and the depression. However, there have only been two published RCTs of CBT for depressed people with diabetes.^{71,72} In the first study, which was performed in the USA, 51 people with diabetes, major depression and suboptimal glycaemic control were randomised to either group CBT or an educational control. At 6 months there was a greater resolution of depression in the CBT group compared with the control group and a significant improvement in HbA_{1c} levels.⁷² The second study took place

in China and involved 59 people with depression, diabetes and suboptimal glycaemic control who were randomised to receive 3 months' group counselling and individual CBT for 8 weeks, or standard diabetes treatment.⁷¹ At 3 months' follow-up there was significant improvement in depression scores and HbA_{1c} in the group who received counselling and CBT.

A stepwise or mixed model approach to the treatment of depression in people with diabetes has gained popularity in recent years. Some patients prefer medication whereas others prefer a more psychologically focused strategy. Three RCTs have studied this approach, all of which used similar intervention models and allowed patients to make their own decisions regarding the treatment course.⁷³⁻⁷⁵ All three studies showed an improvement in depression, but no significant improvement in glycaemic control. The most well-known of these RCTs, the US Pathways study,⁷³ recruited 329 people with major depression or dysthymia and poor diabetes control, and randomly assigned them to either Pathways case management or were given recommendations to work with their GP on issues related to depression.⁷³ Pathways case management involved either a problem-solving intervention from a nurse or antidepressant therapy, and if patients showed no improvement after 12 weeks they could switch treatments or be referred to a speciality mental health service. At 12 months there was a significant improvement in depression in the treatment group compared with the control group, and although a reduction in HbA_{1c} levels was found in both groups, this was non-significant.

Treatment studies show wide variations in the methods used to detect depression and as most have short follow-ups we do not yet know which treatments are most successful in

relapse prevention. The rate of relapse in people with depression and diabetes is thought to be high,²⁵ but large prospective studies are needed to determine factors associated with relapse and the long-term consequences aside from mortality.

Conclusions

Research into the epidemiology of depression in people with diabetes suggests that it is a common and chronic disorder. Depression is associated with multiple adverse outcomes, but its treatment – whether psychological or pharmacological – can alleviate symptoms, at least in the short-term. Research into the pathological mechanisms that may explain the association between depression and diabetes has examined common developmental factors, the psychological response to increased disease burden and potential biological pathways. Further research into these areas will bring with them implications for the treatment of depression in people with diabetes and, potentially, interventions that prevent its onset. What is clear is that assessment and treatment of depression in diabetes is a necessary and integral part of diabetes management.

Conflict of interest statement

K Winkley has received fees for lecturing from Eli Lilly.

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