### **Depression and diabetes**

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### Abstract

There is an epidemic of diabetes mellitus, mainly due to the increasing prevalence of type 2 diabetes, and, as for other chronic medical conditions, the rates of depressive disorder in patients with diabetes are increased two-fold. Depression is associated with multiple adverse biomedical, economic, and psychological outcomes. There may be other psychiatric conditions, such as eating problems, that coexist with depression in diabetes. The pathogenesis of co-morbidity is likely to be complex; there is emerging interest in shared genetic and environmental factors that contribute to both conditions. The well-known problem of poor detection and treatment of depression in the medical setting also applies to people with diabetes. There have been few well-conducted studies evaluating the treatment of depression in diabetes. Nearly all treatments, pharmacological, psychological, and combined or steppedcare models, lead to improvements in mood but there is little evidence that current treatments for depression in diabetes also lead to improvement in glycaemic control. This suggests that treatment probably needs to include diabetes-specific components to improve confidence and diabetes self-management.

**Keywords** antidepressants; diabetes complications; diabetes mellitus; depression; epidemiology; glycosylated haemoglobin; mortality; psychotherapy

Diabetes mellitus is one of the most common chronic diseases worldwide and is characterized by chronic hyperglycaemia which, if untreated, leads to macrovascular complications, such as myocardial infarction and cerebrovascular disease, and microvascular complications, such as nephropathy, retinopathy, and neuropathy. Type 1 diabetes is an autoimmune condition characterized by total insulin deficiency. Its peak ages of onset are around 5 and 18 years. Type 2 diabetes constitutes about 80–90% of all diabetes and is characterized by insulin resistance and insulin deficiency relative to the prevailing glucose levels. Its mean age of onset is 60 years, but increasingly presents in adolescence and early adulthood. The risk factors for type 2 diabetes are obesity, reduced physical activity, family history, and belonging to certain ethnic groups, mainly people of African,

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### **Management of diabetes**

At present, there is no cure, and people with diabetes have multiple self-care tasks such as administering insulin injections and oral medication, implementing specific diet, exercise, weight reduction, and injection sites regimens. Between one-third and one-half of patients with diabetes do not achieve targets for good metabolic control (which includes glycaemic levels as well as lipids, blood pressure, and weight control). Type 2 diabetes is a progressive condition, so that even with optimized intensive medical regimens in controlled settings glycaemic control continues to worsen over time (Figure 1).<sup>1</sup> A significant proportion of patients have clinically relevant difficulties with managing their self-care regimen despite receiving intensive medical, educational, and nursing input such as multiple injection regimens, continuous subcutaneous insulin infusion pumps, and structured



Overweight patients were assigned randomly to intensive or conventional groups; metformin was prescribed to some patients with poor glycaemic control (Adapted from UK Prospective Diabetes Study Group 1998)<sup>1</sup>

Figure 1

education programmes for carbohydrate counting and insulin adjustment. There is now substantial evidence that certain aspects of self-management and suboptimal glycaemic control are associated with a variety of psychiatric and psychological problems. For instance, for people with type 2 diabetes, insulin therapy is associated with weight gain, which leads to a negative effect on body image and contributes to resistance to uptake of insulin treatment.

### Epidemiology of depression in diabetes

Depression is the most common psychiatric disorder associated with diabetes, and may occur at several stages of the natural history of diabetes (Figure 2). It is twice as common in diabetes as in the general population, with a pooled prevalence of 9% using diagnostic interviews and 26% using depressive symptom scores on self-report scales. Prevalence rates at the beginning of the condition in adults (studied only in type 1 diabetes to date) do not appear to be raised,<sup>2</sup> but as the condition progresses the prevalence rates increase, similar to those observed for other chronic medical conditions such as cardiovascular disease.<sup>3</sup> In a systematic review of mainly secondary analyses of retrospective community cohorts, depression was associated with an increased risk of 37% for subsequent diabetes (predominantly type 2) in adults,<sup>4</sup> suggesting a temporal association between the two conditions. Depression is associated with hyperglycaemia, although in a systemic review and meta-analysis of mainly cross-sectional studies only a small pooled effect size (0.17) was observed.<sup>5</sup> There is around a three-fold increased risk of depression in people with diabetes complications,<sup>6</sup> even in children and young adults with type 1 diabetes.<sup>7</sup> There is a two- to five-fold increased risk of death in prospective cohort studies<sup>8–10</sup> (Figure 3). Depression is associated with mortality even when patients are suffering from mild or sub-clinical depression. Elderly patients with type 2 diabetes and those with complications seem to represent a highrisk group.<sup>11</sup>

Depression has a doubling effect on disability. Quality of life is reduced with respect to psychological, physical, and occupational functioning.<sup>12</sup> Diabetes-related burdens are perceived as more severe, and satisfaction with diabetes treatment is lower, when depression is present. Patients with depression and diabetes were less physically active, were more likely to smoke tobacco, had less healthful eating habits, and adhered less to diabetes treatment.<sup>13</sup> Depression is associated with a negative appraisal



Association of depression with diabetes at each stage



## Effect of depression on mortality in 253 patients with their first diabetic foot ulcer



For major depressive disorder, adjusted hazard ratio 2.73 (95% confidence interval 1.38 to 5.40) For minor depressive disorder, adjusted hazard ratio 3.23 (95% confidence interval 1.39 to 7.50) (Adapted from Ismail et al. 2007)<sup>10</sup>

### Figure 3

of insulin therapies in those who are insulin naive,<sup>11</sup> and this could delay diabetes treatment such as initiation of insulin therapy in type 2 diabetes. In a handful of selected clinic samples, the course of depression appears to be of longer duration, with more recurrences and of greater severity in people with diabetes. Diabetes is a costly condition, and co-morbid depression adds to the health care costs; in one study in the USA, there was a fourfold increase.

#### Multiple psychiatric co-morbidities in diabetes

To date, there have been few reports that other psychiatric disorders may coexist with depression in diabetes. Anecdotally, such coexistence is a common problem, but more epidemiological surveys are needed to confirm this observation.<sup>14</sup> Although studied less extensively, prevalence rates of anxiety disorders<sup>15</sup> and eating problems<sup>16-18</sup> are also increased in diabetes compared with those in healthy controls. As these disorders tend to cooccur with depression in the general population, this is likely also to be the case in diabetes. The implications of multiple psychiatric morbidities in diabetes for the prognosis and management of depression, as well as of the diabetes, also remains unknown but is likely to be deleterious. People with diabetes can have unhelpful diabetes-specific cognitions that may be part of, or independent of, depression or integral to the depressive syndrome.<sup>11,19</sup> It is important to enquire about these separately from the assessment of depression, as they may be relevant in the management of diabetes (Table 1).

### Pathogenic mechanisms

The pathogenesis for the association between depression and diabetes is still poorly understood, but there is likely to be a complex and multifactorial interaction between physiological, psychological, and social processes, and several suggestions have been proposed. There are two, not mutually exclusive, questions: (1) why is depression so common in diabetes and (2) what are

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