The prevalence and clinical impact of depression in South Asian and White European people with type 1 and type 2 diabetes in the UK.

Thesis submitted for the degree of Doctor of Philosophy

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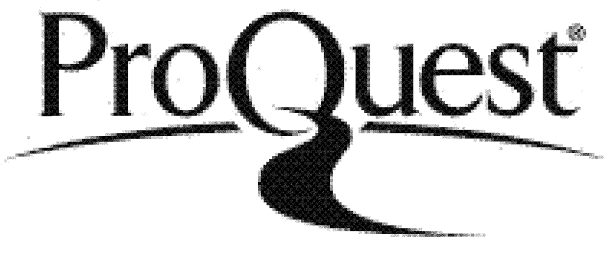

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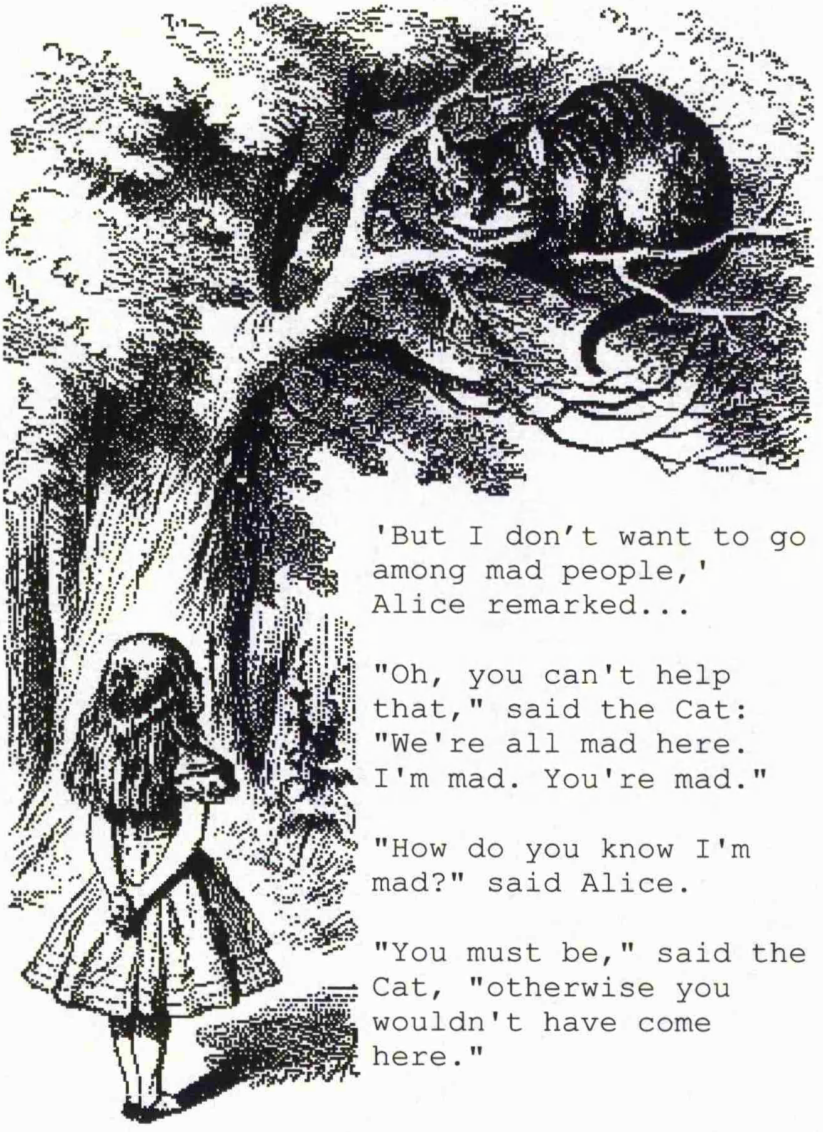
Dedication

To my Uncle Idris



'But I don't want to go among mad people,' Alice remarked...

"Oh, you can't help that," said the Cat: "We're all mad here. I'm mad. You're mad."

"How do you know I'm mad?" said Alice.

"You must be," said the Cat, "otherwise you wouldn't have come here."

Lewis Carroll, Alice's Adventures in Wonderland
Illustration: John Tenniel

Abstract

Depression and diabetes are both common chronic disorders affecting people worldwide. Diabetes is characterised as a metabolic disorder often involving laborious self-management reduced health-related quality of life and often the prospect of diabetes related complications. Depression on the other hand, is a mood disorder associated with high levels of personal disability, lost quality of life, multiple morbidity and an increased risk of mortality. The adverse effects of depression may be especially detrimental in people with diabetes.

This thesis presents the results of a programme of work beginning with two systematic reviews which demonstrate that the prevalence of depression is almost doubled in those with type 2 diabetes relative to those without and in addition is associated with worsened health related quality of life in those with comorbidity.

The second phase of the research involved examining ethnic differences in the prevalence of depression as well as associations between depression and glycaemic control in secondary care patients with diabetes. Although depression did not explain ethnic differences in glycaemic control, the findings suggested that depression may be under-diagnosed in South Asians with diabetes.

A need was highlighted to examine the prevalence of screen detected depression in a multiethnic population with type 2 diabetes relative to a suitable control group. The results from the final phase of the research concluded that although the prevalence of depression was not higher in primary care patients with type 2 diabetes compared to those without diabetes, the prevalence of depression in people with diabetes is nonetheless high, particularly in South Asians. Furthermore, findings from the final stage of the research conclude that depression is seriously under-diagnosed in people with type 2 diabetes, particularly in South Asians. The findings emphasise the need to improve the detection and management of depression to reduce inequalities in both depression and diabetes care.

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"I would challenge anybody in their darkest moment to write what they're grateful for, even stupid little things like the green grass that made them feel good, or the friendly conversation with somebody on an elevator. You start to realise how rich you are."
-Jim Carrey

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Saima xxx

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Abbreviations

ADA =American Diabetes Association
ADDQoL= Audit of Diabetes-Dependent Quality of Life
BDI = Beck Depression Inventory
BMI = Body Mass Index
BNF = British National Formulary
CBT = Cognitive Behavioural therapy
CES-D = Centre for Epidemiologic Studies Depression Scale
CHD = Conroy Heart Disease
CI = Confidence intervals
CIDI = Composite International Diagnostic Interview
COPD = Chronic obstructive pulmonary disease
CVD= Cardiovascular disease
CWS= Clinical work station
DBP/ SBP = Diastolic Blood Pressure / SBP = Systolic blood pressure
DIS = Diagnostic Interview Schedule
D-QOL = Diabetes Quality of Life
DSM-IV = Diagnostic and Statistical Manual of Mental Disorders- Fourth edition
ECT = Electroconvulsive therapy
EMIS = Egton Medical information System
FPG = Fasting plasma glucose
GP = General Practitioner
HADS = Hospital Anxiety and Depression Scale
HANDS National Depression Screening Scale
HbA1c = Glycosylated haemoglobin
HDL = High density lipoprotein
HPA = Hypothalamic Pituitary Andrencortical
HRQOL = Health Related Quality of Life
HUI-III = Health Utilities Index- III
IBD = Inflammatory Bowel Disease
IBS = Irritable Bowel Syndrome
IFD = International Diabetes Federation
IMDS/R = Indices of Multiple Deprivation Score/Rank
LDL = Low density lipoprotein
MAO-I = Mono Amine Oxidase Inhibitors
MI = Myocardial Infarction
MID = Minimally important difference
MIQUEST = Morbidity, Information Query Syntax
MODY = Maturity Onset Diabetes of the Young
NHEFS = Nutrition Examination Survey Epidemiological Follow up Study
NHS = National Health Service
NICE = National Institute of Clinical Excellence
NSF = National Service Framework
OAD = Oral Anti-Diabetic medication
OCD = Obsessive Compulsive Disorder

OGTT = Oral glucose tolerance test
OR = Odds ratio
PHQ-2 and PHQ-9 = Patient Health Questionnaire
PROM = Patient reported outcome measure
PTSD = Post Traumatic Stress Disorder
PPUFA = Polyunsaturated fatty acid
QAYLS = Quality Adjusted Life Years
QOF = Quality and Outcome Framework
RCT = Randomised Control Trial
SA = South Asians
SCID = Structured Clinical Interview for DSM
SCL-90- R = Hopkins Symptom Checklist Revised
SF-36 = Medical Outcome Study Short Form Health Survey
SOAs = Super Output Areas
SSRI = Serotonin Selective Reuptake Inhibitors
TCA = Tricyclic Antidepressants
TIA = Transient Ischemic Attack
WE = White Europeans
WHO = World Health Organisation
WHO-DAS-II = World Health Organisation-Disability Assessment Schedule-II
ZSRD = Zung Self Rating Depression scale

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Chapter 1

General introduction

1.1 South Asians

The diversity in ethnic composition of many industrialised countries has fuelled the need for both researchers and healthcare providers to gain further understanding of the health and well-being of culturally diverse populations. In addition the need to reduce inequalities in health outcomes between minority and majority ethnic groups is increasingly important and now widely recognised by both governmental groups [1] and health care providers [2]. In the UK, Census figures demonstrate that the total population of Black and Asian minority ethnic groups is relatively large and rising. In 2001 the population estimate was 4.6 million (7.9% of the UK population), having risen from 5.5% in 1991 and 4.2 in 1981 [3].

The term 'South Asian' is an umbrella term used to refer to individuals with origins in India, Pakistan, Bangladesh or Sri Lanka. South Asians represent the largest of the minority groups, accounting for approximately 4% of the total UK population. Specifically these groups can be broken down into Indian (1.8%), Pakistani (1.3%), Bangladeshi (0.5%) and other (0.5%). Of these approximately 46% of Indian and Bangladeshi groups and 55% of Pakistanis were born within the UK [4].

The definition of 'ethnicity' and 'ethnic group' is a complex subject and it is important to recognise that South Asians represent a heterogeneous group and that within group diversity is not solely based on the country of origin, but also differences in a range of factors including language, customs, religious beliefs and rural-urban background. For example Indian subgroups are diverse in terms of religion, consisting of Hindus (45%),

Sikhs (29%) and Muslims (13%). In contrast Pakistani and Bangladeshi subgroups represent more homogenous religious sub-groups with 92% identifying themselves as Muslim [5]. There are also wide variations in the languages spoken and levels of literacy. Verbal fluency in a particular language does not necessarily imply literacy in that language or in English [6] and generally these skills become less likely with increasing age as well as in women and those born outside of the UK [7]. The mass migration of South Asians to the UK has typically occurred in two main waves. The first wave of migration in the late 1950s largely included Sikh Punjabis from India and Muslims from Pakistan and India and Pakistanis. These groups were largely manual workers living within deprived inner city areas of the UK [8]. These groups were generally not well-educated with low levels of literacy [8]. Furthermore many second and third generation South Asians born in the UK continue to live in poor, socially deprived inner city areas [8]. The second wave of migration involving East African Asians occurred in the mid 1970s, due to political expulsion from Kenya, Uganda and Zanzibar. This group largely consisted of educated Guajarati's who were established business people in East Africa[8].

There are also large differences in the level of acculturation, which can be defined as a process in which members of one culture may acquire the norms in terms of attitudes, beliefs and behaviour of another (host) culture[9]. Although it is important to note that length of time in the UK and English literacy do not specifically measure the degree of acculturation, they are often used in the literature on minority ethnic communities as proxy measures of acculturation to the host country [9].

1.2 South Asians and health

Regardless of the heterogeneity observed among the South Asians in the UK, some issues remain consistently relevant, for instance disadvantage and discrimination characterise the experience of many minority ethnic groups. These issues are particularly evident in the area of health and healthcare. South Asians in the UK often experience higher levels of morbidity and mortality compared to the majority White population for a range of chronic conditions [10, 11]. For example the 2001 census revealed that South Asians are more likely to suffer from long-term limiting illnesses in comparison to White Europeans [12]. Even after standardising for age, South Asians are at increased risk of diabetes, coronary artery disease, arthritis, stroke, and respiratory disorders which in turn predisposes them to increased levels of disabling long-term illness in comparison to the general population. There is also an increased likelihood of experiencing higher levels of disability in old age and a greater risk of becoming dependent on others at an earlier age than their White European counterparts in the general population [12]. However, despite comprising the highest users of primary care services, South Asians are less likely to access appropriate services and treatment [13]. Communication difficulties as a result of language barriers, different beliefs regarding health and illness, and problems associated with illiteracy may offer some explanation for these disparities [6]. In addition health may be compromised due to socioeconomic factors including poverty, unemployment and poor housing, as well as the psychological and physical impact of racism and discrimination in everyday life [14, 15].

A significant health concern facing South Asians in the UK is in relation to the increased prevalence of diabetes, which may be up to 6 times higher in comparison to White indigenous population [16-19]. The higher prevalence of diabetes in South Asians is also associated with knock on effects to a range of other conditions, particularly microvascular complications including end-stage renal failure [20] and an increased risk of cardiovascular morbidity and mortality [21].

1.3 Diabetes mellitus

The term diabetes mellitus refers to a group of metabolic disorders characterised by elevated levels of blood glucose caused by the body's inability to sufficiently produce and or effectively utilise the hormone insulin [22]. Over 11 different types of diabetes have been classified based on the aetiological origins of the condition, however the majority of cases fall into one of two main categories; namely type 1 diabetes (formerly referred to as insulin dependent diabetes mellitus or juvenile-onset diabetes mellitus) and type 2 diabetes (formerly referred to non-insulin dependent diabetes mellitus) [23, 24].

1.4 Type 1 diabetes mellitus

Type 1 diabetes accounts for 5-10% of those with diabetes and is characterised by absolute insulin deficiency caused by the destruction of pancreatic beta-cells located in the Islets of Langerhans [24]. Beta-cell destruction may be attributable to a cellular-mediated auto-immune mechanism caused by a combination of genetic or

environmental factors (immune mediated), or may occur via a process independent to autoantibodies (idiopathic diabetes) [24]. In those with the auto-immune mediated form of the condition, beta-cell destruction occurs at a rapidly faster rate in infants and children than in adults, leading to a faster progression to the clinical manifestations of type 1 diabetes [25]. Although the peak incidence of this form of type 1 diabetes usually occurs in children and adults, the onset can occur at any age including up to the ninth decade of life [23]. The secretion of insulin is virtually minimal or ceases to exist and as a result individuals are dependent on insulin replacement therapy for survival.

1.5 Type 2 diabetes mellitus

Type 2 diabetes represents the most common form of diabetes accounting for up to 90% of cases [25]. Unlike type 1 diabetes, type 2 diabetes develops progressively and occurs most often in adults [25], although the number of cases in children and younger adults has rapidly increased in recent years [26]. Type 2 diabetes is characterised by increasing insulin resistance, and it is often coupled with a decline in insulin secretion. However the production of insulin may not be entirely compromised and initially people with type 2 diabetes may be managed with lifestyle changes and oral anti-diabetic medication.

People with type 2 diabetes are often obese or may have increased abdominal body fat, which in itself has been associated with insulin resistance [24] therefore insulin sensitivity may be improved to some extent by weight loss [24]. The specific aetiology of type 2 diabetes remains an area of intense research although a number of risk factors

have been identified [24]. These include; age > 40 years, obesity, physical inactivity, history of diabetes in pregnancy (gestational diabetes, presence of hypertension or dyslipidemia and a family history of diabetes. Studies have also demonstrated an inverse association between higher socioeconomic status and type 2 diabetes [27, 28] as well as differential rates in various racial/ ethnic groups [24]. In recent years there has also been suggestion that depressive disorder may also be associated with an increased risk for diabetes [29].

1.6 Diagnosis of diabetes

A diagnosis of diabetes mellitus may be ascertained by any of the three methods detailed in Table 1.1 (ADA recommendations) [24]. Cases are diagnosed on the basis of elevated blood glucose levels or hyperglycaemia, however in the absence of symptoms such as increased thirst, frequent urination and tiredness and fatigue, each method should be confirmed by repeat testing on a subsequent day [24]

Table 1.1 Criteria for the diagnosis of diabetes*

1	FPG ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 hours.
	OR
2	Symptoms of hyperglycemia and a casual plasma glucose ≥200 mg/dl (11.1 mmol/l). Casual is defined as any time of day without regard to time since last meal. The classic symptoms of hyperglycemia include polyuria, polydipsia, and unexplained weight loss.
	OR
3	2-h plasma glucose ≥200 mg/dl (11.1 mmol/l) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.

* Table adapted from ADA 2009 [24]. FPG = Fasting plasma glucose, OGTT= Oral glucose tolerance test

1.7 Epidemiology of diabetes mellitus

The prevalence of diabetes has taken on epidemic proportions and continues to grow. The latest figures from the International Diabetes Federation 2006 (IFD) demonstrate the enormity of the epidemic with an estimated total of 246 million cases worldwide, with 46% of those affected falling within the 40-59 age range [30]. Furthermore these figures predict that at the current rate of increase, the total number of people living with diabetes will rise to 380 million by the year 2025[30]. In the UK the current estimate of diagnosed diabetes is approximately 4% of the total population, although the exact figures will vary according to factors such age, ethnicity and socioeconomic status [31]. However it is clear that not all cases of diabetes are recognised and it is estimated that approximately a quarter of those with diabetes are undiagnosed [32].

The prevalence of type 2 diabetes is up to 6 times more likely in South Asians in the UK in comparison to White Europeans [16-19]. Furthermore the age of onset in South Asians may be up to a decade earlier and the condition can remain undiagnosed in up to 40% of individuals [33]. The reasons for ethnic disparities in the incidence of type 2 diabetes are complicated and likely to be multifactorial. Possible contributors include environmental and genetic factors as well as increased central (intra-abdominal) obesity and hyperinsulinaemia [34]. South Asians have been shown to demonstrate higher levels of insulin resistance even at an earlier age [35]. Furthermore it is also noted that the association between obesity and insulin resistance may occur at a lower threshold in South Asians in comparison to White Europeans. For example several studies demonstrate that Indian patients show an increased risk of glucose intolerance at a

much lower threshold of waist circumference (central obesity) than White Europeans [36].

There appears to have been less interest in examining ethnic differences in the prevalence of type 1 diabetes. Although the few studies available have previously reported a remarkably lower incidence of type 1 diabetes in children living in the Indian subcontinent [37], data suggest that the incidence may be increasing in UK South Asian populations [38], for example a recent UK study involving a large South Asian population demonstrated that the incidence of type 1 diabetes increased in South Asian immigrants to the UK from 3.1/ 100,000 per year to 11.7/100,000 per year over a period of ten years, approaching the figures for the indigenous White European population [39]. It is argued that genetic factors are unlikely to explain such a rapid increase in incidence and alternatively environmental factors may hold an important mediatory role [33].

1.8 Health and resource burden of diabetes mellitus

Chronic hyperglycaemia in those with diabetes is associated with an increased risk of developing a number of specific microvascular diabetes complications (including retinopathy, nephropathy and neuropathy) [40-42] and macrovascular complications (including ischemic heart disease, peripheral vascular disease and cerebrovascular disease) [43-45]. In 2002, deaths due to diabetes related complications accounted for approximately 6% of deaths worldwide[46]. For those with type 2 diabetes cardiovascular disease (CVD) is the leading cause of mortality, accounting for

approximately 70% of all deaths [47]. People with diabetes also have a 4-fold greater risk for having a CVD event than people without diabetes, even after controlling for the effects of traditional risk factors such as age, obesity, smoking, dyslipidemia, and hypertension[48, 49] (21, 22). Although CVD risk factors are common in those with diabetes, research also suggests that diabetes is an independent risk factor for CVD in itself. People with diabetes have a 5-fold increased risk for a first myocardial infarction (MI) and a 2-fold increased risk for a recurrent MI in comparison to those without diabetes but with a history of a previous MI. This suggests that those with type 2 diabetes are already at risk for serious secondary complications [50].

The development of diabetes related complications and the efforts required to prevent them are also known to have a profound impact on quality of life and thus people with diabetes have been shown to experience lowered physical and mental functioning in comparison to people without diabetes [51].

However in addition to the intense burden on patients, diabetes is also associated with significant costs to the National Health Service (NHS) in the UK, accounting for approximately 5% of NHS expenditure[52]. In 2002 this total cost was estimated at £1.3 billion annually, with much of the expenditure aimed at the management of diabetes related complications [53]. One in 20 people with diabetes are also estimated to incur social services cost, with costs increased four-fold in those with diabetes-related complications [54].

As the duration of diabetes is one of the strongest predictors for the development of diabetes related complications, coupled with the fact that South Asians present with diabetes at a significantly younger age in comparison to White Europeans, it comes as little surprise that South Asians are at increased risk for a number of diabetes related complications. Cardiovascular complications of diabetes are more common amongst South Asians, with a 50% higher mortality compared to White Europeans[55], and the development of premature coronary heart disease (below the age of 60) is also disproportionately increased in South Asians. South Asians with type 2 diabetes are also more likely to have higher rates of microalbuminuria (which in turn is associated with end-stage renal failure and cardiovascular mortality in diabetes) [56], end-stage renal failure [57, 58], and an increased risk retinopathy [59] in comparison to their White European counterparts. Mortality rates are 40 per cent higher in South Asians with type 2 diabetes compared to rates in the White European population [13, 60, 61]

Causal factors for these discrepancies in diabetes related outcomes are again likely to be multi-factorial and may be include central obesity, inappropriate diet, the presence of metabolic syndrome, reduced physical activity, as well as biochemical and genetic factors [33]. Cultural and social issues regarding awareness of diabetes, health beliefs and knowledge of preventative behaviours, as well as racism, discrimination and poor use and or access to health resources are also likely to play a significant role [14, 15, 33, 62]

1.9 Management of diabetes

There is currently no cure for diabetes, however results from large multicentre trials demonstrate that improved control of glycaemia as well as blood pressure significantly reduces the risk for both micro and macrovascular complications associated with diabetes [63-66].

The multiple risk factors for diabetes related complications require health care professionals to monitor multiple targets in order to reduce risks of future complications and also to improve health in those with diabetes[67, 68]. These targets include managing obesity, increasing physical activity levels, blood glucose control, blood pressure control, blood lipid control, reduction of thrombogenicity, laser therapy for eye damage, drug therapy to delay kidney damage, local foot care, and symptomatic treatments for various types of nerve damage. As a result, diabetes care is typically complex, time consuming and costly [68].

However, for those living with diabetes, the condition requires self-management on a daily basis in order to achieve optimum glycaemic control. There is a need to consider and maintain a multitude of self-care activities including life style modifications (changes to dietary intake, weight management and maintaining or increasing levels of physical activity), self-monitoring (including monitoring blood glucose concentrations where recommended and foot care) as well as managing and administering medications including oral anti-diabetic medication and in later stages insulin injections. For those receiving insulin therapy there is the added onus of calculating and measuring insulin dosages in response to blood glucose fluctuations and managing hypoglycaemic

episodes. Self-management of diabetes is therefore a complex task, and thus it is clear that patient education and an empowering approach to aid those with diabetes to successfully cope with and maintain life style modifications should play a fundamental role in diabetes management strategies [68].

Despite receiving diabetes education and intensive medical management, a significant proportion of people with diabetes continue to demonstrate clinically relevant difficulties in adhering to self-management activities and maintaining optimum blood glucose levels [63, 69, 70]. However there is now substantial evidence that the management of diabetes and achieving optimal outcomes may be compromised by psychological difficulties. In particular, depression represents one of the most commonly manifest and frequently researched psychological disturbances in people with diabetes.

1.10 Depression classification and diagnosis

The term depression refers to a spectrum of mood disturbance which may range from mild symptoms which affect most people from time to time to severe symptoms. A central feature for a diagnosis of major depressive disorder includes persistent and pervasive low mood, which when severe enough may be accompanied by tearfulness and loss of interest or pleasure in usual activities [71]. As the condition worsens, it becomes more pervasive and a range of other symptoms may develop [72]. These include a phenomenon referred to as negative affectivity, which is characterised by persistent negative views, including feelings of worthlessness, guilt about the past and

pessimism about the future. Suicidal ideation may develop and sleep and appetite disturbances are common. Other physical symptoms can include loss of energy, psychomotor retardation (slowness in movement and speech) and impaired concentration [72]. Criteria according to the Diagnosis and Statistical Manual of Mental Disorders (DSM-IV)[73] are shown in Table 1.2

Table 1.2 DSM Criteria for Major Depression*

Must be present
• Depressed mood • Decreased interest or pleasure
Five or more of the following symptoms during the same two week period representing a change from normal
• Substantial weight loss or weight gain • Insomnia or hypersomnia • Feelings of worthlessness or inappropriate guilt • Recurrent thoughts of death or suicide or suicide attempt • Psychomotor retardation or agitation • Fatigue or loss of energy • Diminished ability to think or Concentrate
**From Diagnostic and Statistical Manual of Mental Disorders, fourth edition [73]*

Diagnostic interviews such as the Structured Clinical Interview for DSM (SCID) are currently considered the gold standard for a research diagnosis of depression [74]. However the expense and time-consuming nature of their administration often precludes such methods for screening depression in epidemiological research. Self-report symptom checklists on the other hand are simpler to administer and consequently inexpensive alternative to diagnostic interviews and as such, represent the most widely used method of depression assessment in studies of people with and without diabetes as well as in clinical practice [75, 76].

1.11 Epidemiology of depression

Depression is common in the general population as well as in those attending primary care general practices. It is estimated that 5% of the general population suffers from depression at any point in time [72].

Causes for depression may include stressful life events and losses, lack of social support, physical illness and pre-disposing familial and genetic factors [72]. One in five people suffering from depression will not recover fully from a first episode, and 70–80% of those achieving remission will relapse at least once [77]. The long-term reoccurring nature of depression magnifies the economic burden associated with the disorder. Depression is a global concern and according to World Health Organisation predictions, by the year 2020 will rank only second to coronary heart disease as the greatest cause of disability[78]. The burden of depression was also highlighted by a recent survey conducted in 60 countries which showed depression to have the strongest impact on worsening health in comparison to other chronic diseases including angina, arthritis, asthma and diabetes [79]. People with depression in addition to another chronic illness were also found to have the worst health measures of all disease states [79]. Depression appears to be strongly associated with physical disease as up to a third of physically ill patients attending hospital are recognised as depressed [71]. Although South Asians in the UK have a higher prevalence of a number of medical conditions including cardiovascular disease and diabetes [16, 20, 21], the incidence of mental health problems in this population is still not fully known.

Risks of suicide and attempted suicide are disproportionally increased in South Asian women in comparison to their White European counterparts[80]. Although depression is believed to precede the large majority of all completed suicides, studies into the rates of depression in South Asians have suggested that the incidence of common mental disorders including depression and anxiety are lower in South Asians in the UK. For example the 4th National Survey of Ethnic Minorities [81] concluded that the rates of both psychotic and non-psychotic mental illness among South Asians were lower in comparison to White Ethnic groups. However the authors of the survey later acknowledged that the instruments used in the survey may not have been culturally or linguistically appropriate, which may have contributed to the apparently low observed prevalence rates [82].

Studies have also focussed on ethnic differences in rates of general practice consultations. Gillam et al [83] examined ethnic variations in the rates of general practice consultations and the outcomes of the consultations among different ethnic groups using retrospective data collected from general practice records. South Asians including those of Pakistani and Indian origin were found to consult their general practitioner (GP) more frequently in comparison to White Europeans, except for in the case of mental disorders, for which there were lower consultation rates, particularly in women. Similarly, studies examining the prevalence of depression based on antidepressant prescribing have found lower rates in practices with a higher number of South Asians in their practice population[84]. Although these findings may be taken to suggest that South Asians may experience lower levels of psychological distress,

differences may also be due to a lack of recognition or differences in presentation of depression.

1.12 Depression in people with diabetes

A plethora of studies have suggested increased rates of depression in people with diabetes as well as an increased risk for a number of adverse diabetes related consequences associated with this comorbidity [75, 85, 86]. A systematic review and meta-analysis of largely cross-sectional studies concluded that the presence of comorbid depression in those with diabetes was associated with hyperglycaemia, although the overall effect size was relatively small (0.17)[85]. In addition cross-sectional studies associate depression with multiple diabetes related complications such as neuropathy [87] and cardiovascular disease [88]. A meta-analysis of 27 studies, including those with both type 1 and type 2 diabetes, concluded a threefold increased risk of depression in those with a range of diabetes related complications including retinopathy, nephropathy, neuropathy, macrovascular complications, and sexual dysfunction [86]. The detrimental impact of this comorbidity may also be additive or synergistic in nature as depression is also associated with increased disability and health status not only in relation to those with diabetes and without depression but also in relation to those with depression but without diabetes [89]. Depression may complicate the management of diabetes via impairments in collaborative self-care strategies, including appropriate dietary behaviour and physical activity [90, 91]. Furthermore, even low levels of depressive symptomatology have been associated with fewer days of glucose self-monitoring and an increased odds for missing medication

[91]. High levels of depression have also been associated with a tendency towards negative beliefs about insulin in insulin naïve people with type 2 diabetes, which may in turn delay the initiation of insulin therapy [92]. Depression in individuals with diabetes is also associated with significantly increased healthcare costs; although there have been no estimates in the UK, a study conducted in the USA reported that in those with comorbid depression with diabetes, the total health care expenditure was 4.5 times higher than that for individuals without depression [93].

The course of depression also appears to be more chronic in those with diabetes with lower rates of remission and higher rates of relapse in comparison to those without diabetes [94-97]. Both major and sub-clinical forms of depression in people with diabetes are also associated with a two to five fold increased risk of mortality in prospective analyses [98, 99].

The pervasive impact of depression throughout the natural history of diabetes is further demonstrated by the suggestion of a temporal association. A systematic review of prospective studies concluded that depression was associated with an increased risk of developing diabetes by 37 percent, a finding which ranks depression as a diabetes risk factor comparable to smoking or lack of exercise [29].

1.13 Pathogenic mechanisms

Several factors are postulated to contribute to the association between depression and diabetes and consequential adverse outcomes. Although the exact mechanisms remain unclear, evidence suggests that a complex interaction between biological, psychological

and social processes is likely to be at play. Talbot and Nouwen [100] conducted a comprehensive review in order to examine whether increased rates of depression in those with diabetes may be attributable to the biochemical effects of the diabetes or its treatment, or whether increased rates are a result of the psychosocial demands or psychological factors linked to diabetes or its treatment. Findings from the review suggested that the initial onset of major depressive disorder was independent of the onset of type 2 diabetes and is thus unlikely to be due the biological impact of diabetes or the psychosocial demands imposed by the illness or its management, although findings were less clear in studies involving type 1 diabetes [100].

Both depression and diabetes are common conditions and it is possible that the two may have shared aetiological origins including environmental and genetic factors [101]. Research has examined the association between depression and changes in certain metabolic pathways which may contribute to insulin resistance and/ or pancreatic beta-islet cell dysfunction, and which may in turn explain the association between depression and the onset of type 2 diabetes as well as adverse metabolic consequences in those with established diabetes[102]. Firstly, depression is associated with an increased release of counter-regulatory hormones, which act to increase blood glucose levels (catecholamines, glucocorticoids, growth hormones and glucagons). Numerous reports suggest that depression is associated with increased activity of the hypothalamic-pituitary-adrenocortical (HPA) axis, resulting in an increase in cortisol, adrenalin and noradrenalin release. Cortisol stimulates glucose production and increases lipolysis and circulating fatty acids and in addition causes a decrease in

insulin production from beta-cells and decreases sensitivity to insulin. It is hypothesised that chronically high levels of cortisol are associated with central adiposity, insulin resistance and the development of type 2 diabetes/ poorer metabolic control [29, 102-106]. Adrenalin may also have an impact on glucose and fat metabolism possibly resulting in increased insulin resistance and type 2 diabetes [29]. Secondly it is hypothesised that increased rates of type 2 diabetes and adverse outcomes may result from dysregulation of the immune system. Emerging evidence suggests that certain inflammatory factors including C-reactive protein, TNF-alpha and proinflammatory cytokines such as interleukin-6 may play a role in the aetiological pathway to insulin resistance; furthermore these factors are also increased in those with depression [102, 107-110]. Most recently there has been a suggestion that the onset of both depression and type 2 diabetes may be related to impairments in Omega-3 polyunsaturated fatty acid (PUFA) metabolism that accompanies these conditions. Omega-3 PUFAs have been associated with cerebral functioning and the depletion of these acids is linked to depression. In addition a low intake of Omea-3 PUFA is associated with the development of well known components of the metabolic syndrome including dyslipidemia, insulin resistance, hypertension and cardiovascular disease [111].

Depression may also be linked indirectly to the development of diabetes and related complications via associations with behavioural factors such as reduced self care [112]and physical inactivity, a strong risk factor for type 2 diabetes and poor control [113]. Symptoms of depression such as a lack of energy and insufficient levels of motivation may explain the reduction in diabetes related self care activities. In addition the association between depression and negative patterns of cognition, internalizing and

pessimistic attribution styles and passive coping as opposed to solution-focused coping strategies may all reduce the likelihood of engagement with collaborative self-management goals and the importance placed on following self care regimens [114-116]. Furthermore, cross-sectional studies have repeatedly demonstrated associations between low levels of physical activity, diabetes, and depression [113]. Longitudinal studies demonstrate that people with higher levels of physical activity have better diabetes related outcomes, and most studies indicate that individuals who are less physically active are more likely to develop depression [117-119].

Depression may also lead to suboptimal patient-provider interactions, possibly as result of poor communication [120]. Communication between patients and providers represents a fundamental aspect of healthcare and may be particularly pertinent for those with depression and diabetes as the quality of communication may predict satisfaction with treatment as well as understanding of self-management and subsequent health care behaviour and glycaemic control [121, 122]. Primary care providers are more likely to view depressed patients as more difficult and also as less able to cope with their diabetes and in turn these perceptions may influence both their communication and management styles [123]. Finally health care utilization and subsequent diabetes care in those with depression may be influenced by factors such as social isolation and stigma.

Overall these findings suggest that depression can be integral to the development of diabetes as well as its clinical characteristics and once manifest, may cause further

detriment via several pathways. Additional research evidence is undoubtedly required in order to substantiate these hypotheses. Furthermore, it is not unreasonable to assume that the exact contribution of these factors may be moderated by a number of factors and thus they are likely to vary from person to person. Such factors may include education, access to healthcare, social support and ethnic/ cultural differences. Data examining the differential rates of and the impact of depression in a variety of cultural/ethnic groups with diabetes are emerging [89, 124-126], although no research has specifically examined the association in South Asians in the UK despite their increased risk for type 2 diabetes and adverse diabetes related consequences. Examining ethnic variations in the relationship between depression and diabetes has the potential to play an important role in the aetiological understanding of this comorbidity and also provide novel targets for tackling inequalities in terms of the rates of diabetes and adverse outcomes observed between different ethnic groups.

1.14 Treatment for depression in diabetes and current UK policy

The benefits of treating depression in those with diabetes are recognised for both improvements in mood as well as diabetes related outcomes, although it is important to consider that the evidence is currently limited. A review of published randomised controlled trials of the effectiveness of three types of interventions for depression, including pharmacological, psychological and managed care packages in people with diabetes concluded that antidepressant therapy may be effective in alleviating symptoms of depression, although they did not show a beneficial effect for diabetes related outcomes including glycaemic control. Psychological treatments on the other

hand appeared to offer superior results in terms of both medical and psychological variables [127]. However the authors concluded that many of the studies included in the review had methodological shortcomings such as small sample sizes and a short duration of follow-up [127]. Also due to study heterogeneity the authors were unable to recommend the single most beneficial treatment based on meta-analysis of the findings [127].

A number of studies in the USA have examined interventions combining both psychological and pharmacological treatment in comparison to standard care. Of these, the Pathways study by Katon et al is possibly the most well-known [128]. Participants with depression and poor diabetes control were randomly assigned to either the Pathways case management intervention or were given recommendations to work with their GP on issues related to depression [128]. The combined intervention involved either a problem-solving intervention from a nurse or antidepressant therapy, and those showing no improvement after 12 weeks were provided with alternative treatment options or were 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, although the reduction in HbA1c levels was not found to be significant [128].

In the UK, guidelines for the treatment and management of depression recommend screening for those with chronic medical illness as well as diabetes specifically [77, 129]. A number of national policy documents also highlight the importance of promoting psychological well-being as well as integrating such care into diabetes

services [130, 131]. The diabetes commissioning toolkit [132] involves the commissioning of services as well as models of best practice to ensure improved quality of care for those with diabetes in the UK. According to the toolkit, the NSF delivery strategy, the Quality and Outcomes Framework (QOF) [31, 133] indicators for depression (Table 1.3) and agreed local pathways to follow up people with diagnosed depression and diabetes can all be used as markers for best practice and evidence for improvement may be demonstrated via audit or measurement of adherence to local protocols [132].

Table 1.3 Quality and Outcomes Framework indicators for depression[31, 133]

Indicators	
DEP 1	The percentage of patients on the diabetes register and /or the CHD register for whom case finding or depression has been undertaken on one occasion during the previous 15 months using two standard screening questions
DEP 2	In those patients with a new diagnosis of depression, recorded between the preceding 1 April to 31 March, the percentage of patients who have had an assessment of severity at the outset of treatment using an assessment tool validated for use in primary care
DEP 3*	In those patients with a new diagnosis of depression and assessment of severity recorded between the preceding 1 April to 31 March, the percentage of patients who have had a further assessment of severity 5-12 weeks (inclusive) after the initial recording of the assessment of severity. Both assessments should be completed using an assessment tool validated for use in primary care

*New Indicator 2009/10[133]

The two standard questions referred to in indicator DEP 1 are;

• 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?

Together these questions form the PHQ-2 and those screening positively are recommended to receive further assessment. It is recommended that the severity of depression is ascertained in all diagnosed cases using one of three screening questionnaires; the Patient Health Questionnaire, Beck-Depression Inventory (BDI) or the Hospital Anxiety and Depression Scale (HADS)[31, 133]. The questionnaires enable depression to be classified as mild, moderate or severe in order to facilitate a stepped care approach to the treatment and management of depression as recommended by the National Institute of Clinical Excellence (NICE)[77], so that different management strategies are offered according to depression severity (Table 1.4). For example mild cases of depression may be managed by watchful waiting, exercise, guided self-help, computerised cognitive-behavioural therapy (CBT), or brief psychological interventions [77]. Antidepressant medication or complex psychological interventions are recommended for those with severe levels of depression [77]. It is yet to be seen whether the introduction of QOF indicators for depression in primary care patients with diabetes will lead to any improvement in either depression or diabetes related outcomes.

Table 1.4 The stepped-care approach to the management of depression. Adapted from NICE 2004 [77].

Level of care	Stage of depression	Intervention
Step 1: GP, practice nurse	Recognition	Assessment
Step 2: Primary care team, primary care mental health worker	Mild depression	Watchful waiting, guided self-help, computerised CBT*, exercise, brief psychological interventions
Step 3: Primary care team, primary care mental health worker	Moderate or severe depression	Medication, psychological interventions, combined Treatments
Step 4: Mental health specialists, including crisis team	Treatment-resistant, recurrent, atypical, and psychotic depression, and those at significant risk	Medication, complex psychological interventions, combined treatments
Step 5: In-patient care, crisis teams	Risk to life, severe self-neglect	Medication, combined treatments, ECT*
**** CBT, cognitive behavioural therapy; ECT, electroconvulsive therapy.***		

1.15 Thesis objectives and outline

The mains objectives of the present thesis are to examine the association between depression and diabetes, specifically in the context of a multi-ethnic UK population.

The remainder of this thesis is organised as follows:

Chapter 2 describes a systematic literature review and meta-analysis which was conducted at the outset of this thesis to examine the prevalence of depression in people with diabetes relative to those without.

Chapter 3 considers the literature examining the association between depression and health related quality of life in those with diabetes.

Chapter 4 examines ethnic differences in the prevalence of diagnosed depression in South Asians and White Europeans with Type 1 and Type 2 diabetes in a secondary care setting.

Chapter 5 presents data regarding the associations between depression and glycaemic control in a mixed ethnic secondary care population with type 1 and Type 2 diabetes.

As the majority of people with diabetes are now managed in primary care, the remaining chapters of this thesis are concerned with examining ethnic differences in the association between depression and type 2 diabetes in this setting.

Chapter 6 describes the methodology for the primary care studies.

Chapter 7 examines ethnic differences in the prevalence of depression in South Asians and White Europeans with and without type 2 diabetes as well as differing rates of depression recognition.

Chapter 8 provides a discussion of the findings from Chapter 7.

And finally,

Chapter 9 presents an overall discussion of the studies presented in this thesis and suggestions for future research.

Chapter 2

The prevalence of comorbid depression in adults with Type 2 diabetes: A systematic review and meta-analysis

2.1 Rationale and aim

Depression is a common mood disorder affecting approximately 5% of the British population[72]. It can manifest itself either as a major depressive disorder or in minor forms characterised by a collection of mental and physical depressive symptoms.

Unsurprisingly, rates of depression are elevated in those with chronic illnesses[134]. Although psychological distress may seem like a natural and inevitable response in such circumstances, the clinical implications of a depressive co-morbidity in either major or minor forms can be of serious consequence. In addition to its implications for physical, mental and social well-being, depression contributes to poor self-care and adherence to medical treatment, diminished quality of life and higher rates of medical morbidity and mortality as well as increased health care costs [90, 112, 135, 136]. The impact of depression in patients with diabetes is a research area of particular interest as it has directly and indirectly been related to poor glycaemic control, which in turn is a major factor leading to the development of both micro- and macro-vascular complications[85] (Chapter 1.8).

Nevertheless, evidence is accumulating to suggest that identification and treatment of depression in patients with diabetes may have a favourable effect on glycaemic control and perhaps even prevent or delay diabetes related complications. Lustman et al [137] demonstrated how Cognitive Behaviour Therapy (CBT) may be an effective option for people with type 2 diabetes and major depression (Chapter 1, Table 1.4), leading to moderate improvement in glycaemic control. In addition, a recent meta-analysis of

psychological interventions for patients with diabetes suggested long-term benefits of glycaemic control [138].

Before planning treatment provision, it is necessary to estimate the prevalence of depression in patients with diabetes. Prior to the work presented in this thesis, Anderson et al [75] had conducted the most recent (2001) systematic review into the prevalence of depression in people with diabetes. They concluded that the prevalence of depression almost trebled in patients with type 2 diabetes (OR = 2.9, 95% CI 2.3-3.7). This finding was based on the analysis of 7 controlled studies. However, some of the studies included in the review involved small sample sizes and control groups of questionable validity. Since Anderson et al's review and recommendations for future research, the literature on this topic has continued to expand. The present review therefore aims to reassess the prevalence and odds of depression in people with diabetes compared to those without diabetes. As the physiological as well as psychological experiences of people with type 1 and type 2 diabetes may vary substantially, the present systematic review is restricted to type 2 diabetes.

2.2 Method

A systematic review was conducted in order to identify published literature on the prevalence of clinically relevant depression in people with type 2 diabetes.

2.2.1 Search Strategy

MEDLINE, EMBASE and PsycINFO databases were searched for papers published between January 1980 and May 2005. The search strategy involved using the explode command with a search under the MeSH terms 'depression', 'depressive disorder', 'major depressive disorder' and 'dysthymic disorder' combined with 'diabetes mellitus' or 'type 2 diabetes mellitus'. This was supplemented with a keyword search of the terms 'depression', 'depressive disorder', 'depressive symptoms' and 'dysthymic disorder' combined using Boolean operators with 'diabetes' and 'diabetes mellitus'. The reference lists of relevant articles obtained were also screened, however no additional studies were identified. Contact was not made with the authors of articles and only studies published in English were considered for review.

2.2.2 Study selection and analyses

Articles were included if a current or life-time rate of clinically relevant depression was identified either by self-report or through diagnostic interviews. Anderson et al defined clinically relevant depression as 'depression severe enough to warrant clinical intervention'[75] which therefore includes major, minor and sub-syndromal depression. Evidence suggests that both major and milder forms of depression may impede social and functional wellbeing for those with diabetes [90, 93, 112, 139]. In

addition treatment for these conditions may lead to improved diabetes related outcomes [137, 138].

Studies selected were limited to those involving adults (>18 years of age) with type 2 diabetes and a sample size of more than 50. Studies involving children and adolescents were excluded as the majority of individuals with type 2 diabetes are adults. Studies were included regardless of the methods used for assessing a diagnosis of diabetes (self-report or doctor verification) as previous studies have established the reliability of self reports of diabetes as a measure of doctor diagnosed diabetes [140, 141]. Studies which failed to specify type of diabetes, or to report depression prevalence by type of diabetes were excluded. Studies were included only if the prevalence of depression was also reported in a non-diabetic comparison group (control group). Comparison groups were not considered to be adequate controls if they included partners, first degree relatives or patients exclusively with other chronic conditions such as hypertension or osteoporosis [135, 142, 143].

The selection of studies was a multi-step process with two reviewers; the author of this thesis and one supervisor working independently to select studies based on the eligibility criteria (Figure 2.1). Potentially relevant articles were first identified for retrieval based on preliminary assessment of the study design and patient characteristics provided in the titles and abstracts of citations obtained from the electronic search. Retrieved articles were then assessed in their entirety with the two reviewers comparing each study with the selection criteria. All disagreements were resolved by discussion.

The use of quality scoring in meta-analysis of observational studies has raised some controversies [144, 145]. Furthermore the existing checklists and quality assessment scales that are available have not been fully validated and fail to include criteria that are associated with effect size. Studies included in the meta-analysis were therefore inverse-variance weighted, so as to ensure that the larger more precise estimates were given relatively more weighting. Subgroup analysis was also conducted in order to explore potential heterogeneity between study methods. Two reviewers independently extracted and recorded the required information from the studies in a standardised manner. Any disagreements with data extraction were resolved by discussion and the involvement of an additional supervisor.

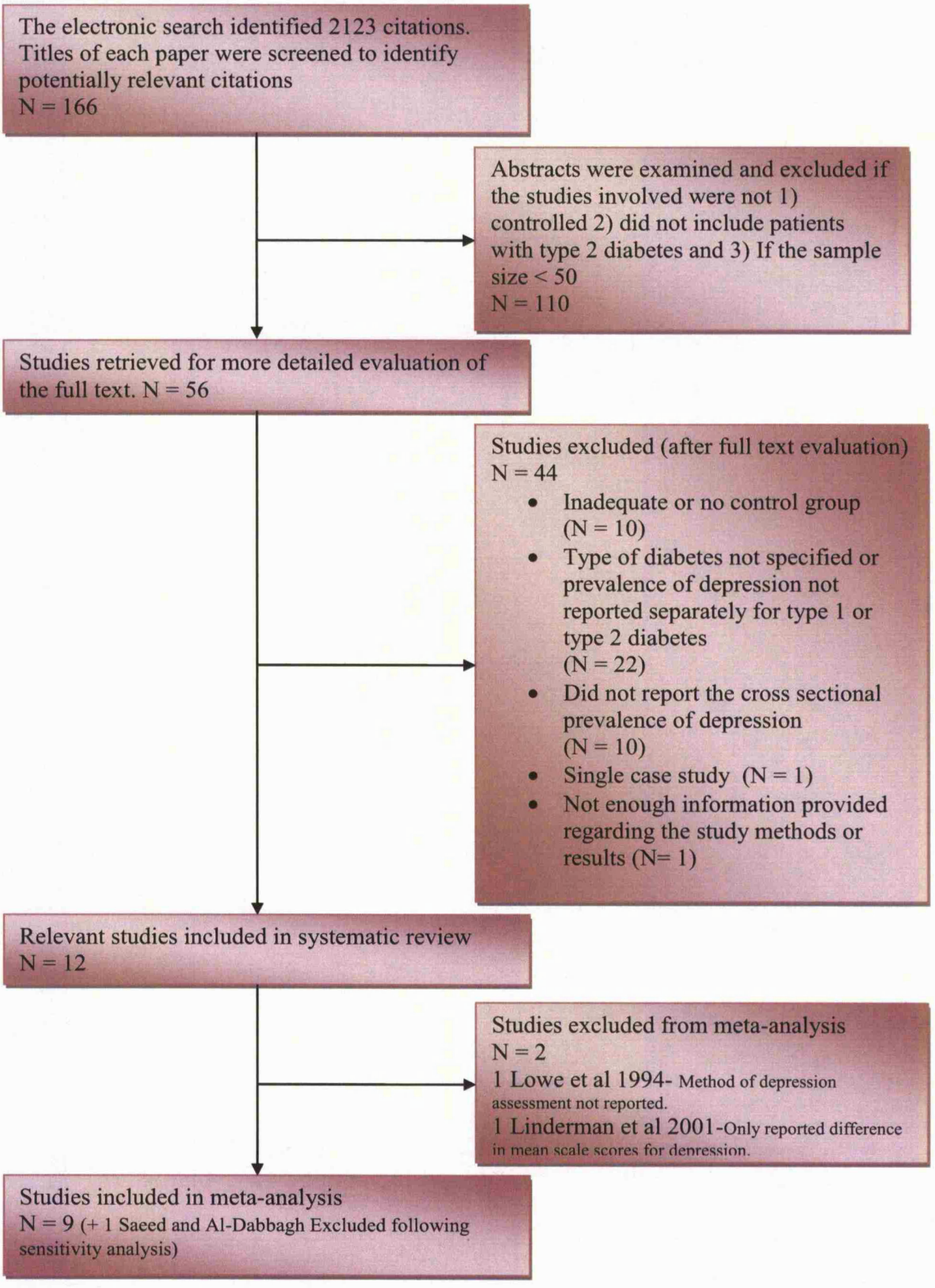
A pooled random effects meta-analysis was conducted using the statistical software Stata v8.0 and non-weighted prevalence rates were calculated. The I^2 value was also calculated. This statistic provides a quantitative assessment of the degree of inconsistency in the results of the studies. The value is expressed as a percentage of the total variation across studies that are attributed to heterogeneity rather than chance. A value of 0% indicates no observed heterogeneity, and larger values show increasing heterogeneity [146].

Publication bias is a significant problem and is known to occur in meta-analyses [147, 148]. Publication bias generally refers to a tendency to publish results that are significant, of higher quality and from larger well-funded studies rather than studies with no statistically significance findings or causal consequences. The interpretation of

any meta-analysis based on a literature search is therefore difficult as the studies involved may be a selected subset (i.e. those demonstrating significant findings). We therefore investigated the likely presence of publication bias using funnel plots and formal tests (Beggs test and Eggers test) [149, 150].

Figure 2.1 Flow diagram of study selection process.

(Adapted from CRD report number 4, 2nd edition)[151]



2.3 Results

2.3.1 Prevalence of depression in type 2 diabetes

The literature search identified 166 potentially relevant articles. Examination of titles and abstracts resulted in 56 articles to be retrieved in order for the full texts to be evaluated in detail (Figure 2.1). Of these only 12 fulfilled the specified criteria to be included in the review. The previous meta-analysis by Anderson et al [75] included nine studies that examined the prevalence of depression in type 2 diabetes compared with those without diabetes. However, only five of these studies were also included in the present review. Three studies were excluded as control groups involved less than 50 participants [152-154]. In addition, one of these studies used spouses of people with diabetes as controls [154]. One study was excluded as the type of diabetes in patients could not be ascertained from the text [139]. A further 7 studies [89, 155-160] were identified in addition to those included by Anderson et al [161-165] (Table 2.1). Linderman et al [160] reported only the statistical comparison between mean depression scale scores in patients with and without diabetes. It was therefore not possible to calculate the prevalence or odds of depression in either group and thus the study was excluded.

One study identified type 2 diabetes patients through screening a population based sample using diagnostic criteria for type 2 diabetes [163] (Table 2.1) the remaining studies identified diabetes using either self-report, physician diagnosis, or through examining patient medical notes.

Six studies identified depressed cases by self-report questionnaire, three using diagnostic interviews and one by examination of patient notes held by general practitioners. One study [165] failed to specify the method for depression assessment and was therefore excluded. A total of 10 studies were therefore included in the analyses. Increased levels of comorbid conditions, such as hypertension and coronary heart disease (CHD) in groups with diabetes were reported in all studies. Only one study reported adjusted prevalence rates for potential confounders such as comorbid disease, age, gender and body weight [156]. One study adjusted rates for age alone[162] , and one adjusted for gender and education [159].

Only one study [158] was conducted in a secondary care setting, the remaining studies were conducted in either population samples (N = 7) or in primary care (N = 2) settings. No statistical difference was found when comparing estimates of the prevalence of depression between patients from these two samples (Table 2.1).

The majority (N = 6) of the studies were conducted in the USA, three studies involved samples from Europe (The Netherlands, Finland and Italy) and one study was conducted in Iraq. The prevalence rates of depression in each of these studies was greater in patients with diabetes compared to those without diabetes ($p<0.0001$). Although there were no differences in the estimates for the prevalence rates in the USA and Europe, significantly elevated prevalence rates of depression in patients with diabetes were observed in the study conducted in Iraq (51.81%) [158] compared to

studies in the USA (12%) and Europe (14.7%) ($p<0.0001$). None of the 10 selected studies examined the prevalence of depression in type 2 diabetes in the UK.

Four studies stated the ethnic background of the participants. One of these described participants as Mexican Americans [89] and one as a White population [155]. Two studies reported a mixed sample, which included black, White and Hispanic individuals [159, 162], but neither reported prevalence rates separately by ethnic group. Only five studies examined different rates of depression in males and females [89, 156, 158, 161, 163], one of which was later excluded from the meta-analysis [158].

An overall prevalence estimate was determined for all studies and then separately by gender (Table 2.1). The prevalence of depression was higher in people with diabetes compared to those without diabetes ($p<0.0001$). This finding was consistent when rates were determined by geographical location, method of depression assessment, sample source and gender.

The overall prevalence of depression was 17.6 % in people with diabetes. This prevalence was elevated in females with diabetes compared to males with diabetes (23.8 vs. 12.8% $p<0.0001$). A higher prevalence of depression was also observed in females without diabetes when compared to males without diabetes (17.0 vs. 8.1% $p<0.0001$).

Table 2.1 Prevalence of clinically significant depression in adults with type 2 diabetes in controlled studies

Study Publication Year	Country and Setting	Race	Participants (Diabetic: *n*) (Control: *n*)	Gender (% Female)	Mean Age (Years)	Age range	Diabetes assessment method	Depression assessment method	Odds Ratio (95% CI)	Prevalence of depression		
										Overall (%)	Males (%)	Females (%)
Amato et al 1996	Italy Community	-	197 1142	67 60	74 74	65+	Medical history	Geriatric Depression Scale	1.67 (1.06-2.64)	14 5	11 7	15 11
Black 1999	USA Community	Mexican American	636 2196	56 58	72 73	65-85+	Self-report	CES-D Scale	1.42 (1.17-1.73)	31 24	23 16	38 30
Eaton et al 1996	USA Community	Mixed: Black and White	148 1600	— —	— —	18-65+	Self report	DIS/ DSM III	1.15 (0.57-2.34)	6 4	— —	— —
Gregg et al 2000	USA Community	White	682 8997	100 100	72 72	65+	Self report	Geriatric Depression Scale	1.91 (1.42-2.57)	8 5	— —	8 5
Nichols and Brown 2003	USA Primary Care	—	16180 16180	48 40	63 63	—	Diabetes register	Patient notes	1.58 (1.49-1.69)	18 12	12 8	23 16
Palinkas et al 1991	USA Community	—	93 1493	40 54	72 68	50+	WHO criteria	Beck Depression Inventory	2.79 (1.41-5.51)	11 5	9 3	14 6
Pouwer et al 2003	The Netherlands Community	—	213 1184	55 48	74 68	55-85+	Self report	CES-D Scale	2.09 (1.39-3.15)	17 9	— —	— —
Saeed and Al-Dabbagh 2003	Iraq Secondary Care	—	110 110	55 55	56 53	35-65	Patients attending diabetes centre	DSM-IV	4.84 (2.62-8.93)	52 18	38 8	62 27
Thomas et al 2003	USA Primary Care	Mixed: Black, White, Hispanic	58 104	73 93	51 32	18-80	Medical history	DIS-IV	1.27 (0.62-2.62	31 26	— —	— —
Viinamäki et al 1995	Finland Community	—	82 115	46 56	67 66	45-64	WHO criteria	Zung-Depression Scale	1.65 (0.61-4.47)	11 7	— —	— —

CES-D, Center for Epidemiologic Studies Depression Scale; DIS/DSM III, Diagnostic Interview Schedule for Diagnostic and Statistical Manual of Mental Disorders, third edition; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, fourth edition; DIS-IV, Diagnostic Interview Schedule for Diagnostic and Statistical Manual of Mental Disorders, fourth edition

2.3.2 Odds ratios of depression in type 2 diabetes

A pooled random effects meta-analysis was conducted using data from 10 studies, which examined the cross-sectional association between depression in people with diabetes compared to those without diabetes. This analysis included data for 18,445 people with diabetes and 32,866 without diabetes. The odds ratio for depression was significantly increased in patients with type 2 diabetes compared to those without diabetes (OR = 1.77, 95% CI 1.5-2.0). The I^2 value was 59%, indicating a moderate amount of heterogeneity in the study results.

Table 2.2 Unadjusted prevalence from controlled studies of clinically relevant depression in patients with and without type 2 diabetes.

	No. of studies	No. of patients	Diabetic subjects (%)	Non-diabetic Subjects (%)
All studies	10	51520	17.8*	9.8
Study by Saeed and Al-Dabbagh	1	220	51.8*	18.2
Excluding study by Saeed and Al-Dabbagh	9	51300	17.6*	9.8
Gender				
Males	5	8795	12.8*	8.1
Excluding Saeed and Al-Dabbagh	4	8745	12.6*	8.1
Females	5	8421	23.8*	17.0
Excluding Saeed and Al-Dabbagh	4	8361	22.15*	10.9

*Prevalence of depression significantly greater in patients with Type 2 diabetes compared with a control group without diabetes ($P < 0.0001$).

2.3.3 Sensitivity analysis

The results of the meta-analysis are shown in Figure 2.2. Examination of this plot reveals that one study [158] lies outside of the normal range. The meta-analysis was therefore repeated, excluding this study. A reduction in the odds ratio was established, and the observed heterogeneity was also diminished (OR = 1.59, 95% CI = 1.5-1.7, I^2 = 3%). The study by Saeed and Al-Dabbagh was therefore excluded from any further analyses.

2.3.4 Subgroup analysis

Of the remaining nine studies, two identified cases of depression using diagnostic interviews, one used patient notes and six used self-report questionnaires. Odds ratios were obtained for studies using each of these methods (Table 2.3). Although not significantly different, a smaller odds ratio was observed in studies utilising diagnostic interviews compared with doctor diagnosis and self-reports of depression. No difference was observed between the odds ratios from the study conducted using doctor diagnosis according to patient notes and self report measures of depression

Only four studies reported the prevalence of depression separately for men and women. A higher prevalence of depression was observed in females both with and without diabetes compared to men. However, when considering the increased risk of depression associated with diabetes, the odds ratio for depression was higher in males (OR = 1.9, 95% CI = 1.7-2.1, I^2 = 29) than in females (OR = 1.3, 95% CI = 1.2-1.4, I^2 = 35).

No significant differences in odds ratios were found between studies conducted in the USA and Europe, or in studies conducted in a primary or population setting.

Figure 2.2 Forest plot for the meta-analysis of depression in patients with and without Type 2 diabetes.

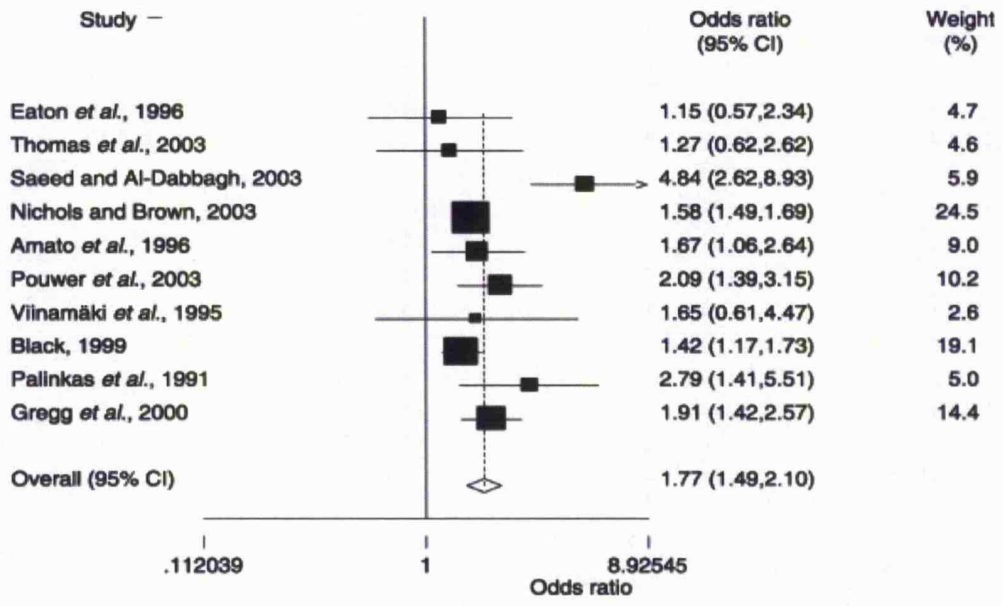


Table 2.3 Odds ratios of depression in patients with and without diabetes: Subgroup analyses.

Subgroups		No. studies	No. of patients	OR	95% CI	I^2
Method of depression assessment	Diagnostic interviews	2	1910	1.2	0.7-2.0	—
	Doctor diagnosed	1	32360	1.6	1.5-1.7	—
	Self-report questionnaire	6	17030	1.6	1.4-1.9	13
Gender	Males	4	8745	1.9	1.7-2.1	29
	Females	4	8361	1.3	1.2-1.4	35

2.3.5 Publication bias

Funnel plots and tests did not suggest evidence of publication bias (Begg's test, p = 0.6; Egger's test, p = 0.2).

2.4 Discussion

This systematic review aimed to estimate the prevalence of depression in adults with type 2 diabetes compared to those without diabetes. The prevalence rate of depression was nearly twice as high in patients with diabetes compared to those without (OR = 1.6, 95% CI 1.5-1.7). This estimate is lower than the figures provided by Anderson et al in their meta-analysis [75], which suggests that the risk may have been overestimated in previous studies. Despite the abundance of literature continuing to emerge on this topic, only five additional controlled studies were identified since the review conducted by Anderson et al 5 years ago. The fact that such a small set of studies was identified for the review reflects the paucity of good quality literature which examines the prevalence of depression in type 2 diabetes.

In order to investigate whether type 2 diabetes is indeed a risk factor for depression, it is vital that comparable control groups are involved so that associations can be reliably determined. Ten studies were excluded solely because there were no or inadequate control groups. In addition, 22 studies, including some with fairly large numbers and of otherwise good quality, were excluded due to a failure to specify the type of diabetes (type 1 or type 2), or to distinguish between the two types in the analyses. Estimating the prevalence rates of depression separately in type 1 and type 2 diabetes is essential considering that the physical burden as well as psychosocial demands associated with these two distinct conditions is likely to vary. Furthermore, only one study involved screening patients using current diagnostic criteria for the identification of type 2 diabetes (WHO criteria) when screening participants from a community sample [161].

Although self-reported diabetes correlates well with doctor diagnosis [140, 141], type 2 diabetes remains largely under diagnosed in some populations [32].

The overall prevalence of depression in people with diabetes was 17.6%, suggesting that 1 in 6 people with type 2 diabetes are likely to experience depression to a degree that may interfere with functional health. Although the prevalence did not vary as a function of the method of depression assessment, or according to whether samples were drawn from primary or population based settings, it is important to bear in mind that only a small sample of studies were involved and therefore the power to detect any differences was low. These prevalence rates should also be viewed with caution as they do not adjust for potential confounding variables.

The prevalence was calculated using data from all studies with the exception of the study conducted by Saeed and Al-Dabbagh [158]. This was the only study carried out in a secondary care population and outside of the USA and Europe. The prevalence of depression in this sample was significantly higher in patients with diabetes (51.8%) and those without diabetes (18.2%) when compared to studies in both the USA and Europe and studies conducted in population or primary care settings. However, the relative influence of these factors on the increased prevalence rate is impossible to deduce from a single small scale study. Samples selected from secondary care settings are likely to differ from those recruited from primary care and population settings with regard to disease stage and severity [166]. Research conducted in such an environment is exposed

to biases of case selection and referral, which in turn may overestimate the prevalence of depression.

Differences were also observed in the prevalence of depression in males and females. Although the rates of depression were higher in both male and female patients with diabetes compared to those without diabetes, females both with diabetes and without experienced a higher prevalence of depression than men. This pattern is similar to that described by Anderson et al [75] in their estimation of rates of depression in a mixed sample of people with type 1 and type 2 diabetes, as well as in the literature reporting rates in the general population and other medical conditions [167-171]. However, as only four studies examined the rates of depression separately in males and females, it is necessary to consider that these results may be influenced by publication bias. In addition, results from the subgroup analysis for gender revealed that the odds ratio for depression was higher in males compared to females. However, again these analyses need to be interpreted with caution as they are based on a small set of studies.

Both major depression and depressive symptoms are associated with adverse outcomes in diabetes [85], in addition they are both highly treatable conditions in this group of patients[137, 138], however these symptoms need to be identified before any efforts can be made for management. There is evidence that depression is under-recognised in people with diabetes [172]. Therefore, training health care professionals to use screening measures to alert them to the presence of depressive symptomatology as well as major depression in people with type 2 diabetes may be useful. Whether screening

for depression actually confers any beneficial effects on diabetes outcomes is a question for future studies. Moreover, it is also important to remember that these findings should be considered with caution as only 2 studies examined the odds ratios using diagnostic interviews and broad confidence intervals were observed.

The present meta-analysis is based on cross-sectional data, which cannot determine the causation or temporality of the observed association. Depression may occur secondary to the hardships associated with diabetes or to the biochemical factors which ensue as a result. In addition evidence also suggests that depression may even precede and act as a causal factor for diabetes through bio-chemical as well as behavioural pathways [102]. A recent meta-analysis by Knol et al [29] concluded that adults with depression have a 30% increased risk for the onset of type 2 diabetes. The complex aetiology of depression in type 2 diabetes therefore remains unclear. However, what remains important is the negative impact of depression on physical and mental health in those with type 2 diabetes [86, 90, 112, 135].

Although this review aimed to provide an overall estimate of the scale of this co-morbidity, a number of factors must be accounted for when considering the accuracy of this estimate. Despite the fact that tests for publication bias were not positive, the possibility cannot be ruled out entirely as the capacity to detect bias may have been limited due to the small number of studies upon which this meta-analysis was based. Also, when determining prevalence rates, it was not possible to conduct any multivariate analysis or take the main confounding variables into account, again largely

due to the small number of studies identified, but also due to the lack of information provided regarding potential moderating factors. Such factors include age, gender, obesity, socio-economic status and additional co-morbid conditions. Furthermore only 2 studies with a combined population of 1910 were conducted using diagnostic interviews based on DSM criteria. The shortage of studies utilising this method for depression assessment may be due to the time and expense required to administer clinical interviews. However in order to determine the prevalence of major depression as well as depressive symptoms in those with type 2 diabetes, it is imperative that such studies are conducted.

In conclusion, a precise assessment of the association between depression and type 2 diabetes is needed in order to direct any form of treatment provision. There is still considerable need for good quality research, which should aim to conduct large, population based cohort studies of the prevalence of depression using standardised diagnostic interviews, diagnostic criteria for type 2 diabetes and control groups that are appropriately matched. In addition, it is important for type 1 and type 2 diabetes to be distinguished as well as for potential biases and moderators to be reported in order for the unique association between depression and diabetes to be determined accurately.

Chapter 3

The Association between depression and Health-related quality of life in people with Type 2 diabetes: A systematic literature review

3.1 Introduction

Although glycaemic control, the development of complications and mortality represent key clinical outcomes in people with type 2 diabetes, patient reported outcome measures (PROMs) are also important. PROMs refer to a range of outcomes which essentially, are obtained directly from the patients' perspective [173]. PROMs may be used to assess multiple aspects of a patient's health. For example they may range from unidimensional symptom scales, such as the diabetes symptom checklist (DSC-R) [174], to complex multidimensional constructs including measures of health status and health related quality of life (HRQOL). Data from PROM are usually obtained via self-report questionnaires or administered via a structured interview. Data collected via classification systems such as the WHO international classification of functioning, disability and health (ICF), which incorporate a providers assessment of patient response are not considered to be PROMs [175] .

HRQOL is increasingly recognised as an important PROM not only as it represents an important goal for health care in its own right, but also due to associations between poor HRQOL and adverse biomedical outcomes in people with type 2 diabetes, including poor response to therapy, disease progression and even mortality [176-178].

Over the years there has been ambiguity around the measurement of PROMs particularly in relation to terms such as HRQOL and health status. This may in part be fuelled by the fact that different concepts are used interchangeably in describing and operationalising HRQOL, health status and related PROMs. There is generally

agreement that QOL represents a broad, multidimensional concept which reflects an individual's sense of well-being or satisfaction with life circumstances. It deals not only with HRQOL but also a range of non-medical experiences such as employment, access to resources, family and social interactions as well as spirituality [179, 180]. Approaches to the measurement of QOL have argued for both subjective indicators which rely on an individual's own personal perceptions, as well as more objective measures such as housing and access to resources, which are less likely to be contaminated by factors such as mood states or cognitive disturbances [181, 182].

HRQOL refers to the ways in which health, illness, and medical treatment impact on the individual's QOL [179]. Central to the understanding of HRQOL is its subjective measurement, that is, it is the individual's personal perceptions of health and well-being that are paramount in defining HRQOL rather than the physical illness itself [180, 183, 184]. Different measurement scales that propose to measure QOL or HRQOL have also been developed. Some are disease specific and are used only for the condition for which they have been developed, whereas others, termed generic measurements, have wider applications across illness groups.

The terms 'functional status' and 'health status' are often used synonymously with the term 'health related quality of life' [180, 185, 186]. Functional status is defined as an individual's ability to perform normal daily activities which are essential in order to meet basic needs, fulfil usual roles and maintain health and well-being [179, 187]. Measures of functional status focus on functional ability and overt behaviour. Although

such measures may represent isolated components of the broader construct of HRQOL, they are not considered to measure HRQOL in a comprehensive fashion.

By contrast, broader measures of health status tend to reflect individuals' subjective perceptions of their health, taking into account the presence of physiological impairment, symptoms and dysfunction and generally involve multiple components including physical, psychological and emotional domains [180]. Currently there is debate concerning the need to distinguish such concepts from HRQOL. Impaired health status may lead to, or co-occur with impaired QOL; however this is not inevitably the case. Similarly, good health and the absence of functional impairments does not necessarily translate to better QOL [179, 188-190].

Measures of HRQOL are also increasingly incorporated within programme and economic evaluations of therapeutic interventions. This recent application of the construct has led to the growth of a subset of instruments which define HRQOL as a quantitative value for a given health state [185] and are referred to as preference based measures. Central to these instruments is the idea that individuals have a quantifiable preference for health outcomes, or 'utilities', with the scores derived reflecting the relative value that people place on living in different health states[191]. Although different methods are used to elicit utilities, they are generally based on the preferences of a community population and the value they attribute to different health states using choice-based valuation tasks or time-trade off [192, 193]. As well as their use as patient reported outcomes and in general population studies, these scores allow the calculation

of quality adjusted life years (QALYs), which have attracted interest for their use in economic evaluations of pharmaceutical and other health care service evaluations [192].

Ideally HRQOL evaluations should include both generic and disease specific measurements to capture the broadest range HRQOL aspects[194]. The importance of psychological factors is also increasingly recognised with the inclusion of such measures recommended in order to provide valuable information that is not incorporated within the other HRQOL instruments [194]. In particular attention has focused on depression, which is a well-established comorbidity in people with diabetes [75, 195]. Measures of depression may share some conceptual identity with HRQOL, particularly in domains pertaining to mental health and emotional functioning; however there is evidence to support the argument that although related, the two concepts should be considered as distinct psychological entities [196]. Furthermore depression is an important determinant of HRQOL.

3.2 Rationale and Aim

Previous studies examining factors associated with HRQOL have largely focused on demographic and disease related factors, including type of treatment for diabetes and the presence of diabetes related complications [197-201]. However considering the emphasis on the subjective measurement of HRQOL, the cognitive processes involved in such reports are likely to be influenced by psychological factors including affective state. Examining the relationship between depression and HRQOL in people with

diabetes represents an important step for both researchers and clinicians in elucidating additional factors associated with HRQOL in this population, which in turn may provide further targets for interventions aimed at reducing the burden associated with this complex condition. The aim of the present chapter was to conduct a systematic review, that is, a review based on explicit, pre-specified and reproducible methods[202] in order to determine the relationship between depression and HRQOL outcomes in people with type 2 diabetes.

3.3 Method

A systematic review was conducted in order to identify published studies examining the association between depression and HRQOL in adults with type 2 diabetes.

3.3.1 Search Strategy

MEDLINE including in-process, EMBASE and PsycINFO databases were searched for English language studies published between January 1980 and December 2007. The review was limited to these databases as they provide an extensive and comprehensive selection of citations from published journals only. The following search strategy was developed for MEDLINE and modified accordingly for each of the databases: the MeSH terms 'depression', 'depressive disorder', 'major depressive disorder' and 'dysthymic disorder'(including all subheadings), supplemented with a keyword search of the terms 'depression', 'depressive disorder', 'depressive symptoms' and 'dysthymic disorder'. This was combined with the search strategy for type 2 diabetes adapted from the Cochrane Collaboration Metabolic and Endocrine Disorders Group [203]. A broad

search strategy was adopted in order to avoid overlooking studies which mentioned the names of particular measures but not the term 'quality of life'. The reference lists of relevant articles obtained were also screened, however no attempt was made to identify unpublished studies because of potential introduction of selection bias if all identified researchers do not respond to requests for details of their studies.

This review examined HRQOL by its commonly accepted definition as a subjective patient-reported construct encompassing multiple dimensions including physical, emotional and social functioning domains. Studies that used only a measure of physical disability were excluded [183].

3.3.2 Study selection

References obtained from the electronic searches were first screened by the author of this thesis in order to exclude articles which were clearly irrelevant. Secondly three reviewers, including two supervisors independently inspected the titles and abstracts of the identified references in order to assess their potential eligibility. Full articles were retrieved for further assessment if the information suggested that the study could potentially meet inclusion criteria based on study design and population characteristics. Full articles were also retrieved for clarification if the abstract provided insufficient information or was unavailable. Retrieved articles were then assessed in their entirety by two reviewers and were included if both reviewers agreed that the study met the following inclusion criteria for the review:

1) The inclusion of people with type 2 diabetes
2) Participants were adults (Aged ≥18)
3) Depression was identified using a previously validated assessment method
4) HRQOL was measured using a previously validated assessment tool
5) A quantitative report of the cross-sectional association between depression and HRQOL was provided

Studies with ≤25 participants were excluded as were studies involving type 1, gestational or borderline diabetes or impaired glucose tolerance only. Studies with a mixed sample of type 1 and type 2 diabetes were considered only if the proportion of type 1 diabetes in the sample was reported to be <5% or the type of diabetes was adjusted for in the analyses.

Any differences in opinion were discussed and, if necessary resolved by a third reviewer. Three supervisors and one external contributor acted in this capacity. Articles provisionally selected were subsequently further examined by two reviewers in order to confirm the appropriateness of inclusion. Citations were not limited to specific publication types and abstracts and letters were considered for inclusion only if investigators had provided sufficient information about study methods and results.

Quality scoring in systematic reviews involving observational studies remains controversial and a clear consensus in terms of methodology has yet to be reached [145, 204]. Our approach for the present review was to set a minimum standard for study

quality through the study inclusion and exclusion criteria. That is, key components of study design which were considered important for study quality, such as the use of appropriate and validated measures, rather than scores derived from quality checklists were identified.

Two researchers collected the characteristics of the included studies independently of each other using a standardised data extraction form. The diversity in study methods, outcome measures and statistical techniques precluded quantitative analysis and synthesis of data, therefore a narrative overview was deemed the most appropriate strategy for summarising the results from the separate studies [202].

3.4 Results

The literature search identified 2083 potentially relevant articles. Examination of titles and abstracts resulted in 141 articles to be retrieved in order for the full texts to be evaluated in detail (Figure 3.1). Fourteen studies involving a total of 14,605 participants met the inclusion criteria (Table 3.1). The most common reasons for excluding articles were that they did not include a measurement of HRQOL or that HRQOL was mentioned but no association with depression was examined.

The majority of selected studies were conducted in the USA (N= 12) with two in Europe (Croatia and Finland). All studies used regression analysis to examine the association between depression and HRQOL. Nine studies examined the impact of

depression on HRQOL and 5 studies examined depression as the dependent variable and its association with HRQOL.

The methods used for depression identification varied between studies with the majority using the Centre for Epidemiologic Studies Depression Scale (CES-D) (N= 9)[205-213] and the remaining 5 studies utilising either, the Hopkins Symptom Checklist Revised (SCL-90-R, N =1)[90], Zung depression inventory (N = 1)[214], the depression module of the Patient Health questionnaire (PHQ-9, N = 1)[215], Harvard Department of Psychiatry National Depression Screening Scale (HANDS, N = 1)[216] or the Composite International Diagnostic Interview (CIDI, N = 1)[217]. The majority of the studies examined HRQOL using generic measures of health status (N = 13)[90, 112, 205-212, 214-217], three of which used utility-based measures [212, 216, 217]. Only three studies involved disease specific evaluations of HRQOL [206, 208, 213] (Table 3.2).

Figure 3.1 Study selection process

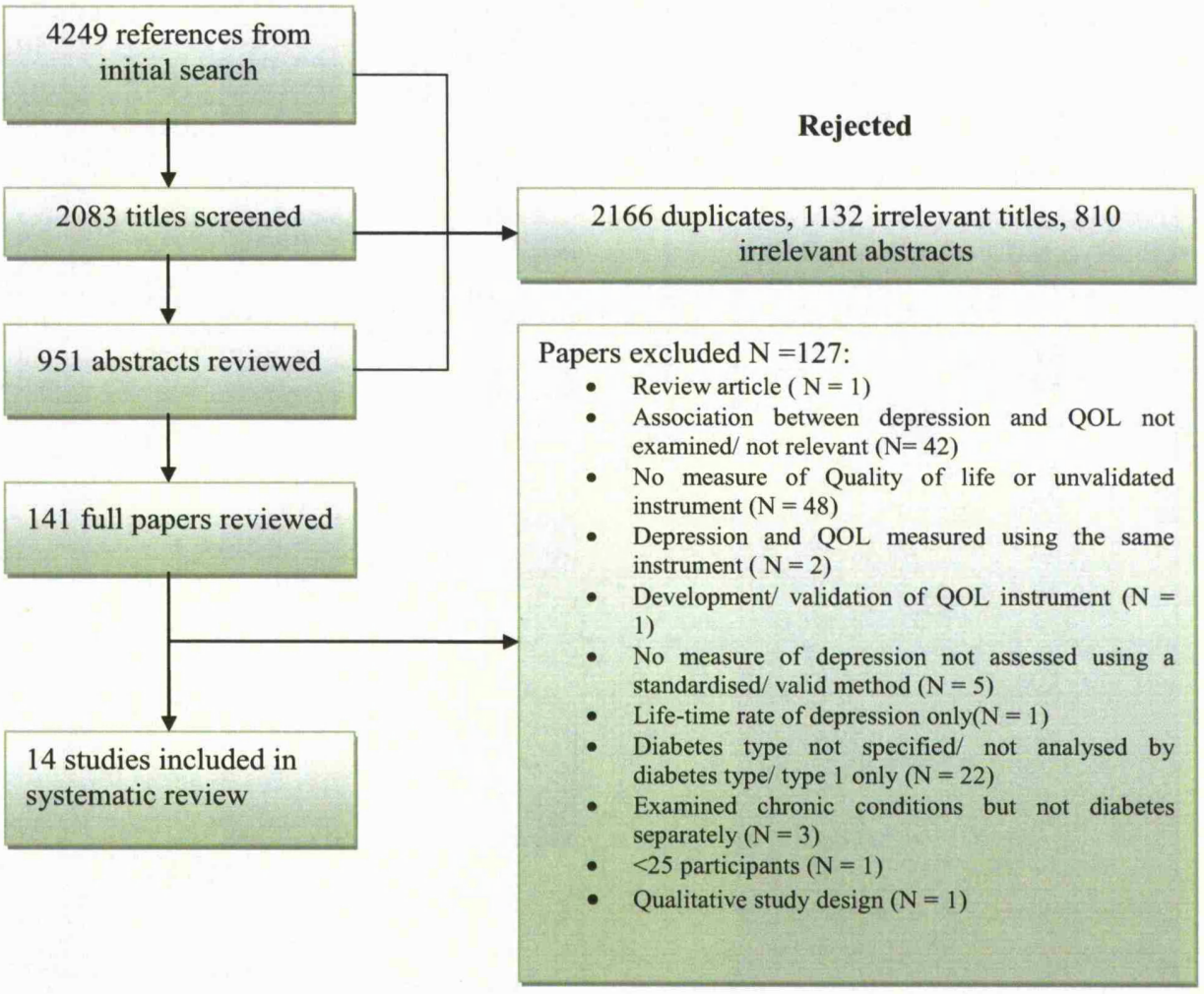


Table 3.1 Summary of studies examining the association between depression and health-related quality of life

Study ref	Country setting	Sample with T2DM				Depression Assessment	HRQOL Assessment		Analyses and findings
		N	Ethnicity	Age	% F		Tool	Domain	
Pawaskar et al 2007[205]	USA community	792	—	71 (±8.7)	60%	CES-D >16	SF-12	Overall HRQOL	Multivariate logistic regression. DV; depression, IV; HRQOL. Reduced HRQOL was associated with increased risk of depression; In all patients with type 2 diabetes (OR 0.97, 95% CI 0.96-0.98); in those on insulin therapy (OR 0.97, 95%CI 0.95-0.99);in those using Sulfonylurea (OR 0.95, 95%CI 0.91-0.99).
Von Korf et al 2004[215]	USA Primary Care	4391	79.6 Caucasian 8.3 black 9.4 Asian 2.3 Other	63.4 (13.3)	49%	PHQ-9	WHO-DAS II < 48 Social functioning subscale from SF-36 <50	Overall HRQOL Social functioning	Logistic regression, DV; HRQOL, IV; depression Depression was associated with a tenfold increase in poor overall HRQOL and social functioning; WHO-DAS II (OR 10.9, 95%CI 7.5-13.5); Social Functioning (OR 9.58, 95%CI 1.5-12.3)
Sundaram et al[206]	USA Specialist diabetes clinic	385	White (93.8%) Black (3.6%) Asian (1%)	<50 (19.4%) 50-59 (27.8%) 60-69 (26%) >70 (26.5%)	57%	CES-D	SF-12 ADDQoL	Physical and mental composite score (PCS and MCS) Diabetes specific HRQOL	Hierarchical multiple regression. DV: HRQOL, IV; depression. Conducted separately for PCS, MCS and ADDQoL Depressive symptoms were associated with significantly lower scores on the SF-12 (both PCS and MCS) and the ADDQoL.
Ciechanowski et al 2003[90]	USA Tertiary clinic	475 (199 T2)	77.7% Caucasians 74% Caucasian T2	48.8 (16) 58.3 (13)T2	52% 50%	SCL-90-R	SF-12	Physical composite score (PCS)	Multiple regression. DV: HRQOL, IV; depression. Depression was significantly associated with poorer physical function and explained the most variance after comorbidities. (Beta -.23, t -5.13, p< 0.01)

Kaholokula et al (2003)[207]	USA (Hawaii) community	141	40.4%Hawaiian 17.1%Filipino-American 14.4%Japanese-American 6.8 Caucasian 21.2% Mixed	59.8 (12.5)	54%	CES-D	SF-36	Physical composite score (PCS)	Hierarchical regression, DV; depression, IV; HRQOL. Inclusion of SF-36 scores in the regression models model significantly increased the variance accounted for in CES-D scores R2 diff = -.16, p<.001 The strength of the negative correlation between CES-D and SF-36 scores varied as a function of HbA1c levels (R2 diff =-.04, P< .01) as well as gender, education level, marital status and social support level (R2 diff -0.03, 4.51, p<0.05, R2diff -.03, 5.17, p,0.05, R2diff -0.05, 4.46, p<0.001, R2diff -0.02, 4.28 p< 0.05)
Hanninen et al 1999 [214]	Finland population	222	—	56.3 (SD 6.9)	46%	Zung depression inventory	SF-20 domains	Physical functioning, role functioning, social functioning, mental health, health perception and bodily pain	Logistic regression. DV; lower quartile of HRQOL subdomain, IV; depression Depression was associated with impairments to HRQOL on all subdomains examined; PF OR 12 (5.5-6), RF OR 4.1 (2.3-7.1), SF OR 8.6 (4.6-16) MH OR 30 (10-88), HP OR 50 (11-220), BP OR 3.8 (1.9-7.5)

Chyun et al 2006[208]	USA Yale university, Hartford Hospital and university of west Virginia medical system	116	91% Caucasian	53%	60.8 (6.5)	CES-D	SF-36	physical functioning, social functioning, role-physical functioning, bodily pain, mental health, role-emotional functioning, vitality, general health	Multivariate linear regression. DV; HRQOL- subdomains, IV; depression Depressive symptoms were associated with poorer HRQOL on the following domains; SF -1.63, RE -1.92, MH -1.31, VIT -0.99, GH -0.77. No significant association between depression and the following subdomains was demonstrated; RP, PF or BP. Depression was associated with worse Satisfaction with treatment (-0.59) and Impact of treatment(-0.32)
							D-QOL	Satisfaction with treatment Impact of treatment	
Caruso et al 2000[209]	USA Primary Care	1238	92% Caucasian	49%	55+	CES-D >20	Pf-10 subscale from SF-36	Physical function	Multiple linear regression. DV; HRQOL subdomain, IV; depression Depression was associated with poorer PF. Regression coefficient -7.14, p< .0001, standardised regression coefficient -0.1185
Pibernik-Okanovic et al 2005[210]	Croatia (primary care/ outpatient clinic)	384	—	57 (7.8)	—	CES-D	SF-12	Physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, mental health	Multiple regression. DV; depression, IV; HRQOL A significant negative association was demonstrated between depression and the following subdomains SF (beta = 2.18), RE (beta = -0.08) and MH (beta = -0.10) No significant association was demonstrates between depression and PF, RP, BP, GH, VIT, GHP and PHT.

Kaholokula et al 2006[211]	USA	179	50% Native Hawaiian 16% Filipino 18% Japanese 16% Mixed-ethnic	52%	—	CES-D	SF-36	Physical functioning, role-physical functioning, role-emotional functioning, social functioning, bodily pain, vitality, general health perception, perceived health transition	Hierarchical regression. DV; depression, IV; HRQOL subscale and interaction. Compared to model with interaction term removed Ethnicity and PF (R2diff = 0.04, P,0.05), BP (R2diff = -0.05 p<0.05), GHP (R2diff = -0.05, p<0.05), VIT (R2diff = 0.04, p< 0.05), RE (R2diff = -0.04, p< 0.05) No significant interaction between RP, SF and HT.
Maddigan et al 2006[217]	USA community	4678	1.8 % indigenous population	61.6 (13.3)	48.3	CIDI >0.90 predicted probability	Health Utilities Index III (HUI-3)	Overall functioning	Multiple regression. DV; HRQOL, IV; depression. Depression was associated with largest amounts of HRQOL deficits.(-0.11 p<0.05)
Wexler et al 2006[216]	USA Primary Care	909	83% White non-Hispanic 17% non White	61.6 (13.3)	49%	Havard Department of Psychiatry National Depression Screening Day Scale (HANDS) and Chart diagnosis	Health Utilities Index III (HUI-3)	Functioning in 8 different health domains-overall measure which includes: Vision Hearing Speech Ambulation Dexterity Emotion Cognition pain	Multiple regression. DV; HRQOL, IV; depression Interactions between depression and sex, heart failure, microvascvular complications, low educational level and presence of severe obesity Depression was the strongest correlate, decreasing utility by 0.37. (parameter estimate -0.37, SE 0.02, p< 0.0001) For chart diagnosis, utility decrement with chart diagnosis was 0.14±0.02 (p<0.0001) Interactions variables were all non-significant (p>0.2)

Gaynes 2002[212]	USA community	537 T2	—	—	—	CES-D >16	Health Utilities index	Overall subdomains ; physical functioning , role function and health	Multiple regression, DV: HRQOL, IV; diabetes and depression and interaction. Depression did not interact with diabetes when examining overall HRQOL When examining subdomains. Depression amplified the effect of depression when examining role functioning.
Fisher et al (2001)[213]	USA community	188	Latino 75 E A 113	L 48.4 ± 8.9 EA 61.7 ± 7.9	L 35% EA 40.7%	CES-D	D-QOL (Functional impact scale)	Functional impact-perceived burden of diabetes on personal, work and social life	Multiple regression conducted separately for each ethnic group DV; depression, IV HRQOL In models accounting for Age, Sex, Education, HbA1c, BMI, Time since diagnosis, No. comorbidities, Financial stress, spouse conflict resolution and Family closeness, functional status accounted for the greatest variance in depression scores L: beta = -0.442, p =0.000 EA: beta=-0.394, p= 0.000

SF-36 and SF-12;PCS physical composite score, MCS mental composite score. SF-36 (SF-20, SF-12) subdomains; PF physical functioning, SF social functioning, RP role-physical functioning, BP bodily pain, MH mental health, RE role-emotional functioning, VIT vitality, GH general health, HT perceived health transition, HP health perception.

Table 3.2 Summary of HRQOL instruments utilised in studies which examine the association between depression and HRQOL in people with type 2 diabetes

Instrument	Description
The Medical Outcomes study questionnaire, including the SF-36, SF-20 and SF-12	The Medical Outcomes study questionnaire, including the SF-36, SF-20 and SF-12 provide an overall score for health status on the basis of respondents' perceived burden of their illness. The overall score encompasses the dimensions of physical functioning (PF), role physical (RP), role emotional (RE), mental health, (MH), bodily pain (BP), general health (GH), vitality (VT) and social functioning (SF). These 8 dimensions can also be summarised into two summary scores of physical and mental health. In addition there is a single item that reports the perception of health transition[218]. The SF-20 and subsequent SF-12 are shorter adaptations of the SF-36, comprising a reduced number of items (20 and 12 items respectively) and were developed as shorter alternative to the SF-36 for use in large scale studies.
HUI-III and The modified HUI	The HUI-III assesses health states as a defined by the level functioning on eight attributes including; vision, hearing, speech, ambulation, dexterity, emotion, cognition, pain and discomfort, to provide an overall score [219] . The modified HUI [220] also allows the summary of scores into categories of functioning within 3 domains; Physical (including mobility and physical activity), Role (including self-care and role activity) and Health problems (difficulty seeing, hearing or pain associated with a medical problem)
The WHO-DAS II	The WHO-DAS II provides an overall assessment of HRQOL by measuring difficulties in performance on a number of domains as a result of health or mental health problems. Domains include self-care, mobility, understanding, communication, interpersonal relations, work and domestic responsibilities [221].
D-QOL	The D-QOL assesses satisfaction with diabetes treatment and the functional impact of treatment. The functional impact scale examines the difficulty diabetes places a burden on work, personal and social life [222].
ADDQoL	The ADDQoL is designed to indicate the impact of their diabetes on those applicable among 18 items domains of life, and also rate how important those domains are in their life. Items relate to physical functioning, symptoms, psychological well-being, social well-being, role activities and personal constructs [223].

3.4.1 Association between depression and measure of health status

Five studies, involving a total of 6184 participants, examined overall scores or component summary scores for health status. These consistently demonstrated a negative association between depression and HRQOL [90, 205-207, 215].

Pawasker et al (2007) [205] examined multiple predictors of depression in an elderly community population of individuals with type 2 diabetes (N = 792). Multivariate analyses accounted for key demographic variables, functional limitations and information regarding health care utilisation. Lower HRQOL, as defined by the overall score on the SF-12, was significantly and independently associated with a higher risk for depression. However caution is needed in interpreting these results due to the possible colinearity between depression and mental health domains encompassed within the overall score for the SF-12.

Von Korf et al (2004) [215] also studied the association between co-morbid depression and overall health status as defined by the WHO-DAS III in a large (N = 4391) primary care population with type 2 diabetes. In analyses which accounted for important potential confounders, including glycaemic control, demographic variables and the presence of complications and co-morbidities, depression was associated with an almost 10 fold increased risk of impaired HRQOL.

Three studies also examined component scores for physical and mental domains separately. Sundaram et al (2007) [206] examined the association between comorbid

depression and SF-12 composite scores for physical and mental functioning in 348 people with type 2 diabetes attending outpatient clinics at a university hospital. Controlling for the effects of demographic and clinical variables, including age, gender, education, diabetes complications and co-morbidities, depression resulted in significant impairments in both physical and mental functioning. Similarly, Ciechanowski et al 2003 [90] reported a significant association between depression and poor overall physical functioning in 475 people with diabetes enrolled at a tertiary care clinic, even when medical comorbidities and complications were accounted for. Finally, Kaholokula et al [207] confirmed a negative association between depressive symptoms and the physical functioning domain of the SF-36 in a multi-ethnic community population with type 2 diabetes in Hawaii (N= 141). However, although the analyses controlled for the effects of knowledge of diabetes, other important potentially confounding factors, including medical comorbidity and diabetes-related complications, were not adjusted for. The study also examined the degree to which the association between depression and the physical component of the SF-36 varied as a function of HbA1c and socio-demographic factors. Results from interaction analyses indicated that the association was stronger in those with higher HbA1c levels, in females, those without a high school degree, people with disrupted marital status and in those with low levels of social support.

Six studies examined individual sub-domains of the SF-36 or its abbreviated versions [208-211, 214, 215]. Of these, two studies examined the association between depression and single sub-dimensions of the SF-36. Caruso et al [209] found that

depression (based on CES-D measurement) was associated with impaired physical functioning in a primary care population of 1238 individuals with type 2 diabetes. However it is unclear whether these analyses adjusted for the duration of diabetes or medical co-morbidities and diabetes-related complications. Depression (based on PHQ measurement) was also associated with impaired social functioning in a large primary care population accounting for important potential confounding factors including demographic and clinical variables [215].

Hanninen et al [214] studied a population-based sample of 520 patients with and without type 2 diabetes in Finland (n with diabetes = 260). The study examined the association between depression (based on ZSRD scale) and each individual sub-dimension of HRQOL as assessed by the SF-20. In analysis adjusted for the presence of diabetes, age, gender, marital status, coronary heart disease and other macrovascular disease, depression was found to be a major determinant associated with impaired HRQOL on each of the six sub-dimensions.

Chyun et al [208] examined the relationship between depression and all 8 subdomains of the SF-36 in 116 people with type 2 diabetes attending diabetes and primary care outpatient practices. Controlling for the effects of demographics, diabetes-related and cardiovascular risk factors, the results demonstrated variation according to the sub-domain examined. Depression was associated with poorer HRQOL in domains pertaining to limitations in social functioning, usual role (emotional), mental health, vitality and general health. However, no significant association was demonstrated

between depression and the HRQOL domains of physical functioning, usual role (physical) activities or bodily pain. The study was limited however, by the small sample size and thus may have lacked adequate statistical power to detect associations between depression and some HRQOL domains. Furthermore participants were previously enrolled on an RCT study and are likely to represent a select group which limits study generalisability.

Variation between the subdomains associated with depression was also demonstrated by Pibernic-Okanovic et al [210] in a Croatian outpatient sample of people with type 2 diabetes (N = 384). In analyses accounting for gender, insulin use, HbA1c, social support and well-being, only the SF-12 mental health and usual roles (emotional) domains were associated with increased risk of depression. No significant association was observed between depression and physical functioning, usual role (physical), bodily pain, general health, vitality and social functioning.

Only one study examined potentially moderating factors for the association between depression and individual subdomains health status measurements. Kaholokula et al (2006) [211] examined ethnic differences in the association between depression and individual facets of HRQOL using SF-36 sub-dimensions, with a population sample of people with type 2 diabetes including Native Hawaiians (N = 94), Filipinos (N = 30), Japanese (N = 35) and those with mixed ancestry (N = 31). In models controlling for age, sex, marital status, education level, social support and HbA1c, ethnicity was shown to moderate the relationship between depression and the HRQOL dimensions of

physical and role functioning, bodily pain, vitality and general health perception. Findings suggested that people of Filipino, Native Hawaiian and mixed-ethnic ancestries with higher levels of depressive symptoms were significantly more likely to report poorer physical functioning, worse perception of general health, more bodily pain, greater impairment of energy, and more emotional problems affecting their usual roles. No significant associations were observed between depression and all eight aspects of HRQOL in Japanese patients.

3.4.2 Association between depression and preference-based measures of HRQOL

Three studies involving 6124 participants with type 2 diabetes, examined the association between depression on HRQOL using utility-based measures.

Wexler et al (2002) [216] examined the association between the presence of depression (as defined by the HANDS) on HRQOL (as defined by the HUI-III) in 909 primary care patients with type 2 diabetes. The presence of depression was shown to be associated with the largest deficits in HRQOL, even in models adjusting for the effects of demographic variables and medical comorbidities. In total the decrement in utility associated with depression was estimated at 0.37-0.38 units, with an increment of 0.03 units representing a clinically significant difference in HRQOL [224].

Maddigan (2006) also studied multiple determinants of HRQOL as assessed by the HUI-III, in a large community population (N = 4678) with type 2 diabetes. In models adjusted for social and behavioural factors as well as medical and demographic

variables, depression as defined by the CIDI was associated with a decrement in HRQOL (-0.11; 95%CI = -0.15, -0.06) second in size only to a diagnosis of stroke (-0.11; 95%CI = -0.17, -0.06).

Gaynes et al (2003) examined whether coexisting depression (as identified by CES-D) amplified the decrements in HRQOL independently observed in people with chronic medical conditions. Data (N = 9898) were obtained from the National Health and Nutrition Examination Survey Epidemiological Follow-Up Study (NHEFS) [225] and involved 703 participants with diabetes, of whom 537 had type 2 diabetes. The study examined the association between depression and both overall decrements in HRQOL (based on the Health Utility Index, adapted for use with NHEFS data) as well as the sub-dimensions of physical functioning, role functioning and health. Findings relating to overall HRQOL indicated that when controlling for sociodemographic factors, both depression and non-insulin dependent diabetes demonstrated a negative association with HRQOL, although no significant interaction between depression and diabetes was found, suggesting that the main effects of these conditions remained the same whether depression was present or not. However in analyses of sub-dimensions of HRQOL, a synergistic relationship between depression and non-insulin dependent diabetes was observed on the dimension of role, but not on physical or health dimensions.

3.4.3 Diabetes-specific measures

Three studies including a total of 689 participants examined the association between depression and measures of diabetes-related quality of life. Fisher et al (2001) [213]

examined factors associated with depression (CES-D) in 188 people with type 2 diabetes from managed care settings. In models accounting for demographic characteristics, diabetes-related factors, comorbidities and family levels of stress, HRQOL (as measured by the functional impact subscale of the DQOL) was shown to predict depression in both European Americans and Latinos. Furthermore, functional status was shown to explain the highest proportion of variance in depression scores in both ethnic groups, accounting for more variance than time since diagnosis, HbA1c, BMI and number of comorbid conditions.

Chyun et al (2006) [208] examined the association between depression (CES-D) and the DQOL domains of satisfaction with and impact of treatment. In models accounting for demographic and biological indicators, depression was associated with poorer treatment satisfaction and a greater perceived functional impact of treatment in 116 people with type 2 diabetes. Finally, Sundaram et al (2007) [206] studied the effects of depression on diabetes-specific HRQOL (as defined by scores on the ADDQoL) in 377 patients with type 2 diabetes recruited from a University Hospital clinic. In models adjusting for key demographic and medical variables, depression was shown to be associated with poorer diabetes specific HRQOL.

3.5 Discussion

The past few decades have witnessed an expansion of HRQOL research, particularly in people with diabetes for whom outcomes such as physical, social and mental well-being comprise vital components of treatment evaluation and control [201]. Although a variety of disease-related factors including treatment, long-term complications and comorbidities have been shown to affect HRQOL adversely in those with diabetes [197, 199, 200], emerging literature also proposes the contribution of psychological factors in people with diabetes, particularly depression. According to the understanding of this author of this thesis, this is the first systematic review to examine the relationship between depression and HRQOL in people with type 2 diabetes.

Overall these findings reveal significant impairments of both generic and diabetes-specific measures in those with comorbid depression and type 2 diabetes. The impact of depression was far reaching with studies demonstrating detrimental associations on a diverse array of HRQOL subdomains. However variation was observed between studies with respect to the particular subdomains associated with depression. Whereas associations between mental components of HRQOL were uniformly portrayed, findings were less consistent for domains pertaining to physical functioning. Although the associations between mental health components of HRQOL and depression may be expected due to the inherent overlap between the constructs [226], a variety of factors may contribute to the observed differences for physical functioning. It is possible that a lack of association merely reflects the small sample sizes involved and a lack of power for detecting significant relationships [208, 210, 211]. Furthermore each study used

only one measure per construct of HRQOL which may be insufficiently sensitive to demonstrate the detrimental impact of depression on these domains.

Alternatively, these differences may be related to the extent to which possible confounding variables were controlled for. For example, studies conducted in both community and treatment settings demonstrated a significant associations between depression and HRQOL domains [207, 209, 214], however it is well recognised that the presence of comorbid conditions or complications contributes to diminished HRQOL in people with diabetes particularly in respect of physical domains [227, 228] and the lack of accounting for these variables may explain why associations were observed in some studies, but not those that accounted for at least some of these factors [208, 210].

Cognitive factors such as illness representations are also important determinants of HRQOL in people with diabetes, and in turn, may mediate the relationship between depression and indices of HRQOL [229]. It is also likely that health beliefs and representations of illness may vary between cultural and ethnic groups [211]. However no attempt was made to adjust for these effects in the studies included in this review and therefore it is not possible to determine the extent to which variations between the aspects of HRQOL influenced by depression are due to possible differences in health beliefs between the study populations.

Additionally, the association between depression and specific aspects of HRQOL is known to vary across distinct ethnic groups [211, 230]. It is also increasingly

recognised that a comprehensive assessment of HRQOL should ideally include both generic and disease specific measurements of HRQOL [183, 231]. However, only one of the 14 studies examined involved both a generic and disease specific assessment of HRQOL [206]. The lack of association between depression and certain aspects of HRQOL in some studies could therefore be because these were truly unrelated factors or because the measures used did not include the aspects of HRQOL particularly pertinent to the population studied.

Variability may also be explained by study setting. Depression was identified as a major determinant for poor function on all six subdomains of the SF-20 when studied within a population sample despite controlling for the presence of comorbidity and complications. However associations between depression and physical aspects of HRQOL were less likely to be identified in studies conducted in managed care settings [208, 210, 232], suggesting that the effects of depression may be particularly detrimental to functioning in community populations rather than settings in which people can potentially access further support for physical, social and mental-wellbeing. However further research is required to examine the moderating influence of patients' environment on the association between depression and HRQOL.

It is imperative to note that these explanations for the observed differences between study results reflect mere speculation and due to the small number of studies it was not possible to conduct any analyses to systematically study the impact of potential modifying factors or to make generalisations based on particular study characteristics.

Only two studies formally examined potential moderating factors between depression and overall HRQOL as well as specific subdomains [207, 211]. However, again, due to the small sample sizes involved and the lack of accounting for potential confounding, the generalisabilty of these findings is limited. Undoubtedly, there is a need for further research to elucidate specific factors that may mediate the effects of depression on specific sub-domains of HRQOL.

Due to the cross-sectional nature of the studies examined we cannot determine whether decreased HRQOL is a cause or consequence of depression, although it is likely that the relationship is bidirectional. Perceptions of poor physical, social and emotional functioning can directly or indirectly lead to the development of psychological distress and depression [233]. Furthermore it is possible that the association between depression and HRQOL in people with diabetes is related to the behavioural factors underlying the development of diabetes related complications, which in turn impede HRQOL [86, 194]. To illustrate, the cognitive-affective symptoms of depression may impair the capacity and motivation to maintain lifestyle modifications such as exercise, healthy eating and smoking cessation as well as adherence to self-management regimes all of which are essential to manage and mitigate diabetes-related complications [86].

However depression was associated with HRQOL even when the presence of comorbidities was controlled for. Alternatively, it is possible that the association between depression and decreased HRQOL may be confounded by cognitive biases associated with an enhanced focus on somatic symptoms and negative events [233,

234]. Symptoms of depression, by definition instigate a general disposition to experience negative mood states, a phenomenon referred to as negative affectivity [235]. Individuals with high negative affectivity may focus on and selectively recall negative experiences, which in turn may lead to worse reports of perceived health and symptoms even though their underlying health may not be worse [236, 237]. This negative reporting bias may lead to inflated HRQOL decrements in those with depression in comparison to individuals without depression [187].

It may be argued that the confounding associated with negative affectivity may be inherent in all outcome evaluations involving self-reported questionnaires. Although findings from this review can be supported by the negative effects of depression on measurements less susceptible to the effects of mood state, such as mortality [238] and disability days [239], it is important to emphasise that HRQOL is not an objective criterion, rather it is a construct intended to complement more objective criteria with the subjective experiences reported by patients themselves.

However research has attempted to delineate negative affectivity from both depression and HRQOL [196, 240]. One study used structural equation modelling to test a conceptual model of both generic and disease-specific HRQOL [240] in patients with coronary artery disease. The model included a range of variables including biomedical, environmental and individual factors, including depression. The model was tested at 3 separate points in time (baseline assessment of chest pain and one and three month follow-ups). Although depression was a major determinant of emotional aspects of

HRQOL, there was no evidence for a direct influence on global HRQOL. However, depression had a major impact on physical functioning and general health domains, indirectly exerting a major effect on global HRQOL at baseline and 3 months later. However no effect was observed after one month. The results demonstrated that reports of HRQOL shortly after treatment were influenced by perceptions of physical functioning, but 3 months later the indirect effect of depression regained an influence on reports of HRQOL. The authors thus concluded that the assessment of HRQOL is distinct from the assessment of depression, although depression was associated with a significant indirect influence on the course of HRQOL in patients with coronary artery disease. Further prospective study is needed to consider the impact of negative affectivity and the association between depression and HRQOL in people with diabetes.

This review highlights methodological vulnerabilities to be considered when designing and reporting future studies examining the impact of depression on HRQOL. As stated earlier, depression shows a modest amount of variance with mental health components of HRQOL [226]. Depression may also have a greater magnitude of effect on specific dimensions of HRQOL. These findings highlight the potential for misinterpretation of data based on overall HRQOL scores. Future studies should account for this in their design and researcher should exercise caution when interpreting findings from global scales.

In addition, this review questions not only whether a relationship exists between depression and HRQOL in people with type 2 diabetes and whether there are any

moderating factors, but how strong any relationship is and whether it has clinical significance. Since statistical significance does not always translate to clinical relevance, HRQOL research focus has shifted to the notion of minimally important difference (MID) [234, 241], broadly defined as the smallest difference in HRQOL score that patients perceive as important and which would lead healthcare providers to consider change in a patient's therapy. However the small number of studies, heterogeneity of measures of HRQOL, study design and discrepant reporting of study outcomes precluded meta-analysis to describe the size of these relationships or to interpret the overall clinical relevance within or across different indicators of HRQOL. Investigators can enhance interpretation of the impact of depression on HRQOL scores by providing the MID of an instrument and reporting mean differences between groups or a change in score in relation to the MID.

Further studies are also needed to examine whether the association between depression and HRQOL varies in the presence of diabetes, since only one study to date has demonstrated that comorbid depression with diabetes may interact such that HRQOL decrements are higher in people with diabetes and depression rather than depression without diabetes [212]. This would further strengthen the argument that depression is a relevant comorbidity associated with additional HRQOL deficits seen in people with diabetes.

It is acknowledged that the present systematic review may arguably be constrained by incomplete inclusion of all of the relevant literature, since it was limited to articles

published in the English language only. This limitation is mitigated by the large number of abstracts generated by a broad search strategy, greatly enhancing the sensitivity of the search and giving some weight to the present findings.

Overall the present review indicates that self-reported depressive symptoms markedly impair HRQOL in several domains. If depression adversely affects HRQOL in patients with diabetes, then clinical priority should be given to the effective identification and treatment of coexisting affective disorder. Likewise therapeutic approaches that focus on facets of HRQOL could potentially be a fruitful avenue in addressing symptoms of depression in those living with type 2 diabetes. These findings also have implications for future research, in that any analyses of HRQOL should account for depression as a possible confounder. Further prospective evaluations are warranted in order to confirm the direction of causation as well as the degree to which the interventions for depression can improve HRQOL outcomes and vice versa.

Chapter 4

The prevalence and risk factors for diagnosed depression in South Asian and White Europeans with Type 1 and Type 2 diabetes in Secondary Care

4.1 Rationale and Aims

A growing body of literature continues to demonstrate increased rates of depression in people with diabetes relative to those without [75, 195, 242] (Chapter 2). Although the exact aetiology of this relationship is still a subject of research, evidence to suggest negative associations between depression and glycaemic control as well as the development of diabetes related complications is presented in recent meta-analyses [85, 86]. The examination of risk factors for depression in diabetes is key in terms of improving understanding of the relationship as well as enabling healthcare professionals to identify high-risk groups. However, despite an emerging interest in racial and ethnic variations in the rates of this co-morbidity in recent years [126, 207, 243, 244], the literature has so far failed to examine the association in migrant South Asian populations. Epidemiological studies conducted in various parts of the world have observed a dramatic increase in the prevalence of type 2 diabetes in South Asian, with reports of up to a 4-fold increased risk in comparison to the White Europeans [17, 245-248]. Furthermore, poor glycaemic control, microalbuminuria, retinopathy and cardiovascular disease mortality have been shown to be higher in this group compared to White Europeans [58, 249, 250].

The present study aims to address this gap in the literature by comparing the prevalence and risk factors for diagnosed depression in South Asian and White European people with type 1 and type 2 diabetes managed in secondary care.

4.2 Method

4.2.1 Design

A cross-sectional study was conducted using data derived from the computerised database at a secondary care diabetes and endocrinology clinic.

4.2.2 Data Source: The clinical workstation

The clinical workstation (CWS), at the Leicester Royal Infirmary and University Hospitals of Leicester UK, is a purposively created electronic patient record system, used for recording clinical data and routine correspondence, as well as for audit and research purposes. The database used for this study includes all routinely collected demographic and clinical data including problems, diagnoses and treatments for all patients attending a secondary care diabetes and endocrinology clinic, either through referral or for regular diabetes reviews. Data from all consultations are collected routinely using a standardised patient clinic sheet completed by clinicians at each patient encounter. Once complete, forms are conveyed to the diabetes information analyst for data entry onto the clinical workstation. Also integrated within the system is the storage of clinical correspondence, including notes and letters as well as links to specialist datasets (APEX system) for the latest as well as previous laboratory results.

4.2.3 Data collection

A search was performed on the CWS and most recent data were retrieved for all patients visiting the clinic between January 2003 and March 2005. Demographic data collected included age, gender, postcode and ethnicity.

Postcodes were obtained in order to derive Indices of Multiple Deprivation scores (IMD scores) as a proxy for socioeconomic status. IMD scores provide a means to measure the level of deprivation within local areas in England. Scores are calculated from measurements of 7 domains: income, employment, health, education and training, housing, crime and geographical access to services, with greater scores indicating a higher level of deprivation[251].

Patient ethnicity was originally self-defined into one of the following categories: White British, Irish or Scottish which were then recoded to 'White European' for the purposes of the analyses, and Indian, Pakistani, and Bengali which were re-coded as 'South Asian'. Other racial/ethnic groups including Black African, Black Caribbean, Chinese, other Asian, other Black, mixed or Jewish were not included in the final analyses of ethnic differences as the group as a whole was considered to be too heterogeneous and the numbers (n=318) too small for meaningful analysis.

Medical data extracted included type and duration of diabetes, current use of insulin and oral anti-diabetic medication (OAD), smoking status, Body Mass Index (kg/m^2), systolic and diastolic blood pressure (mmHg), cholesterol (mm/l), HbA1c (%), the presence of one or more comorbid conditions (coronary heart disease, cerebrovascular disease, asthma, chronic obstructive pulmonary disease, heart failure, peripheral vascular disease, inflammatory bowel disease, irritable bowel syndrome, epilepsy, hypothyroidism, transient ischemic attack, fibromyalgia and malignant neoplasm), one

or more diabetes related complications (peripheral neuropathy, diabetic retinopathy, nephropathy, neuropathy and microalbuminuria), psychotic disorder and psychiatric disorder.

It is recognised that there may be imprecision in the reporting of depression in administrative data, therefore with the aim of maximising sensitivity, an algorithm was developed in order to identify patients diagnosed as having depression through a combination of case documentation in the patient's list of problems and/ or a prescription of antidepressant medication above or equal to the minimum therapeutic dosage recommended for depression (BNF 52) [252]. The rationale for including patients receiving antidepressant treatment but with no diagnosis was to ensure the inclusion of all those who were recognised as depressed but not charted as such, a common occurrence in general practice notes. However, the therapeutic dosage for many anti-depressants also overlaps with that prescribed for a number of psychiatric complaints as well as neuropathic pain. Such disorders include obsessive compulsive disorder, post-traumatic stress disorder, bulimia, panic disorder and social anxiety. In the absence of specific categorising of psychiatric disorders, ambiguous cases were not coded as having depression if there was evidence of psychiatric or psychotic disorder.

4.2.4 Available data

A total of 7035 patients attended the diabetes and endocrinology clinic between January 2003 and March 2005. Data were retained for those classified as having either type 1 or type 2 diabetes mellitus only. Patients seen at the clinic for reasons other than diabetes

were excluded, as were patients with gestational diabetes and Maturity Onset Diabetes of the Young (MODY). Twenty-six duplicate cases were also removed, leaving a final sample of 6230 individuals (Figure 4.1).

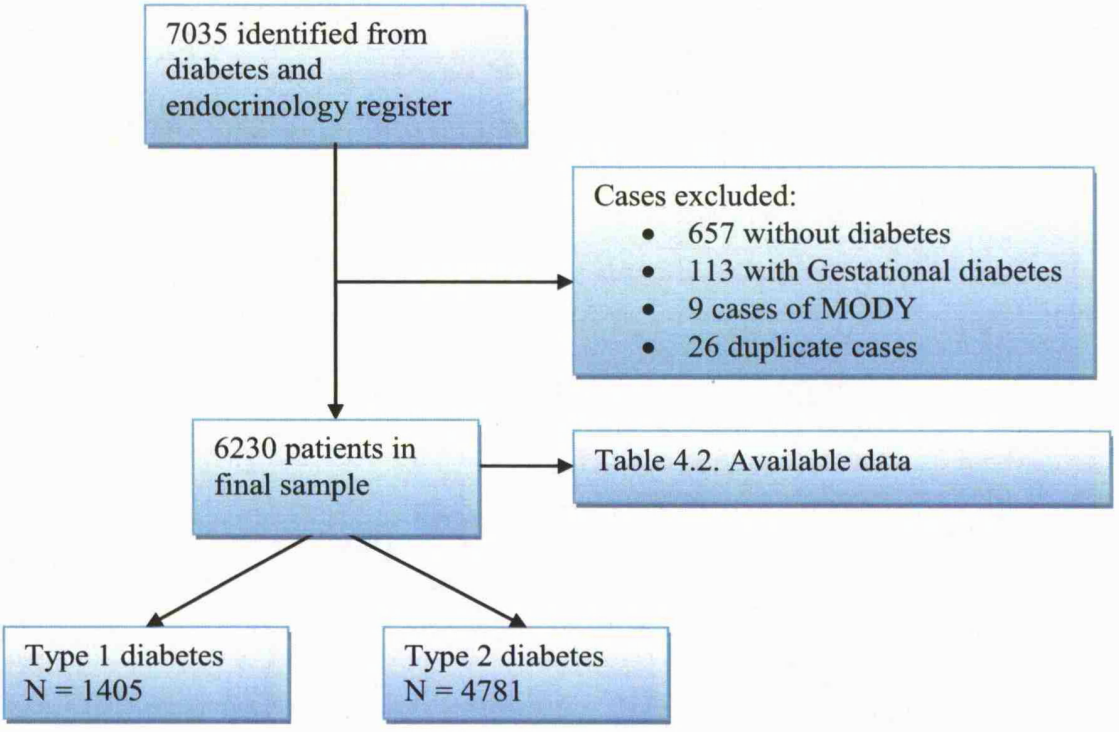


Figure 4.1. Flow diagram of available data

4.2.5 Treatment of missing data

Missing data is a common problem in clinical databases and incomplete data was observed for BMI (30%), cholesterol (5%), blood pressure (32%) and HbA1c (3.2%). These deficiencies in the dataset may be attributable to data not being coded onto the clinic template despite being measured or patients not receiving an annual review due to a recent history of good metabolic control. Such circumstances can arise when patient notes are sent to, or requested by other departments within the hospital, sooner than it has been possible to electronically input data onto the clinical workstation.

Efforts to retrieve missing data, as well as correcting anomalies within the dataset (<0.1%) involved examining clinical letters as well as laboratory results in the pathology database via links through the clinical workstation. In 448 patients (7.2%), the type of diabetes was not specified. In line with previous research, we classified patients as having type 1 diabetes if they had been diagnosed under the age of 35 years and were receiving insulin therapy only [253]. Forty-four (0.7%) of the sample were unclassified due to insufficient information.

Ethnicity data were unavailable for 17.4% of patients. Missing cases were further examined and patients of South Asian ethnicity were identified using the computer program 'Nam Pehchan' [254] supplemented by a visual inspection of surnames and forenames. This method for ascribing South Asian ethnicity has been shown to have high reliability in UK populations [254, 255].

Variables with missing data and the percentage of data retrieved via the methods described above are shown in Table 4.1. Data were excluded for cases with values outside of the normal range for cholesterol (N =6) and Hba1c (N = 8) and years of diabetes (N =1).

Despite efforts for retrieval, 30% of cases included no data for BMI. Cases with and without missing data for BMI were compared for demographic and clinical variables. Cases with missing data were more likely to have type 2 diabetes and be aged >60 years. Values for SBP, cholesterol and HbA1c were lower in cases with missing data

for BMI and they were less likely to be taking insulin and OAD medication and were less likely to have diabetes complications.

Due to the high proportion of missing data for BMI, the multiple imputation technique proposed by Rubin 1987 [256] was applied in order to generate a complete dataset for analysis. This technique was only applied to generate a complete set of data for BMI and not additional variables with comparable rates of missing data (e.g. blood pressure) due the importance of BMI as a potential confounder.

The variables used to predict missing values for BMI were: age, female gender, South Asian ethnicity, duration of diabetes (years), HbA1c, IMDS and insulin use. These variables were selected due to their theoretical associations with BMI. Five sets of imputed data for BMI were produced using STATAv9 (StataCorp 2005, Stata Statistical Software, College Station, TX).

Complete information on all variables entered into logistic regression analysis was available for 1265 cases with type 1 diabetes. For cases with type 2 diabetes complete information was available for 3845 (Table 4.2).

Table 4.1 Missing data retrieval

Variable	Original dataset No. available (%)	No. missing (%)	Method of additional data extraction.	Missing data retrieved N (%)	Final dataset No. available (%)
Age	6226 (99.9)	4 (0.1)	Apex and letters	0	6226 (99.9)
Gender	6229 (99.9)	1 (0.1)	Examining patient names	1 (100%)	6230 (100)
Diabetes type	5782 (92.8)	448 (7.2)	Apex and letters	404 (90.3%)	6186 (99.3)
Insulin	6205 (99.6)	25 (0.4)	Checked on CWS	18 (75%)	6223 (99.9)
OAD	6205 (99.6)	25 (0.4)	Checked on CWS	9 (25%)	6214 (99.7)
Ethnicity	5145 (82.6)	1085 (17.4)	Nam Pechan software supplemented by visual inspection of surnames	1085 (100)	6230 (100)
BMI	2298 (36.9)	3932 (63.1)	Apex and letters	423 (10.8%)	4355 (70)
SBP	3468 (55.7)	2762 (44.3)	Apex and letters	841 (30.5%)	4309 (69)
DBP	5893 (55.7)	337 (5.4)	Apex and letters	836 (30.2%)	4245 (68.1)
Cholesterol	5550 (89.0)	337 (5.4)	Apex and letters	-6*	5887 (95)
HbA1c	6034(96.8)	196 (3.2)	Apex and letters	-8*	6026 (97)
Years of diabetes	5716 (91.7)	514 (8.2)	Checked on CWS	-1*	5715 (91.7)

SBP =Systolic blood pressure, DBP = diastolic blood pressure, OAD = oral anti-diabetic medication* Patient data were excluded due to anomalous values

Table 4.2 Available data

Variable	Type 1 N = 1265		Type 2 N 3845	
	Available	Missing	Available	Missing
Age	1403	2	4779	2
Gender	1405	0	4781	0
IMDS	1394	11	4722	59
Diabetes type	1405	0	4781	0
Years of diabetes	1377	28	4336	445
Insulin	1405	0	4775	6
OAD	1403	2	4768	13
SA or WE ethnicity	1344	61	4524	257
BMI (imputed)	1405	0	1405	0
Systolic blood pressure	1118	287	3181	1600
Diastolic blood pressure	1103	302	3132	1649
Cholesterol	1354	51	4502	279
HbA1c	1395	10	4595	186
Depression	1375	30	4673	108

4.2.6 Statistical analysis

Demographic and medical characteristics were compared between South Asian and White European patients with type 1 and type 2 diabetes. All subsequent analyses were performed separately for type 1 and type 2 diabetes.

Patients with and without depression were compared using t-tests for normally distributed continuous variables (systolic and diastolic blood pressure). Variables failing to display a normal distribution were transformed using Log base10 transformation (HbA1c, Cholesterol and BMI) and differences in geometric means were examined. When a normal distribution could not be achieved despite logarithmic transformation, variables were divided into categories using either quantiles or conventional cut-points (age, years of diabetes, IMD scores). As no standard cut-points exist for IMD scores, the variable was categorised into 4 equal groups, with 0 representing the lowest level of deprivation and 4 the highest. Differences in terms of categorical variables (including gender, insulin and/ or oral anti-diabetic medication use, ethnicity, smoking status and the presence or absence of diabetes complications and co morbidities) were examined using χ^2 tests. Differences were considered to be significant at the $P<0.05$ level.

Multiple logistic regression modelling was conducted in order to examine the variation in the risk of depression according to ethnicity, while controlling for age, gender, comorbidities, complications, insulin and oral anti-diabetic medication use (type 2 only), BMI, HbA1c, duration of diabetes and deprivation (based on IMD scores). Each

of these variables has been shown to be associated with depression in previous studies [213, 243, 257, 258]. Individual logistic regression models were carried out with each imputed data set for BMI. The method described by Van Buuren 1999 [259] was used in order to pool the results from the analyses and produce ORs and CIs that incorporate missing data uncertainty.

To examine whether factors associated with depression differed between South Asian and White European patients with diabetes, logistic regression was performed separately for each ethnic group. Controlling for the effects of age, gender, comorbidities and complications, each variable was entered into the model individually in 6 separate analyses. The regression models were repeated with depression as the dependent variable and each independent variable entered separately with the interaction between the variable in question and ethnicity. Each model was adjusted for age, gender, comorbidity and complications.

Hosmer-Lemeshow tests were conducted with each model to indicate the degree of goodness of fit ($P>0.05$). Analyses were performed using SPSSv14 (SPSS, Chicago, IL, USA)

4.3 Results

Of the 6230 cases in the study sample, 22.5% (n= 1405) had type 1 diabetes and 76.7% (n= 4781) had type 2 diabetes.

4.3.1 Type 1 diabetes

Table 4.3 shows medical and demographic characteristics of the study population with type 1 diabetes. The majority of patients were aged ≤59 years (80%) and had had diabetes for 15 or more years (57.4%). Fifty-seven percent were female and similar proportions of the sample were represented in each group for IMDS. Twenty-five percent of the sample had one or more comorbid condition and 54.9% had one or more diabetes related complication. HbA1c levels ≥7% were observed in 1123 patients (84%) and 298 (24.9%) had a BMI >30 kg/m^2.

A greater proportion of South Asians scored within the most deprived group in comparison to WEs (28.2% vs. 16.9%, p< 0.001). South Asians had a significantly higher mean HbA1c level (8.9% vs. 8.3%, p<0.001) but lower systolic blood pressure (136mmHg±19 vs. 142mmHg±18, p= 0.001). White Europeans were significantly more likely than South Asians to be smokers (30.5% vs. 16.9%, p<0.001) and to have had diabetes for at least 15 years (59.7% vs. 45.4%, p=0.003).

Table 4.3 Demographic and medical characteristics of people with type 1 diabetes

	Type 1			Total
	South Asian N (%)	White European N (%)	P	Type 1 N (%)
N	166	1178		1405
Age (Years)				
< 59	141 (84.9)	934 (79.4)	.118	1123 (80)
>60	25 (15.1)	242 (20.6)		280 (20)
Sex				
Males	103 (62)	673 (57.1)	.264	810 (42.3)
Females	63 (38)	505 (42.9)		595 (57.3)
IMDS (Quartiles)				
1	23 (14.1)	429 (36.7)	.001	468 (33.6)
2	34 (20.9)	311 (26.6)		360 (25.8)
3	60 (36.8)	232 (19.8)		308 (22.1)
4	46 (28.2)	198 (16.9)		258 (18.5)
Duration of diabetes (years)				
0-5	35 (21.5)	177 (15.3)		227 (16.5)
6-14	54 (33.1)	289 (25)	.003	359 (25.6)
15+	74 (45.4)	689 (59.7)		791 (57.4)
Insulin	--	--	--	--
OAD	20 (12.1)	67 (5.7)	.003	93 (6.6)
Comorbidities	49 (29.9)	291 (24.7)	.185	350 (25)
Complications	77 (47.8)	663 (56.5)	.047	766 (54.9)
Smoker	28 (16.9)	359 (30.5)	.001	402 (28.6)
Depression	16 (10)	91 (7.9)	.355	110 (8)
HbA1c ≥7%	146 (88.5)	977 (83.5)	.126	1123 (84.1)
BMI >30 Kg/m^2	38 (26.4)	245 (24.4)	.674	298 (24.9)
HbA1c*	8.91	8.30	.000	8.38
BMI*(Original)	26.72	26.79	.863	26.82
BMI (imputed data)	27.8 (5.5)	27.7 (5.4)	.869	27.7 (5.5)
Systolic BP	136.43 (18.7)	141.88 (17.8)	.001	141.4 (18.1)
Diastolic BP	74.62 (12.6)	75.5 (11.7)	.454	75.4 (11.8)
Cholesterol	4.628 (1.0)	4.8 (1.0)	.581	4.8 (1.0)

*** Geometric means**

Associations between the presence of diagnosed depression and patient characteristics are shown in Table 4.4. The prevalence of depression was higher in females than in males (p= 0.001) and this pattern was mirrored when examined separately by ethnicity for White Europeans (p= 0.001), however, a significant gender difference was not found in South Asians (p= 0.193). Rates of depression were also higher in patients with one or more comorbidity (p= 0.002), one or more diabetes related complication (p= 0.026) and in smokers (p= 0.016).

Table 4.5 presents the results from the multiple logistic regression. Female gender (OR 2.10, CI 1.38-3.19, p< 0.001), the presence of one or more diabetes related complication (OR 1.84, CI 1.10-3.03, p= 0.018) and the presence of one or more comorbidity (OR 1.89, CI 1.20-2.95, p= 0.005) were significantly and independently associated with depression. Logistic regression models conducted separately by ethnicity showed that in White Europeans, female gender (OR 2.1, CI: 1.3-3.2, p= 0.001), comorbidities (OR 1.8, CI: 1.15-2.96, p= 0.011), complications (OR 1.7, CI 1.1-2.7, p= 0.027) and smoking (OR 1.7, CI 1.1-2.6, p= 0.025) were significantly associated with depression, however none of the variables examined showed a significant association with depression in South Asians. No significant interactions were observed between ethnicity and the independent variables examined. Results from Hosmer-Lemeshow test were >0.05, indicating no statistical evidence of a poor fit between the logistic model and observed data.

Table 4.4 Association between depression and demographic and medical variables in people with type 1 diabetes

	N	Depressed	P
Ethnicity			
South Asian	160	16 (10)	.446
White European	1154	91 (7.9)	
Age			
< 59	1096	85 (7.8)	.568
>60	277	25 (9.0)	
Sex			
Males	794	46 (5.8)	.001
Females	581	64 (11)	
South Asian			
Males	99	7 (7.1)	.193
Females	61	9 (14.8)	
White European			
Males	661	37 (5.6)	.001
Females	493	54 (11)	
IMDS			
1	463	34 (7.3)	
2	353	26 (7.4)	.752
3	302	26 (8.6)	
4	246	23 (9.3)	
Years diabetes			
0-5	215	19 (8.8)	
6-14	350	24 (6.9)	.663
15+	782	63 (8.1)	
OAD			
Yes	89	6 (6.7)	.799
No	1284	104 (8.1)	
Comorbidities			
Yes	341	27.1 (12.0)	.002
No	1031	68 (6.6)	
Complications			
Yes	752	71 (9.4)	.026
No	614	37 (6.0)	
Smoker			
Yes	394	43 (10.9)	.016
No	981	67 (6.8)	
HbA1c			
>7.5	1011	28 (2.8)	.413
< 7.4	384	7 (1.8)	
BMI			
> 30	298	7(30.7)	1.0
<29	901	23 (2.6)	

	N	Control	Depressed	P
* HbA1c	1365	8.35	8.65	.069
* BMI (original)	1172	26.75	27.35	.251
Imputed BMI	1375	27.7 ± 5.4	28.3 ± 6	.210
Systolic BP	1096	141.9 ± 17.9	136.1 ± 20.1	.004
Diastolic BP	1081	75.5 ± 11.8	75.2 ± 12.1	.807
Cholesterol	1325	4.8 ± .97	4.8 ± 1.2	.785

**Geometric mean. Equal variance not assumed for imputed BMI and HbA1c and cholesterol for type 2 diabetes.*

Table 4.5. Odds ratio for diagnosed depression in people with type 1 diabetes

	Type 1 N = 1265	
	OR (CI)	P
WE vs. SA[1]	0.86 (0.46-1.60)	0.638
Age<59 vs. 60+	1.10 (0.65-1.86)	0.721
Females vs. Males	2.10 (1.39-3.19)	<0.001
Comorbidities vs. None	1.89 (1.21-2.96)	0.005
Complications vs. none	1.84 (1.11-3.04)	0.018
Insulin yes vs. no	--	--
OAD yes vs. no	--	--
BMI *(5 unit change)	1.02 (0.97-1.06)	0.454
HbA1c (1 unit change)	1.05 (0.93-1.17)	0.411
Duration of diabetes		
6-14 vs. 0-5	0.65 (0.33-1.26)	0.203
15+ vs. 0-5	0.58 (0.31-1.11)	0.104
IMDS		
2 vs.1	0.92 (0.53-1.62)	0.796
3 vs.1	0.71 (0.63-1.95)	0.710
4 vs.1	1.08 (0.59-1.96)	0.794

[1] WE= White European, SA= South Asian* including imputed data, OAD: Oral anti-diabetic drug

4.3.2 Type 2 diabetes

The majority of the sample were aged ≥60 (65.5%) and similar proportions of men and women (52.8% and 47.2%) and each IMDS group were represented. Fifty-six percent were using insulin therapy and 68.6% were prescribed oral anti-diabetic medication. One or more comorbid condition was present in 46.4% of the sample, and one or more diabetes related complication in 47.2%. Sixty eight percent had a HbA1c ≥7% and 55.1% had a BMI>30 kg/m^2 (Table 4.6)

In comparison to White Europeans, a greater proportion of South Asians scored within the most deprived quartile group (30.8% vs. 24.5% respectively, p<0.001), had been diagnosed with diabetes for 15 years or more (28.4% vs. 21.6%, p = 0.001) and had a

significantly higher mean HbA1c level (8.06% vs. 7.64%, p<0.0001). White Europeans with type 2 diabetes in comparison to South Asians, had a higher mean BMI (32.2 ± 6.8 vs. 29.9 ± 5.9, p< 0.0001) and systolic blood pressure (147.2mmHg ± 22.2 vs. 142.7mmHG ± 21.4, p< 0.0001) (Table 4.6).

Table 4.6 Demographic and medical characteristics of people with type 2 diabetes

	Type 2			Total
	South Asian N (%)	White European N (%)	P	Type 2 N (%)
N	1331	3193		4781
Age (Years)				
< 59	660 (49.6)	896 (28.1)	.001	1651 (34.5)
>60	671 (50.4)	2295 (71.9)		3128 (65.5)
Sex				
Males	686 (51.5)	1712 (53.6)	.214	2523 (52.8)
Females	645 (48.5)	1481 (46.4)		2258 (47.2)
IMDS (Quartiles)				
1	146 (11.1)	893 (28.3)	.001	1088 (23)
2	238 (18.1)	849 (26.9)		1144 (24.2)
3	524(39.9)	641 (20.3)		1234 (26.1)
4	405 (30.8)	774 (24.5)		1256 (26)
Duration of diabetes (years)				
0-5	441 (36.2)	1232 (42.8)		1762 (40.6)
6-14	431 (35.4)	1028 (35.7)	.001	1532 (35.3)
15+	346 (28.4)	621 (21.6)		1042 (24.0)
Insulin	730 (54.9)	1806 (56.6)	.291	2678 (56.1)
OAD	942 (70.9)	2166 (68)	.059	3273 (68.6)
Comorbidities	603 (45.4)	1507 (47.3)	.255	2212 (46.4)
Complications	631 (47.7)	1486 (46.8	.630	2244 (47.2)
Smoker	153 (11.5)	590 (18.5)	.001	783 (16.4)
Depression	100 (7.7)	320 (10.3)	.007	435 (9.3)
HbA1c ≥7%	942 (73.5)	2004 (65.4)	.001	2946 (67.8)
BMI >30 Kg/m^2	397 (41.7)	1230 (61.1)	.001	1738 (55.1)
HbA1c*	8.06	7.64	.000	7.77
BMI*(Original)	29.15	31.94	.000	31.02
BMI (imputed data)	29.9 (5.9)	32.2 (6.8)	.000	31.6 (6.8)
Systolic BP	142.7 (21.4)	147.2 (22.2)	.000	145.9 (22.1)
Diastolic BP	73.3 (13.9)	76 (13.4)	.230	75.9 (13.5)
Cholesterol	4.6 (1.1)	4.6 (1.1)	.164	4.6 (1.0)

*** Geometric means**

In comparisons (Table 4.7), the prevalence of depression was 10.3% in WEs compared to 7.7% in South Asians (p= 0.008). The rates were also higher in patients aged ≤59 years old (p< 0.0001), in females (p< 0.0001), patients with a longer duration of diabetes (p= 0.005), patients on insulin (p< 0.0001), those with one or more comorbidity (p= 0.0001), one or more complication (p<0.0001), and patients who were smokers (p= 0.013). A significant association was also demonstrated with BMI (p< 0.0001) and cholesterol levels (p= 0.040).

In multiple logistic regression analyses (Table 4.8), White Europeans ethnicity was a significant independent risk factor for depression . The odds of depression were also increased in those aged ≤59 years, with complications, comorbidities, in those using insulin and in patients with a higher score for deprivation.

In models conducted separately by ethnicity, being aged < 59 years (White European OR 1.7, CI 1.3-2.2, p< 0.001, South Asian OR 2.31, CI 1.5-3.6, p< 0.001), female gender (White European OR 1.5, CI 1.2-1.9, p< 0.001, South Asian OR 1.7, CI 1.14-2.7, p= 0.009) comorbidity (White European OR 1.5, CI 1.2-2.0, p<0.001, South Asian OR 1.9, CI 1.23-2.9, p= 0.004) and insulin (White European OR 1.4, CI 1.1-1.8, p= 0.017, South Asian OR 1.9, CI 1.2-3, p= 0.009) use were associated with depression. Complications (White European OR 1.6, CI 1.3-2.1, p< 0.001) and BMI (WE change in 5 units (OR 1.02, CI 1.00-1.03, p= 0.029) were associated with depression in White Europeans but not South Asians. No significant association was demonstrated between ethnicity and any of the independent

variables examined. Results from Hosmer-Lemeshow test were >0.05, indicating no statistical evidence of a poor fit between the logistic model and observed data.

Table 4.7 Association between depression and demographic and medical variables in people with type 2 diabetes

	N	Depressed	P
Ethnicity			
South Asian	1305	100 (7.7)	.008
White European	3116	320 (10.3)	
Age			
< 59	1598	183 (11.5)	.000
>60	3073	252 (8.2)	
Sex			
Males	2198	189 (7.6)	.000
Females	2475	246 (11.2)	
South Asian			
Males	675	39 (5.8)	.011
Females	630	61 (9.7)	
White European			
Males	1676	146 (8.7)	.002
Females	1440	174 (12.1)	
IMDS			
1	1068	83 (7.8)	
2	1123	101 (9.0)	.124
3	1204	121 (10.0)	
4	1219	127 (10.4)	
Years diabetes			
0-5	1720	136 (7.9)	.005
6-14	1497	168 (11.2)	
15+	1024	104 (10.2)	
Insulin			
Yes	2622	294 (11.2)	.000
No	2045	140 (6.8)	
OAD			
Yes	3196	311 (9.7)	.141
No	1464	122 (8.3)	
Comorbidities			
Yes	2162	242 (11.2)	.000
No	2500	191 (7.6)	
Complications			
Yes	2205	253 (11.5)	.000
No	2440	180 (7.4)	
Smoker			
Yes	755	89 (11.8)	.013
No	3918	346 (8.8)	
HbA1c			
>7.5	2467	75 (3)	.796
< 7.4	2128	61 (2.9)	
BMI		73 (4.2)	
> 30	1738		.028
<29	1414	38 (2.7)	

	N	Control	Depressed	P
* HbA1c	4495	7.76	7.87	.207
* BMI (original)	3080	30.81	32.79	.000
Imputed BMI	4673	31.5 ± 6.6	32.9 ± 7.0	.000
Systolic BP	3111	146.18 ± 22.1	144.69 ± 22.2	.250
Diastolic BP	3063	75.91 ± 13.6	75.83 ± 13.4	.927
Cholesterol	4406	4.602 ± 1.0	4.737 ± 1.3	.040

**Geometric mean. Equal variance not assumed for imputed BMI and HbA1c and cholesterol for type 2 diabetes.*

Table 4.8. Odds ratio for diagnosed depression in people with type 2 diabetes

	Type 2 N = 3845	
	OR (CI)	P
WE vs. SA[1]	1.60 (1.22-2.10)	<0.001
Age<59 vs. 60+	1.63 (1.28-2.07)	<0.001
Females vs. Males	1.48 (1.19-1.84)	<0.001
Comorbidities vs. None	1.53 (1.22-1.92)	<0.001
Complications vs. none	1.33 (1.04-1.71)	0.023
Insulin yes vs. no	1.53 (1.17-2.00)	0.001
OAD yes vs. no	1.06 (0.82-1.36)	0.664
BMI *(5 unit change)	1.01 (0.99-1.03)	0.121
HbA1c (1 unit change)	1.00 (0.94-1.07)	0.879
Duration of diabetes		
6-14 vs. 0-5	1.16 (0.88-1.53)	0.299
15+ vs. 0-5	0.99 (0.71-1.38)	0.942
IMDS		
2 vs.1	1.30 (0.94-1.81)	0.117
3 vs.1	1.55 (1.11-2.15)	0.009
4 vs.1	1.49 (1.09-2.07)	0.013

[1] WE= White European, SA= South Asian* including imputed data, OAD: Oral anti-diabetic drug

4.4 Discussion

This study represents the first report of the prevalence and risk factors for depression in a large multiethnic population with either type 1 or type 2 diabetes. In addition the study is unique in that it presents data for migrant South Asians, a previously understudied group, as well as a comparison with White Europeans.

The unadjusted rates for depression identified are similar to reports from a large population-based survey of participants from over 60 countries, which identified prevalence rates of depression to be between 7.3-11.3% in people with diabetes [79]. Depression prevalence estimates vary widely, however, depending on a range of factors including the medical and demographic characteristics of the population

studied [75, 213]. Comparisons between the present findings and previous studies should therefore be exercised with caution. For example a meta-analysis of 43 studies of the prevalence of depression in people with type 1 and type 2 diabetes concluded that the rates were generally higher in studies conducted in clinical settings (32%) as opposed to population settings (20%)[75]. Furthermore, differences have been associated with the method used for depression identification with a higher prevalence observed in studies using self-report questionnaires (31%) than with diagnostic interviews [75] (Chapter 2). It is important, however to make a distinction between these findings and the present study, in that the present observations of depression prevalence are based on cases recognised by a physician and/or treated using antidepressant medication. A similar process for depression identification has been applied in only one previous study. Nichols and Brown reported unadjusted rates of diagnosed depression to be 17.9% in a large US population sample with type 2 diabetes [156]. Although the rates of diagnosed depression identified in the present study are considerably lower, population characteristics and geographical differences make between-study comparisons problematic.

Nevertheless, factors associated with depression are consistent with past reports [75, 126, 156, 213, 257, 258, 260] suggesting that cases with diagnosed depression as identified in our study may not be markedly distinct from cases identified by Nichols and Brown, or previous studies utilising diagnostic interviews or self report tools. In type 1 and type 2 diabetes, the odds of depression were increased in females, smokers and those with complications and comorbidities. An increased odds for depression in those with type 2 diabetes was also associated with the

duration of diabetes, insulin use and cholesterol levels, although these associations were not demonstrated in those with type 1 diabetes.

Risk factors associated with depression varied in type 1 and type 2 diabetes and also by ethnicity, demonstrating the importance of observing these subgroups separately when examining the relationship between depression and diabetes. The findings also suggest that research is needed to identify additional risk factors that are associated with depression in South Asians, particularly with type 1 diabetes.

Rates of depression in people with diabetes have been found to be either similar or higher in ethnic minorities [126, 230, 257, 258, 260]. In contrast our results showed that White Europeans exhibited significantly higher rates of diagnosed depression relative to South Asians, although this difference was not observed in type 1 diabetes. Interaction analyses revealed that these findings are not explained by any of the variables we examined including socioeconomic status, suggesting there may be other cultural factors exerting a mediating effect.

It is possible is that our findings reflect true differences in the underlying prevalence of depression between these two ethnic groups. However, although a small number of studies have identified lower rates of depression among the South Asian population in the UK in comparison to White Europeans [81, 261, 262], these findings have been criticised on methodological grounds. For example it has been argued that traditional westernised methods for depression assessment may be inappropriate and therefore fail to recognise depression in South Asian populations

in whom the manifestation and expression of depression may differ from their White European counterparts [168, 263, 264].

Similarly, lower rates of observed depression in South Asians with type 2 diabetes may be due to difficulties in case recognition of depression and/or treatment initiation due to problems associated with language, stigma and beliefs about health care, as well as cultural differences in the presentation of depression [81, 264] [168, 263, 265, 266]. These issues may be particularly accentuated in the South Asian elderly (those who migrated to the UK in late childhood or adulthood) rather than the generally younger 'second generation' South Asians who may have a greater cultural affinity to western idioms of depression [82, 267] as well higher rates of English literacy [4]. This in turn may explain why ethnic disparities in the rates of depression were observed in people with type 2 diabetes (the majority of who were aged $\geq$60) and not in people with type 1.

Limitations of the present study include the fact that the data are from a single geographically located hospital and thus results may not be generalisable to other settings. Furthermore, our data are limited to the coding strategies implemented within the clinical workstation and therefore without explicit categorisation of various diagnostic subgroups of depression, we are unable to provide estimates specifically for the rate of major depression. As with research utilising self-report tools, our figures for depression most likely correspond to individuals with differing levels of depressive symptoms which may or may not constitute major depression. Our categorisation for ethnicity also represents broad groups and therefore any differences which may exist within subgroups (for example, between people of

Indian and Pakistani origin) are not accounted for in this analysis. In addition, the data in the present study are cross-sectional, and therefore risk factors represent correlational associations, which in turn limit analysis concerning the direction of causation.

The accuracy of these prevalence rates is also dependent on the completeness of routinely recorded information and there is likely to be under recording of depressive symptoms. In order to maximise sensitivity we incorporated the receipt of antidepressant medication into our algorithm for identifying depressed cases. However our data cannot account for cases in which physicians had failed to record a diagnosis and the patients in question were in receipt of non-drug management, such as counselling only. As such our figures are likely to be an underestimation of the prevalence of diagnosed depression. Furthermore our rates are likely to underestimate the prevalence of depression in people with diabetes, as it is well established that rates of recognition of depression are low in both primary and secondary-care services [268-270].

Despite these limitations, to our knowledge the present study offers the first insight into the prevalence of depression in a large multi-ethnic secondary care population with type 1 or type 2 diabetes in the UK. Depression in diabetes represents a significant impediment to the interests of public health, with research documenting its contribution to poor glycaemic control, a reduction in functional status and quality of life as well as the development of both micro- and macrovascular disease [85, 86, 213]. These issues may be of particular concern in the South Asian communities within the UK who are at increased risk for both diabetes [17, 245-

248] and adverse outcomes associated with comorbidity [58, 247, 249, 250]. The findings from this study identify important ethnic disparities in the rates of diagnosed depression in people with type 2 diabetes. Once recognised, depression in people with diabetes can be effectively treated with, improvements demonstrated in both glycaemic control as well as reduced risk of mortality [138, 271, 272]. Further research is needed in order to identify the underlying reasons for these ethnic disparities. In the meantime health care providers should continue to be alert to the possibility of depression in all patients with diabetes.

Chapter 5

The association between diagnosed depression and HbA1c in a multiethnic secondary care population

5.1 Introduction

HbA1c is an important measure of long term glycaemic control which indicates the degree of hyperglycaemia over approximately the prior 120 days from the point of testing. Guidelines for management of both type 1 and type 2 diabetes recommend efforts to normalise HbA1c without detriments to HRQOL [44, 273-276] in particular increased weight gain and increased risk of hypogycaemia. However, maintaining glycaemic control can be a psychologically demanding task which requires those with diabetes to adhere to a complex regimen of medical care and lifestyle modification. Failing to achieve glycaemic control is a major risk factor for diabetes related complications in both type 1 and type 2 diabetes mellitus,[66, 69] furthermore evidence suggests a continuous association between glycaemia as determined by HbA1c levels and the risk for micro and macrovascular complications and mortality [69]. Improved glycaemic control on the other hand has been shown to reduce the incidence of both long-term and end-stage micro-vascular complications [63, 64, 66, 277-279].

Depression is a common affective disorder and there is ample evidence to suggest that people with diabetes suffer from particularly high levels (Chapter 2 and 4). Both depression and its treatment via antidepressant medication may interfere with glycaemic control through a number of mechanisms. Most obviously, common symptoms of depression such as decreased energy, concentration and motivation may impair the ability to adhere to medication or self care regimes including physical activity, smoking cessation and healthy eating which in turn may worsen glycaemic control [112, 280, 281]. However, there is also evidence to suggest that the impact of depression on behavioural aspects of self-care may not fully explain

the association between depression and poor glycaemic control. For example Gary et al [114], in their study of primary care attenders with type 2 diabetes, demonstrated that, when controlling for the effects of age, gender, income, social support, and duration of diabetes, depressive symptoms as assessed by the CES-D were associated with worse metabolic control. However this relationship was not explained by behavioural factors including diet, exercise and self-monitoring behaviour. In those with type 1 diabetes, Lustman et al[282] also demonstrated that self-care activity did not mediate the association between depression and poor HbA1c control.

These findings raise the possibility that depression may also impair glycaemic control via psycho-physiological processes. For example depression has been associated with increased cortisol secretion within the hypothalamic pituitary adrenal (HPA) axis resulting in reduced glucose uptake and elevated glucose levels [283-285]. Major depression has also been associated with hyperactivity of the sympathoadrenal system followed by increased secretion of several counter-regulatory hormones which act to amplify insulin resistance and worsen glycaemic control [102, 285].

Although successful remission of depression using antidepressant medication has the potential to improve glycaemic control through behavioural change [286], various antidepressant medications are also demonstrated to have direct associations with glycaemic levels. For example tricyclic antidepressants (TCAs) such as Nortriptyline may impair HbA1c control by increasing glucose levels and reducing insulin levels independently of weight loss [286-288]. Conversely, there is evidence

to suggest that some selective serotonin reuptake inhibitors (SSRIs) including Fluoxetine and Paroxetine may have a favourable impact on HbA1c and reduce insulin dosage requirements [289-293].

To add this complexity, the association between depression and HbA1c is also likely to be bi-directional as studies suggest that poor glycaemic control may in fact have a reciprocal effect by initiating or exacerbating depressed effect in people with diabetes. Fluctuations in blood glucose levels may provoke symptoms of depression via a direct influence on brain structure[294] or, alternatively, the association may be driven indirectly via the development of diabetes related complications, functional impairment or decreased quality of life[100].

Despite various pathological propositions, findings from studies which examine the association between depression and poor glycaemic control are inconsistent. Although a meta-analysis of 24 studies demonstrated that depression was significantly associated with hyperglycaemia in both type 1 and type 2 diabetes[85], it is important to consider that the results reported only a small to moderate association and in fact a large proportion of the studies included in the meta-analysis reported no association between depression and hyperglycaemia.

Since Lustman et al's meta-analysis[85], research into the association between depression and glycaemic control in people with diabetes has continued to expand with numerous studies continuing to add to a conflicting and complex knowledge base. However, emerging evidence appears to suggest that the association may be

clustered or more pronounced within certain clinical or demographic subgroups that may be more susceptible to the effects.

It has been argued that the heterogeneity in findings may be due to differences in the diagnostic distinction between type 1 and type 2 diabetes. When examined meta-analytically, the association between depression and hyperglycemia was greater in studies conducted in those with type 1 diabetes, in comparison to those involving type 2 diabetes (effect size 0.28 vs. 0.15) [85]. It may be that the behavioural or neuro-chemical mechanisms through which depression may impair glycaemic control may be more pronounced in those with type 1 diabetes, which is characterised by complete insulin deficiency in comparison to those with type 2 diabetes who may still produce some insulin. Several cross-sectional studies have reported an association in those with type 1 diabetes but not in those with type 2 diabetes [90, 295]. In contrast, Surwit et al (2005) found no association between depression and HbA1c both in those with type 1 and those with type 2 diabetes [296]. However, further subgroup analysis in those with type 1 diabetes revealed a negative association between depression and HbA1c in those taking at least 3 daily insulin injections but found no association in those prescribed a less intensive treatment regimen. This finding suggests that the association between depression and HbA1c may be moderated by the intensity of self-care regimens.

Depression may also be particularly influential in those who adhere to a strict regimen such that any depression-induced change in self-care behaviour would produce a significant negative effect on glycaemic levels in comparison to those managed using a less-intensive regime. For example insulin therapy which requires

regular blood glucose monitoring and dose adjustments in response to diet or physical activity levels may be particularly venerable to the effects of depression in comparison to those treated using oral medication. This premise has received some preliminary support. Aikens et al (2008) [297] examined the association between depression and glycaemic control in people with type 2 diabetes and demonstrated a significant negative relationship in patients prescribed insulin therapy but not in those taking oral anti-diabetic medication alone, even when controlling for the effects of diabetes duration. However further analyses revealed that the association was not mediated by the influence of depression on treatment adherence and therefore the exact mechanism for the moderating effect of treatment type is unclear.

Studies also suggest that the association between depression and HbA1c may differ across gender [298, 299] A study by Lloyd et al (2001) demonstrated an association between depression and HbA1c in men but not women with type 1 and type 2 diabetes in the UK[300]; on the other hand findings from Pouwer and Snoek (2001) showed a positive association between depression and HbA1c in women with diabetes but not in men[299]. These findings suggest that there may be cultural differences in the relationship between gender and coping styles which may modify the association between depression and HbA1c in people with diabetes, However, further research in this area is required [301].

Due to wide ranging methodological differences between studies, including differences in the assessment of depression, variations in the cut-points for HbA1c (when examined dichotomously) and the diversity of study designs and populations

considered, it is difficult to systematically study and accurately identify specific moderators of the association between depression and glycaemic control. However what is clear is that significant gaps in the literature remain. In particular research examining the association between depression and glycaemic control in the UK is limited and the few available studies are criticised for using small non-representative samples or failing to control for potential confounding factors such as complications and type of diabetes[300, 302]. Furthermore, the association between depression and HbA1c has been demonstrated in a number of ethnic groups [303, 304]. Although the reasons are likely to be multi-factorial, no previous study has examined psychological explanations, such as the presence of depression for disparate outcomes in achieving glycaemic control between South Asian and White European people with diabetes.

5.2 Aims

This study aimed to examine the association between glycaemic control and depression in a large multiethnic population with both type 1 and type 2 diabetes independently, while controlling for potentially confounding factors. In addition the study aimed to investigate the extent to which the association between ethnicity and poor glycaemic control was moderated by depression.

5.3 Method

5.3.1 Design

A cross-sectional study was conducted using data collected from the routine medical records of all patients attending a UK hospital diabetes and endocrinology clinic over a two year period (2003-2005).

5.3.2 Data collection

Cases included male and female patients with type 1 or type 2 diabetes attending the clinic for a referred appointment or for their annual diabetes review. Details regarding the data source and collection are provided in Chapter 4 (sections 4.2.2 and 4.2.3). Data were collected retrospectively from the diabetes clinical work station. Variables extracted included: age (< 59 and 60+), gender, IMDS (4 groups), duration of diabetes (0-5, 6-14 or 15+ years) diabetes type (type 1 or 2), insulin use, OAD use, Ethnicity (South Asian or White European), BMI, HbA1c and depression. Data were limited to South Asian and White European patients only. In addition data were collected regarding smoking status as well as the class of antidepressant medication prescribed (SSRI, MAO-I or TCA).

As detailed in Chapter 4 (section 4.2.3) patients with a diagnosis of depression were identified through a combination of case documentation in the patient's list of problems and or a prescription for antidepressant medication above or equal to the minimum therapeutic dosage recommended for depression using the UK prescribing formulary (BNF 52)[252].

5.3.4 Statistical analysis

All analyses were performed separately for patients with type 1 and type 2 diabetes.

Demographic and medical characteristics were previously compared between South Asian and White Europeans and between those with and without diagnosed depression using χ^2 tests (Chapter 4, Table 4.3 and Table 4.6).

HbA_{1c} was categorised into 2 groups in order to allow for a non-linear relationship between depression and glycaemic control. HbA_{1c} was categorised into good and poor control, with values $\geq$7% corresponding to poor glycaemic control. This cut-off for HbA_{1c} was selected as current clinical guidelines recommend additional clinical action for patients whose HbA_{1c} levels fall within this range [305]

The likelihood of poor glycaemic control was examined in people with depression in comparison to those without depression. Logistic regression analyses were conducted in order to compute adjusted and unadjusted odds ratios (OR) and 95% confidence intervals (CI). Adjusted analyses included covariates that were considered most likely to be related to both depression and Hba1c values on the basis of previous research. These were age, gender, oral anti-diabetic medication (OAD) medication, insulin (type 2 only), smoking, complications, comorbidities, duration of diabetes, deprivation and BMI [85, 112, 213, 306]. To investigate ethnic differences in the association between depression and glycaemic control, the interaction between ethnicity and depression was entered into a second adjusted model. Hosmer-Lemeshow statistics were obtained in order to assess goodness of fit.

The above analyses were repeated in order to examine the degree of linear association between depression and glycaemic control. HbA1c values were transformed using the Log_{10} transformation in order to achieve well-fitting models. Differences in geometric means for HbA1c values were compared for patients with diagnosed depression in comparison to those without using the independent samples t-test. Multiple linear regression analysis was used to compare the HbA1c values of

patients with depression with those of patients without depression. Results from the linear models were exponentiated in order to derive the ratio of geometric means and confidence intervals. Statistical analyses were performed in STATAv9.2 (StataCorp 2005, Stata Statistical Software, College Station, TX).

5.3.5 Treatment of Missing data

To impute the missing data for BMI, the imputations by chained equations (MICE) were calculated using the STATA software package ICE[307], with missing at random assumptions (Chapter 4). Variables used in the imputation procedure were age, gender, ethnicity, duration of diabetes, HbA1c, deprivation and insulin use.

Five copies of the data, each with missing values suitably imputed, were analysed separately, and then estimates of parameters of interest were averaged across the 5 models to provide a single mean estimate, and standard errors were adjusted using to Rubin's formula [256].

5.3.6 Sensitivity analyses

Previous research has suggested that different classes of antidepressant medication may have varying effects on glycaemic control [286-293]. Follow-up analyses were therefore conducted to examine the differences in HbA1c by antidepressant class. χ^2 tests were conducted to examine differences in poor glycaemic control (HbA1c = $\geq$7%) between patients prescribed selective serotonin re-uptake inhibitors (SSRIs) vs. those prescribed tri-cyclic antidepressants (TCAs).

5.4 Results

The final study sample consisted of 5868 people with type 1 (N =1344) and type 2 diabetes (N= 4524). Demographic and medical characteristics of the study sample are described in Chapter 4 (Table 4.3).

5.4.1 Type 1 diabetes

Of the 107 patients with depression 31 (29%) were prescribed TCAs, 56 (52%) were prescribed SSRIs, 6% (N = 6) were prescribed an 'other' antidepressant and 13% (N = 14) had a diagnosis of depression recorded in their notes but were not currently prescribed any antidepressant medication.

Eighty-four percent (N = 1131) of patients with type 1 diabetes had HbA1c values ≥7%. In both adjusted and unadjusted analyses (Table 5.1), having a diagnosis of diabetes for 15 or more years was associated with an increased risk for poor glycaemic control. No increased risk for poor HbA1c control was observed in those with depression in comparison to those without in either adjusted or unadjusted analyses (p> 0.05). Results from Hosmer-Lemeshow test were >0.05, indicating no statistical evidence of a poor fit between the logistic model and observed data.

Similarly no difference in mean HbA1c values was observed in those with depression (geometric mean HbA1c = 8.7%, range 8.5 to 8.8%) versus those without (geometric mean 8.4%, range 8.3 to 8.4%), P = 0.07 (overall mean HbA1c value for people with type 1 diabetes = 8.5, SD = 1.7). In multivariable analyses (table 5.2), higher HbA1c values were associated with South Asian ethnicity (P<

0.001), being a smoker (P <0.001) and higher levels of deprivation (P<0.001). An increased risk for poor glycaemic control was not evident in those with depression in comparison to those without (P = 0.258).

In order to examine whether possible associations between depression and HbA1c differed by ethnicity, the interaction between depression and ethnicity was entered into the complete models. No significant interactions between depression and ethnicity were observed in either logistic regression or linear models (OR 0.415 95%CI 0.072-2.393 p=0.325 and Ratio geometric mean 0.947, 95% CI 0.847-1.060, p = 0.342 respectively).

Table 5.1 The association between medical and demographics factors and glycaemic control in people with type 1 diabetes

Variable	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
60+ vs. <59	1.034 (0.713-1.501)	0.850	1.000 (0.668-1.496)	0.999
Females vs. males	0.832 (0.614-1.127)	0.235	0.837 (0.614-1.143)	0.263
No OAD vs. OAD	1.418 (0.720-2.794)	0.313	1.404 (0.687-2.873)	0.352
SA vs. WE	1.501 (0.896-2.514)	0.123	1.535 (0.899-2.621)	0.117
Depression vs. none	1.686 (0.886-3.208)	0.111	1.611 (0.836-3.101)	0.154
Smoking	1.356 (0.961-1.912)	0.083	1.409 (0.985-2.013)	0.060
Complications	1.223 (0.907-1.651)	0.187	0.978 (0.684-1.400)	0.905
Comorbidities	0.960 (0.684-1.347)	0.812	0.827 (0.575-1.188)	0.304
Years of diabetes				
6-14 vs. 0-5	1.359 (0.873-2.117)	0.175	1.384 (0.877-2.185)	0.163
15+ vs. 0-5	1.689 (1.138-2.508)	0.009	1.865 (1.182-2.941)	0.007
IMDS				
2 vs. 1	1.064 (0.731-1.548)	0.746	1.051 (0.719-1.536)	0.799
3 vs. 1	1.330 (0.877-2.016)	0.179	1.288 (0.842-1.971)	0.243
4 vs. 1	1.356 (0.866-2.124)	0.184	1.306 (0.821-2.076)	0.260
BMI	1.002 (0.966-1.040)	0.904	1.005 (0.967-1.044)	0.816

* N = 1304 due to small numbers of missing data for complications, comorbidities, OAD and depression

Table 5.2 The association between medical and demographic variables and glycaemic control (continuous) in people with Type 1 and Type 2 diabetes

Variable	Type1 = 1304 Ratio geometric means	P	Type 2 =4386 Ratio geometric means	P
60+ vs. <59	0.976 (0.949-1.003)	0.079	0.969 (0.956-0.983)	0.000
Females vs. males	0.983 (0.962-1.004)	0.114	1.006 (0.994-1.019)	0.293
OAD vs. no	1.018 (0.974-1.065)	0.420	1.044 (1.030-1.059)	0.000
Insulin vs. no	--	--	1.134 (1.119-1.149)	0.000
SA vs. WE	1.064 (1.030-1.100)	0.000	1.052 (1.035-1.068)	0.000
Depression vs. none	1.022 (0.984-1.062)	0.258	0.994 (0.975-1.014)	0.573
Smoking	1.061 (1.036-1.086)	0.000	(1.003 (0.987-1.019)	0.729
Complications	1.004 (0.980-1.029)	0.721	1.000 (0.987-1.013)	0.986
Comorbidities	0.996 (0.971-1.021)	0.738	0.986 (0.975-0.998)	0.021
Years of diabetes				
6-14 vs. 0-5	0.985 (0.951-1.020)	0.389	1.022 (1.005-1.040)	0.010
15+ vs. 0-5	0.988 (0.956-1.021)	0.465	1.028 (1.009-1.047)	0.004
IMDS				
2 vs. 1	1.007 (0.980-1.034)	0.624	0.990 (0.972-1.008)	0.276
3 vs. 1	1.031 (1.002-1.061)	0.039	0.994 (0.978-1.12)	0.523
4 vs. 1	1.060 (1.028-1.093)	0.000	1.004 (0.988-1.021)	0.621
BMI	0.999 (0.997-1.002	0.478	1.001 (1.000-1.003)	0.037

5.4.2 Type 2 diabetes

Of the 420 individuals with type 2 diabetes and depression, 181 (43%) were prescribed TCAs, 188 (45%) were prescribed SSRIs, 4 (1%) were prescribed another antidepressant and 47 (11%) had a diagnosis for depression but were not currently prescribed any antidepressant medication.

Sixty-eight percent (N =3061) of people with type 2 diabetes had HbA1c values ≥7%. In unadjusted logistic regression analyses (Table 5.3), an increased risk for poor glycaemic control was evident in those aged 60 years and above (P<0.001), in those using insulin (P<0.001), in those not using OAD (P<0.001), in South Asians (P<0.001) and in those with a longer duration of diabetes (P<0.001). However in multivariable analysis (Table 5.3), in addition to the variables associated with poor

control in unadjusted analysis, good HbA1c control was observed in patients with a diagnosis of depression in comparison to those without (OR= 0.78, 95% CI = 0.61-1.0, P = 0.038). Results from Hosmer-lemeshow test were >0.05, indicating no statistical evidence of a poor fit between the logistic model and observed data.

The mean HbA1c value for people with type 2 diabetes was 8.0% (SD = 1.7). No statistically significant difference was observed between those with diagnosed depression (geometric mean HbA1c = 7.9%) in comparison to those without (geometric mean HbA1c = 7.7%), P = 0.159. In contrast to the finding from multiple logistic regression, no significant association was observed between depression and HbA1c in linear regression analyses (p= 0.573). Finally no significant interactions between depression and ethnicity were observed in either logistic regression or linear models (p=0.325 and p= 0.342 respectively).

Table 5.3 The association between medical and demographics factors and HbA_{1c} ≥7% in people with type 2 diabetes, N =4386 *

Variable	Unadjusted OR (CI)	P	Adjusted OR (CI)	P
60+ vs. <59	0.780 (0.679-0.897)	0.000	0.803 (0.682-0.945)	0.008
Females vs. males	1.071 (0.938-1.222)	0.311	1.101 (0.956- 1.268)	0.182
Insulin	3.408 (2.982-3.894)	0.000	1.655 (1.414-1.936)	0.000
No OAD vs. yes	1.506 (1.312-1.729)	0.000	3.139 (2.693-3.660)	0.000
SA vs. WE	1.466 (1.263-1.701)	0.000	1.464 (1.222-1.753	0.000
Depression vs. none	0.962 (0.775-1.194)	0.724	0.779 (0.615-0.987)	0.038
Smoking	1.154 (0.969-1.375)	0.108	0.933 (0.769-1.132)	0.482
Complications	1.970 (1.728-2.245)	0.000	1.176 (1.008-1.373)	0.040
Comorbidities	1.036 (0.911-1.178)	0.593	0.888 (0.770-1.023)	0.101
Years of diabetes				
6-14 vs. 0-5	2.118 (1.798-2.494)	0.000	1.453 (1.210-1.745)	0.000
15+ vs. 0-5	2.976 (2.456-3.607)	0.000	1.779 (1.420-2.230)	0.000
IMDS				
2 vs. 1	0.898 (0.744-1.085)	0.264	0.894 (0.730-1.094)	0.278
3 vs. 1	0.912 (0.760-1.095)	0.323	0.847 (0.693-1.037)	0.107
4 vs. 1	0.979 (0.815-1.175)	0.816	0.924 (0.757- 1.127)	0.434
BMI	1.005 (0.994-1.017)	0.386	1.007 (0.995-1.020)	0.240

* Due to small numbers of missing data for complications, comorbidities, OAD and depression

5.4.3 Sensitivity analysis

No significant differences in the likelihood of poor glycaemic control were observed between depressed patients prescribed either TCAs or SSRIs, in either type 1 (90% vs. 89% respectively, P =1.000) or type 2 diabetes (68% vs. 64% P =0.528).

5.5 Discussion

Optimal glycaemic control is an essential component in preventing the potentially serious complications of diabetes [44, 64, 273-276, 279]. Numerous studies[85] have demonstrated a significant association between psychological concerns, particularly depression, and poor glycaemic control. The main objective of the present study was to investigate whether this association was also observable in a large multi-ethnic population in a UK specialist clinic.

Findings in those with type 1 diabetes suggest that there is no association between diagnosed depression and HbA1c control. This is in contrast to a vast body of research which has frequently suggested that people with type 1 diabetes may be particularly susceptible to poor glycaemic control in the presence of depressive symptomatology [85, 90, 295, 300]. Owing to the large sample size (N = 1304), these results are unlikely to be attributable to a lack of statistical power and alternatively a number of factors may account for the lack of an observed association in this population.

Firstly it is important to distinguish depressed cases included in the present analyses from those studied in previous reports. In the present study, these cases were defined as those currently recognised in their medical records as depressed, whereas previous studies which involved screening participants for depression used either self-report questionnaires or a clinical diagnostic interview. It is also worth noting that these studies failed to control for those in receipt of treatment for depression [85]. The majority of those recognised as depressed in the present study were currently in receipt of anti-depressant medication.

It is plausible that treatment for depression and subsequent alleviation of depressive symptoms would reduce any potential association with glycaemic control, as studies suggest that glycaemic control may possibly be improved with appropriate treatment of comorbid mental disorders [137, 286]. In addition, the majority of patients recognised as depressed were treated with SSRIs which several studies imply may have a direct influence on improved metabolic control [289-293]. However, these explanations remain speculative and, due to restrictions associated with the data available from routine medical records, it was not possible to ascertain the success of depression management and current severity of depressive symptomatology in those recognised as depressed. Furthermore due to the small number of cases receiving non-pharmacological management of depression we were unable to make comparisons with those prescribed and not prescribed antidepressants.

Alternatively, there has been recent suggestion that the association between depression and poor HbA1c control in those with type 1 diabetes may in fact be attributable to the complexity of diabetes regimens [296, 297]. However due to the lack of information regarding differences in insulin regimens, it was not possible in the present analyses to examine the moderating impact of this variable and future research is necessary to determine whether or not the association between depression and poor glycaemic control in those with type 1 diabetes is more pronounced in those adhering to a more complex insulin regimen.

In Lustman et al's review, the effect sizes were greater in studies which assessed depression using clinical interviews or standardised criteria as opposed to symptom severity checklists, suggesting that those fulfilling diagnostic criteria for depression may be expected to have greater abnormalities in HbA1c[85]. However in the present study details regarding the manner of diagnosis or the severity of depressive symptoms at the time of HbA1c measurement are not known and therefore could not be adjusted for. It is possible that symptoms of depression did not exceed a threshold required to disrupt the associated metabolically significant biological pathways [102, 283-285]. Furthermore it is not known whether the severity of depressive symptomatology was sufficient to impair adherence to prescribed dietary and lifestyle management of diabetes. Finally it should also be noted that patients attending secondary diabetes services were receiving support from a specialist diabetes team which could possibly reduce any behavioural impact of depression on glycaemic control.

The findings regarding the association between depression and HbA1c in those with type 2 diabetes are more perplexing. Contrary to expectation those with diagnosed depression were more likely to achieve an HbA1c target <7% in comparison to those without diagnosed depression. This is not, however, the first report of better HbA1c control in those with psychological disturbance in comparison to those without. Kruse et al (2003)[308] also examined the association between blood glucose control and common mental disorders assessed by diagnostic interview in a US community sample. They demonstrated that those with affective and anxiety disorders more frequently achieved adequate glycaemic control (HbA1c <7%) in comparison to those without mental disorders. Further analyses revealed that people

with mental disorders also had a greater number of physician visits per year, which the authors postulated may be associated with improved glycaemic control [308]. This may possibly offer some explanation for the disparity in glycaemic control observed between those with and without diagnosed depression in the present analyses. However, further research is necessary in order to determine whether depression is in fact associated with increased service utilisation in the present population and whether in turn this may be associated with better control in those with type 2 diabetes.

It is also important to consider alternative explanations. Firstly, the classification of depression in the present study represents a key point to consider. Cases of diagnosed depression include all those who were recognised as such and were either coded in their medical notes as having this diagnosis (a known rarity in medical record keeping) and/ or were receiving antidepressant treatment. Although the recording of prescribing data is likely to be highly accurate, this method of identifying depressed cases cannot account for those with recognised depression without a formal documentation in their medical records (unless they were in receipt of antidepressant medication) and also for those with unrecognised depression. Given that half the cases of depression in diabetes may go undetected by health care professionals [257], and the relatively lower prevalence of depression identified in this population in comparison to studies based on screening for depression (Chapter 4), the actuality of a non-depressed control group in the present analyses is questionable. As a result it is possible that failure to achieve adequate control (HbA1v <7%) in those without diagnosed depression, may be attributable to the impact of unrecognised and/ or untreated depression.

However, it is also worth noting that the association between depression and HbA1c was not a linear one, suggesting the possibility of two distinct groups. One of these groups is characterised by glycaemic control reaching a target of <7% with simultaneous high levels of depression and a second group is characterised by elevated HbA1c values but a lower prevalence of depression. It is important to acknowledge that achieving recommended HbA1c targets for many people with type 2 diabetes, particularly those referred to a secondary care diabetes clinic, can be physically and psychologically arduous. Achieving such goals often involves a complex treatment programme including intense monitoring and insulin dosing as well as fears due to the increased risk of hypoglycaemia. Results from recent clinical trials have also identified the previously unrecognised detrimental effect of imposing strict targets in those with diabetes [274, 309] and it is therefore increasingly recognised that targets for HbA1c in people with type 2 diabetes and the efforts required to attain them should correspond with an individual's clinical context and personal preferences. Those requiring hospital management in the UK generally have a more complicated course of diabetes with longer duration and increased co morbidity compared to those receiving diabetes care in the community, therefore it is possible that for those in the present study, the substantial efforts required to achieve an HbA1c target of <7% exceeded their capacity to cope physically and psychologically, causing decrements to health-related quality of life and an increased risk of depression.

However at present these possibilities remain suggestive and not conclusive. Further research is necessary to examine the impact of undiagnosed and untreated depression in those with type 2 diabetes as well as factors mediating the increased risk for depression in those with good glycaemic control.

Both those with type 1 and those with type 2 diabetes had mean HbA_{1c} values that exceeded the recommended levels that would be associated with increased risk of coronary heart disease and mortality [44, 275, 276]. As expected, South Asians were at increased risk of sub-optimal glycaemic control in comparison to White Europeans. Previous studies have failed to examine whether South Asians are at increased risk for the possible detrimental association between depression and poor glycaemic control. In the present study, interaction analyses revealed no ethnic differences in the relationship between depression and HbA1c. However, it is important to be cautious when interpreting these findings as there may be bias as a result of undiagnosed depression, particularly in South Asians (Chapter 4). Future studies should examine the impact of both diagnosed and undiagnosed depression on the association between depression and glycaemic control.

Although no significant difference between HbA1c values was observed between those prescribed SSRIs or TCA medication in the present study, antidepressants have been implicated with disturbances in metabolic control either in a favourable or detrimental manner [286-293]. However, due to the small sample size, it was not possible to make comparisons between those receiving antidepressant treatment compared to those that who were not prescribed pharmacological treatment.

It is also important to consider that data were derived from a single large hospital clinic; furthermore the intensive treatment received from diabetologists and specialist diabetes teams may not be typical of the majority of patients with diabetes who are managed in primary care. The results may therefore not be generalisable to other health care settings or localities.

Although a number of limitations have been highlighted, the present study also has a number of strengths. Firstly this study adds to the very sparse literature on depression and diabetes in the UK and it includes the first large scale analysis regarding the association between depression and glycaemic control in a UK population with both type 1 and type 2 diabetes. The analyses also controlled for the effects of a number of potentially confounding factors including the duration of diabetes, type of treatment, complications, comorbidities, ethnicity and the type 2 diabetes, many of which previous studies have failed to account for [85]. This study represents the first in the UK to examine ethnic differences in the impact of depression on HbA1c control. Failure to achieve metabolic control presents a major public health concern, particularly in South Asians with diabetes, and efforts to identify possible predictors of poor control and in turn effective strategies to reduce this inequality are vital.

The present study provides no evidence that depression is associated with worse metabolic outcomes in those with depression and either type 1 or type 2 diabetes in the UK. However, this does not to suggest that previous evidence for an association between depression and impaired glycaemic control cannot be considered to reliable. A number of limitations with the present study have been highlighted and

future research should aim to examine the impact of a number of potential modifying factors including service use, treatment complexity and intensity, antidepressant medication and the impact of undiagnosed and untreated depression, preferably in longitudinal analyses.

Chapter 6

Depression in people with type 2 diabetes in primary care: Introduction, Aims and Methodology

6.1 Introduction

The aims of the present chapter are to describe the aims and the rationale for the studies conducted to examine the prevalence of depression in a multiethnic primary care population in Leicester, the results of which are presented in Chapter 7. This chapter will also describe the rationale for the depression assessment method as well as procedural details.

6.2 Background and Rationale

Research evidence has accumulated to suggest a strong association between depression and diabetes. Chapter 2 described the results of the most recent meta-analysis of published research which concluded that the prevalence of major depression as well as depressive symptoms are almost twice as likely in individuals with type 2 diabetes compared to those without diabetes [195]. Both major or sub clinical forms of depression have serious implications for physical and functional health, for example results from a recent meta-analysis presented in Chapter 3 demonstrated associations between symptoms of depression and diminished health related quality of life in those with type 2 diabetes. In addition depression has been associated directly and indirectly with poor glycaemic control, a major factor leading to the development of diabetes related complications [85, 172]. In turn these findings suggest that identification and treatment of depression in people with diabetes may have a favourable effect on glycaemic control and perhaps even prevent or delay diabetes related complications [138].

However Chapter 2 also identified a number of important limitations in the current literature. Firstly few studies have compared the prevalence of depression in those with type 2 diabetes relative to a control group. In order to investigate whether type 2 diabetes is indeed associated with an increased risk for depression, it is vital that suitable control groups are involved so that associations can be reliably determined. Secondly many studies fail to account for potentially confounding factors including the presence of comorbid conditions as well as diabetes related complications. Further research is warranted in order to address these methodological limitations and to control for potential biases and moderators in order for the unique association between depression and diabetes to be determined accurately.

Examining risk factors for the development of this depression is also critical in improving understanding of the relationship between depression and diabetes as well as enabling health care professionals and researchers to identify high-risk groups and to develop appropriate prevention and treatment interventions. Socio-demographic characteristics such as female gender, low education and socioeconomic status have been related to increased risks of depression in patients with diabetes [213]. However results from meta-analyses examining the relationship between depression and diabetes conclude that only approximately 3% of studies examined race or ethnicity as a contributing factor in the prevalence of depression [75, 195]. Although some studies have demonstrated cultural differences in the prevalence of co-morbid depression with diabetes [126, 213, 243, 302], controlled studies in the UK and in particular studies involving South Asian people with diabetes are non-existent.

The rates of type 2 diabetes are up to six times higher in South Asians in comparison to White Europeans with an age of onset of almost a decade earlier [245]. In addition the prevalence of poor glycaemic, blood pressure and lipid control, microalbuminuria, hypertension, retinopathy and CHD have been shown to be higher in this group compared to White Europeans [21, 58, 249]. Considering the evidence to suggest a bidirectional relationship between depression and diabetes [29], it is reasonable to question whether depression acts as an influencing factor in diabetes related disparities among South Asians. If so, treatment and prevention programmes for depression may be of particular relevance for this group. However planning health services or estimating the level of need is made difficult by the lack of evidence relating to the prevalence of depression in these individuals.

Chapter 4 described the results from the first, and to date, only study to examine differential rates of depression among South Asian and White European people with type 1 and type 2 diabetes in the UK. The findings suggested lower rates of depression in South Asians in comparison to White Europeans, however it is essential to consider that the chapter examined rates of diagnosed depression and thus the finding may alternatively be interpreted to suggest lower rates of depression recognition in South Asians. It is therefore clear that further research is required to examine the relationship between depression and diabetes in South Asians in the UK, using screening methods for depression assessment.

Although the majority of diabetes care is currently delivered in primary care [310] and primary care is the initial point of contact for most patients suffering from depression, the literature generally suggests that general practitioners may face

obstacles in recognising and treating patients with depression [311] and in many cases patients with depression are frequently under-recognised and inadequately treated in general practice [72]. Explanations may stem from both the patients and the consultation process, for example patients may feel discouraged from disclosing depressive symptoms due to the stigma associated with the diagnosis, or because of time constraints and attitudes towards the appropriateness of such discussions during GP consultations [71]. General practitioners may also struggle with diagnosing and treating depression for a variety of reasons including a lack of relevant training or resources and assumptions about mental health [312-314]. In addition ethnic differences may also influence the rates of detection and treatment of depression in people managed in primary care [84, 266, 315-317].

Difficulties in diagnosis may be further exaggerated with the presence of a chronic illness such as diabetes [71, 318]. It is reported that depression may be recognised in fewer that one third of such cases [172]. Diagnosing and managing depression in patients with diabetes can be problematic for a number of reasons. Symptoms of depression may be considered to be a natural response to challenging physical illness and concerns about physical illness may crowd the independent importance placed on a 'secondary' diagnosis of depression and thus treatment may be deferred [71, 318]. Alternatively the presence of diabetes may mask the problem, for example symptoms of depression such as insomnia, fatigue and appetite disturbances which may overlap with symptoms of hyperglycaemia [71, 172, 313, 318].

In view of the detrimental associations between diabetes and co-morbid depression and the possibility of improvement through both pharmacological as well as psychological therapies [138, 319, 320], it is essential that primary care physicians are proactive in diagnosing depression in those with type 2 diabetes and are able to offer appropriate treatment.

6.3 Aims

The study described in the present chapter had the following objectives:

1) To compare the prevalence of depression between people with and without type 2 diabetes (and to examine the prevalence separately in South Asian and White European participants)
2) To compare the prevalence of depression between South Asian and White European people with type 2 diabetes
3) To determine the rates of detected and undetected depression in South Asian and White European general practice attenders with and without type 2 diabetes

6.4 Depression assessment

6.4.1 Measuring depression in South Asians

Although inherent within the majority of epidemiological research, problems of validity may be particularly problematic within the context of transcultural epidemiology- which is defined as research in which the 'views, concepts or measures of the investigator extend beyond the scope of one cultural unit' [321, 322]. In selecting an appropriate tool, it was therefore necessary to consider not only the construct of interest i.e. depressive symptomatology and the tool's

psychometric properties, but also issues regarding cultural relevancy and validity [322].

Although there may be similarities in the pattern of depression across cultures [323], differing ways of expressing the experience of mental and emotional health suggests that structured self report tools developed in western culture may have poor fit for the experiences of South Asians, particularly non-English speakers[267].

It has been suggested that some groups may experience 'culturally-bound' syndromes. This refers to a collection of symptoms that are restricted to particular cultural groups, for example a 'sinking heart' as described by Punjabi South Asians[324]. Furthermore it has been suggested that certain South Asian groups may be more likely than their British White counterparts, to describe psychological distress in terms of physical symptoms, which are less likely to be identified as mental illness in both epidemiological research and in clinical practice, although the evidence is largely anecdotal[267].

The assessment of depression in different ethnic and cultural subgroups has therefore evoked some debate and two broad methodologies have emerged. One approach advocates the development of instruments that include culturally specific domains, referred to as the 'Emic' approach. This approach to the development of assessment tools in South Asian groups requires the incorporation of observations and idioms of mental health that are culturally specific to a particular group. Simply importing instruments from the countries of origin e.g. the Amritsar Depression Inventory from India for the application with UK Punjabis, have shown little

success which may reflect the impact of acculturation on the expression of mental health [323, 325] and therefore as cultural perspectives and experiences may change over time, tools also need to be specific to groups at a particular period in time as well as place.

However, it is clear that if rates of depression are to be compared between different ethnic and cultural groups then the methods should be conceptually and functionally equivalent and appropriate for all groups compared. Therefore the Emic approach for developing different instruments for use in different ethnic groups may not be constructive[326] . Furthermore the process is highly resource intensive and given the financial and time constraints of the present thesis, it was not considered to be a feasible option.

The alternative 'Etic' approach requires that existing tools developed and validated in English are translated and adapted for use in different ethnic groups. This approach was considered to be the most appropriate option for the present thesis due to the need to make comparisons between the rates of depression between South Asian and White European groups. In anticipation of a high number of non-English speaking South Asian participants it was necessary to consider an instrument that was available in the common South Asian languages spoken in Leicester, namely; Gujarati, Urdu, Punjabi and Bengali. Issues of validity, however, may become particularly problematic when instruments are translated from their original language [327].

Ideally translation and the cross-cultural application of tools also requires a rigorous validation process to take place and several guidelines have been proposed regarding the appropriate methodology, although there appears to be little consensus to support one particular method over another [327-333]. Overall the translation process aims to achieve an accurate re-statement of the meaning rather than exact linguistic precision and the process usually involves the comparison of several independent translations and back translations as well as focus groups with local groups to ascertain the appropriateness and acceptability of translations [328].

However, once translated further psychometric assessment is also required before using translated instruments in research studies or clinical practice. This includes ensuring the tool's reliability, both in terms of reproducibility and internal consistency, its validity in terms of whether it truly measures depression and the preciseness and interpretability of scores [328].

Unfortunately, studies which use systematic and appropriate methods for examining validity are rare in trans-cultural epidemiology [322] and as a result information regarding the validity of tools for use in the British South Asian population is scarce.

6.4.2 Identification of depression: tool selection

A wide range of tools is available for the assessment of the clinical construct of depression. However, a number of factors warranted consideration when selecting the most appropriate assessment tool for the purposes of this thesis, namely a tool for use in a multiethnic population of people with and without type 2 diabetes.

Issues which are of primary concern include the validity of the tool in patients with diabetes and other illnesses likely to be encountered in general practice settings, as well as the tool's validity for use in different ethnic groups and in its linguistically translated versions.

Although diagnostic interviews such as the Structured Clinical Interview for DSM (SCID) are currently considered the gold standard for a research diagnosis of depression [74], (Chapter 1 section 1.10), due to the time and financial constraints of the present research, the use of diagnostic interviews to screen for depression was not considered to be a feasible option. Self-report symptom checklists on the other hand are simpler to administer and consequently inexpensive alternative to diagnostic interviews and as such, represent the most widely used method of depression assessment in studies of people with and without diabetes [75, 76].

A variety of self-report tools for depression are available and are used in people with diabetes both in research and for screening in clinical practice [31, 75], However it is important to be aware that these tools have not specifically been designed to be used with people with diabetes. Research has therefore recently begun to question the appropriateness of these measures in the diabetic population [334, 335]. For example there is largely an issue with specificity; an important feature of self-report tools for depression which warrants consideration is that many capture a range of overlapping emotional disturbances. The literature suggests that these tools have good sensitivity in terms of screening for common mental disorders (including depressive disorders as well as general anxiety states) within the general population; however they often show poor specificity for depression [75].

Although there may be a considerable overlap of patients with depression and the common mental disorders observed in people with diabetes as well as the general population, such as anxiety and depression, it is essential to acknowledge that the two subgroups are not identical. Specifically in people with diabetes, both anxiety and depression have been shown to have an independent impact on glycaemic control [336] furthermore the management of these conditions may vary depending on whether they occur together or alone [337]. With these factors in mind, the argument to separately determine levels of anxiety and depression is clinically relevant.

In addition there may be difficulties in assessing the certainty of depression when assessment tools also involve somatic symptoms for depression [338]. Symptoms such as fatigue, changes in sleep patterns and changes in appetite and body weight are legitimate symptoms of depression however may also be attributable to and overlap with the physical symptoms of diabetes. This in turn suggests that the sensitivity and utility of measurements of depression may be compromised. For example physical symptoms associated with hyperglycemia may influence a person's response to somatic items included in measures of depression. Responses to items may therefore vary with changes in health status which would inevitably compromise the accuracy of case detection.

Considering the above information, the Hospital Anxiety and Depression Scale (HADS) was selected to be the most appropriate for the purposes of the present study due to be the fact that it is the only available tool to separately determine

levels of depression and anxiety, to exclude somatic items and which was also available in the four main South Asian languages, namely Urdu, Gujerati, Punjabi and Bengali.

6.4.3 The Hospital Anxiety and Depression Scale (HADS)

The Hospital Anxiety and Depression Scale (HADS) is a well-validated self-report tool commonly used in research and clinical practice to assess the distinct dimensions of anxiety and depression, independent of somatic symptoms [339].

The ease and speed with which the HADS can be administered as well as its patient acceptability has led to its application in a wide variety of clinical populations in whom significant levels of anxiety and depression may co-exist with physical illness.

Although the HADS was originally developed in the UK and for use in medical patients, it has generally been shown to perform well in identifying cases of depression and anxiety as well as symptom severity not only in medically ill patients but also in the general population [339]. The HADS therefore represents an ideal tool for the assessment of depression and to allow the comparison of rates between diabetic and non-diabetic populations.

6.4.4 Questionnaire format and administration

The Hospital Anxiety and Depression Scale (HADS) is a one page document consisting of 14 items. For each item participants are to select one response from a multiple choice of 4 (Appendix I). The scale is divided into two subscales with

separate scores calculated for anxiety (HADS-A) and depression (HADS-D). Each scale comprises of seven questions rated using a score of 0 to 3 depending on the severity of the problem described in each question. The 7 Items for depression assessment focus specifically on the cognitive and emotional aspects of depression, particularly anhedonia and somatic items which may be related to either mood or physical disorders are not included. The score for the HADS range from 0-21 for the depression subscale and 0-21 for the anxiety subscale. The anxiety and depression scores are categorised into four ranges: normal (scores between 0-7), mild (8-10), moderate (11-14) and severe (15-21) [340]. The HADS is a self-administered questionnaire, however in the case of illiteracy, or poor vision it may be interviewer assisted [341].

6.4.5 Validity

Two comprehensives reviews have examined the validity of the HADS [339, 342]. Bjelland et al (2002)[339] identified 747 papers involving the HADS and examined a range of factors related to the tool's validity including the factor structure and internal consistency, as well as the performance of the HADS as a case finder for depression and anxiety. The findings from their review generally supported a two factor structure for the HADS, corresponding to the independent dimensions of depression and anxiety. The robustness of the scale was also supported by measures of internal consistency which were reported in the range of .68 to .93. Finally, analyses of the sensitivity and specificity involved studies that compared HADS scores with diagnoses according to structured or semi-structured diagnostic interviews. Overall the optimal cut-offs for the HADS varied between studies, however the majority of studies reported an optimal balance between sensitivity

and specificity for the depression subscale of the HADS (HADS-D) using a cut-off value of 8 and above, with overall sensitivity and specificity in the range of 0.70 to 0.90. This threshold was generally supported by studies conducted in the general population as well as in those with medical illness, including those in primary care [339].

6.4.6 HADS translations

Professionally translated and linguistically validated versions of the HADS questionnaire are available in Gujerati, Urdu, Punjabi and Bengali. The questionnaires were purchased from the licence holding organisation NFER-Nelson, however information regarding the translation process is limited and it is known only that the instruments were forward and back translated to ensure conceptual equivalence and cultural relevance.

Following a review of studies using of the use of the HADS in UK South Asians, Collins et al [343] identified only one study reporting the results of psychometric testing using the translated questionnaires available from Nfer-Nelson. Songua Barke et al [344] reported internal and test-retest reliability for the HADS in UK South Asian females and reported acceptable results for the Gujarati and Urdu translations (Gujarati: Internal consistency = $\alpha < .73$, test-retest reliability = $r > .92$, $P<0.01$; Urdu: $\alpha <.84$, test-retest, $r > .86$, $P<0.01$).

6.5 Population setting and participants

The study was conducted in general practice settings during 2006-2008. Fourteen general practices were selected from among those served by Eastern Leicester and

Leicester City West Primary Care Trusts (now combined as Leicester City Primary Care Trust) and one practice from Leicestershire County and Rutland Primary Care Trust. Together these Trusts serve a socioeconomically and ethnically diverse community with some practices serving a high proportion of South Asian populations.

6.5.1 Patient inclusion criteria

Patients attending selected general practices were eligible for inclusion if they were > 35 years of age and did not meet the exclusion criteria. Patients with low levels of literacy or a lack of fluency in English are often excluded from health-related research [345] however the present study included individuals who were able to read or speak English, Punjabi, Hindi/ Urdu, Gujarati or Bengali.

6.5.2 Patient exclusion criteria

Patients were excluded if they identified themselves as, or were identified from practice records as having either gestational or type 1 diabetes mellitus. Patients considered by general practice staff to be unsuitable to be approached (e.g. due to terminal illness or severe mental disabilities) were also excluded.

6.5.3 Study design

A controlled cross-sectional study was conducted between December 2006 and July 2008 using a combination of patient self-reported and routinely coded general practice data.

6.6 Procedure

6.6.1 Practice recruitment

Letters of invitation to participate (Appendix II) and an information sheet (Appendix III) were sent to all practices within Eastern Leicester and Leicester City West PCTs. Practices which agreed to participate were asked to return a consent form (Appendix IV), details of the practice patient demography and also information regarding the storage of patient information, including the computer system used. Only practices using the clinical systems EMIS (Egton Medical Information Systems) LV or EMIS PCS were eligible for study inclusion due to compatibility of EMIS systems with MIQUEST data extraction software.

6.6.2 Pilot study of patient recruitment methods

In order to secure enrolment of the target number of participants with type 2 diabetes, a number of methods of recruitment were tested at a pilot practice. Initially all participants with type 2 diabetes attending a routine primary care diabetes clinic were invited to participate in the study by the nurses running the diabetes clinics or by the practice reception staff who identified patients before their appointment. Participant eligibility was assessed through conversation and all those matching the selection criteria were provided with a study information pack and the opportunity to study its contents. The study information pack included a participant invitation letter (Appendix V) participant information sheet detailing the purpose of the study and the procedure for patients consenting to take part (Appendix VI), a consent form (Appendix VII), a self-report questionnaire (Appendix I) and an envelope in which to return the questionnaire and consent form. Each pack was available in following languages: English, Bengali, Gujarati, Punjabi and Urdu.

In addition to the Hospital Anxiety and Depression scale, the questionnaire included demographic questions including gender, marital status (married or living with a partner, divorced, widowed or single), occupation and smoking status (categorised as 'no never', 'quit over a year ago', 'quit 1 year ago' or 'yes'). Patient name and date of birth were also recorded on a detachable slip attached to the questionnaire. These details were used to cross link the questionnaire to the patient's GP data and to cross link a unique ID number assigned to each participant for the purposes of the study. After this point, the slips were detached from the questionnaires and patient names and any other patient identifiable information were not retained.

Once the consent form was complete, those who agreed to take part were asked to complete the questionnaire which was then returned to the practice nurse or a member of staff at reception in the envelope provided. A bilingual researcher was present at each practice when the need for language interpretation was considered a possibility.

Due to the intense demand placed on practice staff time, this method was not considered feasible for the remainder of the project; therefore an alternative recruitment strategy was adopted. This involved the inclusion of a pre-paid envelope within the study pack. Potential participants were then asked to study the contents at home and return questionnaires directly to the study investigator. However owing to financial constraints and the lower response rate observed in comparison to the previous method, the use of pre-paid envelopes was also abandoned.

6.6.3 Patient recruitment and data collection; stage 1

Finally, participants were recruited by the study investigator during regular visits to the practices. Initially potential participants were approached by the practice reception staff or the nurses running the diabetes clinics, who were able to assess patient eligibility through personal knowledge or by examination of clinical records during patient check-in. Initial verbal consent to discuss the study with a researcher was obtained by this member of the practice staff. Participants wishing to take part or those requiring further details were directed towards the researcher who provided patients with the study information pack as well as further discussion regarding the study process. Once consent forms were complete, the study questionnaire was either self-completed or interview-administered by the study investigator either before or after the patients' consultations with their GP or practice nurse. In order to maximise the opportunity to recruit participants with type 2 diabetes, the investigator visits were coincided with the scheduling of the practice's diabetes nurse clinic or during the practice's annual routine retinal screening for people with diabetes. The retinal screening programme is an NHS service which travels to general practices within Leicestershire on an appointment basis to perform retinal screening on all patients with diabetes registered at the practice. Control patients (i.e. those without diabetes) were consecutive general practice attendees who were recruited via a similar process to those with type 2 diabetes.

Once completed, questionnaires were stored in a locked filing cabinet at the practice for a period of one week to allow participants to withdraw their consent for the second part of the data collection should they decide to do so.

The process was conducted between December 2006 and February 2008. Study Ethnical approval was obtained from the Leicestershire, Northamptonshire & Rutland research ethics committee (REC Ref: 06/q2502/25).

6.6.4 Data collection; Stage 2- EMIS System

Over 90% of primary care patient medical records are now electronically recorded [346]. In response to this a number of clinical information systems have been developed in order to support the management of patient data. The EMIS system is an example of a commonly used clinical electronic database. The system can be used to code details of all general practice patient encounters, including diagnostic records, prescriptions and any additional notes about the consultation, using a combination of Read codes and free text terms. Data are entered directly into the system by general practitioners, practice nurses and administrative staff. Patients' diagnoses are coded using the Read code system, a hierarchical directory of symptoms and morbidities which is currently the standard method for coding clinical data in the UK [347]. At the point of entering a diagnosis, clinicians type in the problem title or diagnosis and are then presented with a 'picking list' of relevant diagnostic categories from which they select the most appropriate code. One of the great strengths of the UK general practice systems is that it also includes a complete and accurate record of prescribing data as well as blood pressure and the latest laboratory test results [348] which are automatically transferred from the laboratory to the general practice database via an electronic link. A number of studies have examined the accuracy and completeness of electronic primary care records [349]. Thiru et al 2003 [350] conducted a systematic review in which they identified 52 studies that examined the quality of data in general practice records. In most cases

the quality of the data was examined using comparisons of rates derived from electronic records using an external standard. Although the data regarding prescriptions was complete, the recording of diagnosed diseases varied, with completeness generally higher for diseases with clear diagnostic criteria, such as diabetes.

6.6.5 Data collection; Stage 2-Data extraction from EMIS

The Morbidity, Information Query Syntax (MIQUEST) is a program designed to search and retrieve data from electronic primary care records. Although largely used for audit purposes, its potential for research in general practice is also recognised [351]. MIQUEST queries may be written to extract pre-defined data from a specified sub-set of the practice population and at a specified point in time. As the same search (or queries) may be performed on any primary care system with which the software is compatible, MIQUEST allows identical searches to be conducted across different general practices. For the purposes of the present study, specific MIQUEST queries were created in order to collect a standardised set of data for each patient who had consented to take part and had completed the questionnaire at stage 1 of the research. Once all questionnaires at a given practice were complete, a list of patient practice identification numbers was generated and queries were executed in order to collect data retrospectively from the specified groups of patient records, with the date of the search pre-set to the date of completion for the final questionnaire at that practice. For practices in which data were collected over several months, data were collected in sets with the date for extraction pre-set to the end of each calendar month.

The unique practice ID ascribed for each patient on the EMIS system was used to cross-link self-report data collected at stage 1 with data extracted from patients' medical records. Data extracted from patient records included age, the type and duration of diabetes and current smoking status (yes/ no). Patient postcodes were also extracted in order to derive measures of deprivation using IMD data from 2004. Each English local authority area (n = 353) is geographically divided into 'Super Output Areas' (SOAs, n = 32 482) of approximately equal population. The SOAs do not overlap each other or the geographical borders of local authority areas. For each geographical area (SOAs), a number of routinely available indicators of deprivation are weighted under one of seven 'domains' including income, employment, health, education, housing, crime and living environment deprivation. In terms of the ranking, 1 is the most deprived and 32842 is the most deprived SOA in England[352].

Patients had been identified as having type 2 diabetes via the search for relevant Read codes. However examination of participants without a code for diabetes revealed a number of inconsistencies. For example, 80 participants had data for duration of diabetes but no formal diagnosis was coded. These participants were coded as type 2 diabetes unless they were diagnosed under 35 and treated with insulin straight away in which case they were coded as type 1 (N = 7).

In order to identify the presence of comorbid conditions and diabetes related complications, the MIQUEST queries searched for Read codes for 17 types of diagnosis and symptoms (anxiety, myocardial infarction (MI), angina, cardiovascular disease (CVD), transient ischemic attack (TIA), heart failure,

peripheral vascular disease, hypertension, asthma , chronic obstructive pulmonary disease (COPD), inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), epilepsy, retinopathy, nephropathy, peripheral neuropathy and peripheral vascular complications) (Table 6.1).

Clinical data included the most recent results (including dates) for blood pressure (systolic, diastolic and total), cholesterol (HDL and LDL), triglycerides BMI and the 3 most recent figures (including dates) for HbA1c.

Data extracted also included whether the patient was currently in receipt of insulin or oral anti-diabetic (OAD) medication using BNF drug codes[252] and whether they were prescribed antidepressant medication (including the name, dosage and whether prescribed currently, in the previous 3, 6, or 12 months). A diagnosis of depression was identified using the Read codes detailed in Table 6.1; the queries identified whether the patient had been diagnosed with depression 3, 6, 12 and over 12 months ago, or whether they had been newly diagnosed in the last 3 months.

6.6.6 Identifying physician's diagnosis of depression

The majority of comorbid conditions and complications identified in medical records, including the presence of diabetes, are largely based on objective diagnostic criteria. In contrast, inconsistent coding may be a cause for particular concern in the case of a general practitioner's diagnosis and coding of depression. A truly objective diagnosis of this condition may be difficult and often relies on the coding general practitioner's interpretation of a patient's symptoms and history. Furthermore, when coding a diagnosis of depression onto the EMIS system, general

practitioners are presented with a picking list of a number of depression sub-categories ranging from depressed mood to major depressive disorder. This list of detailed codes is displayed as a drop down menu and continues over several pages. This array of choices, together with the fact that general practitioners already face time constraints within the short consultation period, means that the coding of depression may not always reflect a carefully informed choice. In addition, the order in which the list is displayed is determined by how often items are used in the practice. On examination of the lists at 5 practices, it was revealed that the code for 'depression not otherwise specified (NOS)' featured highly amongst the commonly used codes for depression. Due to these concerns regarding the precision of coding, for the purposes of the present study, individual subgroups of depression were not differentiated and individuals were defined as 'currently recognised' if any code for depression was entered in the 3 months prior to the date of questionnaire completion. It is also commonly acknowledged that there is likely to be under recording of depression and depressive symptoms in routine databases, therefore cases were also identified as depressed if patients were currently in receipt of antidepressant medication at a dose recommended for the treatment of depression according to the BNF [252] (as described in Chapter 4 section 4.2.3). However, a number of antidepressants may be prescribed for reasons other than depression including neuropathic pain, bulimia, obsessive compulsive disorder (OCD), post-traumatic stress disorder (PTSD), panic disorder and general anxiety. For cases in which the recommended dosage for the treatment of depression overlapped with the dosage suggested, according to the BNF, for alternative indications, these cases were not coded as depressed if there was no history of a depression diagnosis in the 12 months prior to questionnaire completion and there was evidence for bulimia or

any form of anxiety disorder, also taking into account the antidepressant in question. A small number of cases were prescribed antidepressant medication at dosages lower than those suggested by the BNF for the treatment of depression or alternative indications; these cases were only defined as depressed if there was a history of depression in the previous 12 months prior to completing the questionnaires.

As data were collected retrospectively from patient records, all dates for antidepressant prescriptions were examined to ensure an initiation date prior to questionnaire completion. The study procedure is summarised in figure 6.1.

Figure 6.1 Participant recruitment

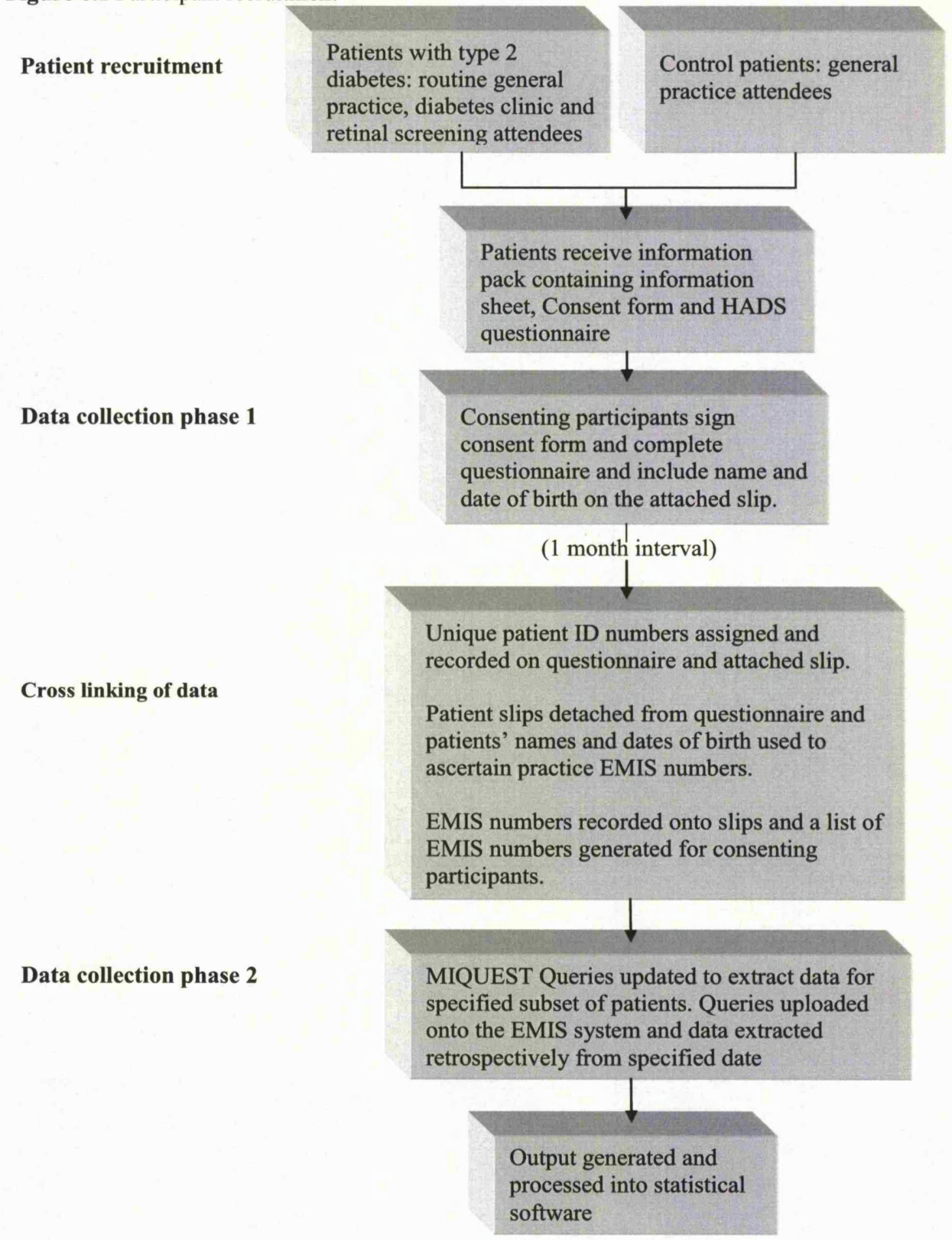


Table 6. 1 Read codes for comorbid conditions and complications

Diagnosis	Read codes
Diabetes	"C10E%" (type 1) "C10F%" (type 2) "C10" (unknown)
Anxiety	Eu41%","Eu45%","Eu341","E200%","E207%"
MI	G30%","G35%","G38%","Gyu34"
Angina	662K%","G33%","G311%","14A5
Cardiovascular disease	"G61%","G610%"-"G616%","G618%"-"G61z%"\,"G63y0" "G63y1","G64%","G66%","G6760","G6W","G6X"\,"F4236"
TIA	G65"-"G654","G65y"-"G65zz"
Heart failure	"G58%","G1yz1","585f","585g"\ ,"G5yy9","G5yyA"
Peripheral vascular disease	"G70%","G71","G710%"-"G713%"\ ,"G715%","G718%","G74%","7A1%","7A4%","G73z0"
hypertension	G2","G20%","G24%","G2y","G2z"
Asthma	H33%
COPD	"H3","H31%"-"H3100","H310z"-"H31z"\,"H32%","H36%"-"H3z"
Inflammatory bowel disease	J40%","N0311","N0453","J08z9","J41%"\ ,"N0454","N0310","14C4"
Irritable bowel syndrome	"J521%"
Epilepsy	F25","F2510","F2511","F2512","F2513"\ ,"F2514","F2515","F251y","F25z","F1321","SC200"
retinopathy	F4201"-"F420z","2BBL","2BBM","2BBR"-"2BBY"\ ,"2BBk"- "2BBo","8HBH","8HBG","C105%","C10E1","C10E7","C10EF"\ ,"C10EP","C10F1","C10F6","C10FE","C10FQ","C105%","C1081 "\ ,"C1087","C108F","C1091","C1096"
Nephropathy	"R110"-"R1100","R110z","K190X","Kyu5G"\ ,"C10E0","C10ED","C10F0","C10FC","C10FL","C10FM","C104 %"\ ,"C1080","C108D","C1090","C109C"
Peripheral neuropathy	"F3y0","F372%","F35z0","F3450","M2711","F1711"\ ,"29B9","29BA","C10E2","C10EB","C10EC","C10EJ"\ ,"C10EQ","C10F2","C10FA","C10FB","C10FH","C10FR"\ ,"C106%","C1082","C108B","C108C","C108J","C1092"\ ,"C109A","C109B","C109H"
Angiopathy/ peripheral vascular complications	"2G44"-"2G47","2G54"-"2G57"\ ,"2G61","2G62","2G5A","2G5B","2G5F"-"2G5H"\ ,"2G5J"-"2G5L","2G5S"-"2G5W","7L060"-"7L064"\ ,"7L08%","7L07%","C10E5","C10E6","C10EG","C10F4"\ ,"C10F5","C10FF","C107%","C1085","C1086","C108G"\ ,"C1094","C1095","C109F"
Depression	E112%","E113%","E118","E11z2"\ ,"Eu32%","Eu33%","E2B%","E135","Eu341","E2003"\ ,"Eu412","E130","E0021","E291","Eu920","Eu204"\ ,"8G1%","8G6%","9NJ1","212S"

Chapter 7

The prevalence of depression in South Asians and White European people with and without type 2 diabetes in primary care: Analyses and Results

7.1 Introduction

The rationale, aims and methods for the present study are detailed in Chapter 6. Briefly this chapter aims to;

1) To compare the prevalence of depression between people with and without type 2 diabetes (and to examine the prevalence separately in South Asian and White European participants)
2) To compare the prevalence of depression between South Asian and White European people with type 2 diabetes
3) To determine the rates of detected and undetected depression in South Asian and White European general practice attenders with and without type 2 diabetes

consecutive general practice attenders with and without type 2 diabetes were screened for depression using the depression subscale of the Hospital Anxiety and Depression Scale (HADS-D) during routine appointments in primary care. Demographic and medical data were also extracted from participants' general practice records.

7.2 Sample size calculations

Aims 1: To compare the prevalence of depression between people with and without type 2 diabetes (South Asians)

Pilot data were obtained for the local Leicestershire population. The prevalence of depression was estimated to be 10% in South Asian patients with diabetes and 5% in those without. It was therefore estimated that 950 patients (475 in each group)

would be required to detect a significant difference with 80% power at the 0.05 significance level.

Aims 1: To compare the prevalence of depression between people with and without type 2 diabetes (White Europeans)

A significant difference in the prevalence of depression in White European patients with and without diabetes should be detectable in a sample size of 108 patients in each arm with a power of 80% and alpha <5%, based on an estimated prevalence of 18% in those with diabetes (estimate from pilot data) and a 5% prevalence of depression in control patients [72].

Aim 2: To compare the prevalence of depression between South Asian and White European people with type 2 diabetes

Based on pilot study data which shows that the prevalence of depression in South Asian and Caucasian patients is 10% and 18% respectively, it was estimated that 233 Caucasian patients with diabetes and 466 South Asian patients with diabetes would be required to determine a significant difference with 80% power at the 0.05 significance level.

7.3 Statistical analyses

Categorisation of variables

For ease of interpretation a number of variables were re-categorised. As the numbers were too small to examine individually, comorbid conditions were grouped as follows: cardiovascular-related comorbidities (MI, angina, TIA, heart failure and peripheral vascular disease), other comorbid conditions (Sleep disorders, Asthma,

COPD, inflammatory bowel disease, irritable bowel syndrome, epilepsy, hypothyroidism, peptic ulcer, liver disease and any tumour/ lymphoma/ leukaemia) and diabetes related complications (retinopathy, nephropathy, peripheral neuropathy and peripheral vascular complications). Co-morbidity status in respect of each of these groups was categorised as: none, one, or two or more conditions.

Due to the small number of participants in some categories, smoking status was re-categorised as never, former and current and marital status was dichotomised as currently married/living with a partner and not currently married or living with a partner. Age and duration of diabetes were categorised using conventional cut points (< 50 and ≥60+ and 0-3, 4-14 and ≥15 years respectively). Treatment for diabetes was coded into one of four groups: none/life style intervention, oral anti-diabetic medication, insulin, or a combination of insulin and oral anti-diabetic medication. IMD ranks (Chapter 6 section 6.4.5) were organised into 4 categories based on national quartiles [352] (lowest quartile: 0-8,120, lower middle quartile: 8,121-16,241, upper middle quartile 16,242-24,361 and upper quartile 24,362+). Participants were categorised as obese based on a BMI >30 [353] and poor glycaemic control was defined as HbA1c ≥7 [24].

Sample characteristics and group comparisons

The prevalence of depression and demographic and medical characteristics were compared between South Asian and White European participants with and without type 2 diabetes. Participants with and without depression were compared using χ^2 tests to examine differences between categorical variables and independent samples t-tests for normally distributed samples and the Mann-Whitney U test for non-

normally distributed variables. Comparisons were conducted separately for depression defined as a HADS score of 8 and above (corresponding to mild-severe depression) and a HADS score of 11 and above (corresponding to moderate to severe). Analyses were also conducted for diagnosed depression, i.e. depression recorded in patient medical records.

Aim 1: The prevalence of depression in Type 2 diabetes in comparison to those without diabetes

Multiple logistic regression models were used to compare the odds of depression (using a HADS cut point > 8 and HADS≥11 and Diagnosed depression) in people with and without type 2 diabetes before and after controlling for potential confounding factors. Models adjusted for age, gender, deprivation, ethnicity, the presence of cardiovascular related comorbidities and non-cardiovascular related comorbidities and BMI. Variables were selected as each had been shown to have associations with depression in previous studies. In order to examine whether the association between depression and type 2 diabetes differed between South Asians and White Europeans, separate models were conducted for each ethnic group. The moderating influence of ethnicity, gender and age (<59 vs. ≥60) on the relationship between depression and type 2 diabetes was also examined via three separate models adjusting for age/ gender/ ethnicity (as appropriate) as well as cardiovascular-related comorbidities and other comorbidities and BMI.

Aim 2: The prevalence of depression in South Asian vs. White European people with type 2 diabetes

Multiple logistic regression was used to model ethnic differences in the prevalence of depression whilst controlling for the effects of age, gender, deprivation, cardiovascular and non-cardiovascular related comorbidities, diabetes related complications, duration of diabetes, treatment for diabetes, BMI and HbA1c. As with previous analyses, each of these variables has strong evidence for an association with depression in previous research with people with diabetes [75, 213, 354]. Models were conducted separately for mild to severe (HADS≥8), moderate to severe (HADS≥11) and diagnosed depression (depression recorded in patient notes).

To examine whether factors associated with depression differed between South Asian White European patients, logistic regression was performed separately for each ethnic group. Controlling for the effects of age, gender, cardiovascular-related and other comorbidities and diabetes complications, each variable was entered into the model individually in 6 separate sets of analyses. Each set of analyses was repeated with the population of type 2 diabetes as a whole and with the addition of ethnicity as an independent variable as well as the interaction between ethnicity and each explanatory factor (in separate analyses).

Hosemer-Lemeshow tests were conducted with each model to assess the degree of goodness of fit.

Aim 3: comparison of recognised and unrecognised depression in South Asian and White European people with and without type 2 diabetes

Analyses were conducted in order to compare the rates of diagnosed and undiagnosed depression separately by diabetes status and ethnicity.

7.4 Results

7.4.1 Response rate

Fifteen of the 65 practices within Eastern Leicester and Leicester City West Primary Care Trusts responded, of these 14 used the computer the EMIS computer system. An 85% participant response rate was achieved at the pilot practice, however following the introduction of response by pre-paid envelope this was reduced to 5%. Using the final recruitment strategy (Chapter 6 section 6.4.2 and 6.4.3), a high response rate was achieved in both South Asian and White Europeans with type 2 diabetes, with an overall response rate estimated at 98%. However, although it was not practically feasible to obtain a precise figure, a lower response rate was observed in those without type 2 diabetes. Reasons for declining to participate were almost always attributable to lack of time, which was observed to be particularly problematic in those without type 2 diabetes due to the shorter length in waiting time before general practice appointments.

7.4.2 Available data

A total of 1868 questionnaires were returned of which 1505 were included in the final analyses (Figure 7.1). Questionnaires with unsigned consent forms or incomplete information to allow questionnaires to be cross-linked to GP data were discarded (N = 14). A further 121 questionnaires were excluded on the basis of

failing to satisfy eligibility criteria, that is: patients aged < 35 years of age and those with type 1 diabetes. Participants were excluded if the details provided on the questionnaire slip did not match with any case on the practice register or if they had recently joined the practice and electronic data were currently unavailable (N = 59). In some instances, participants had completed questionnaires on more than one occasion; in these cases only the earliest questionnaire was retained, resulting in exclusion of 18 questionnaires. Three cases were excluded due to evidence of psychotic disorder and 2 participants contacted the research investigator to withdraw consent.

Due to time constraints participants were often unable to fully complete questionnaires and therefore incomplete data were also observed in participants' responses on the HADS questionnaires. The scoring guidelines for the HADS advocate that scores for missing items may be inferred from the scores for the remaining items for either subscale so long as no more than 20% are missing [355]. Therefore questionnaires with one item missing from a subscale were included (with the missing value calculated using the average of the remaining scores), however subscales with 2 or more items missing were rendered invalid and were thus excluded (cases excluded due to missing data for both the anxiety and depression subscale (N = 100). Missing data were observed for 18 participants for the HADS-A scale only and for 16 cases with the HADS-D only.

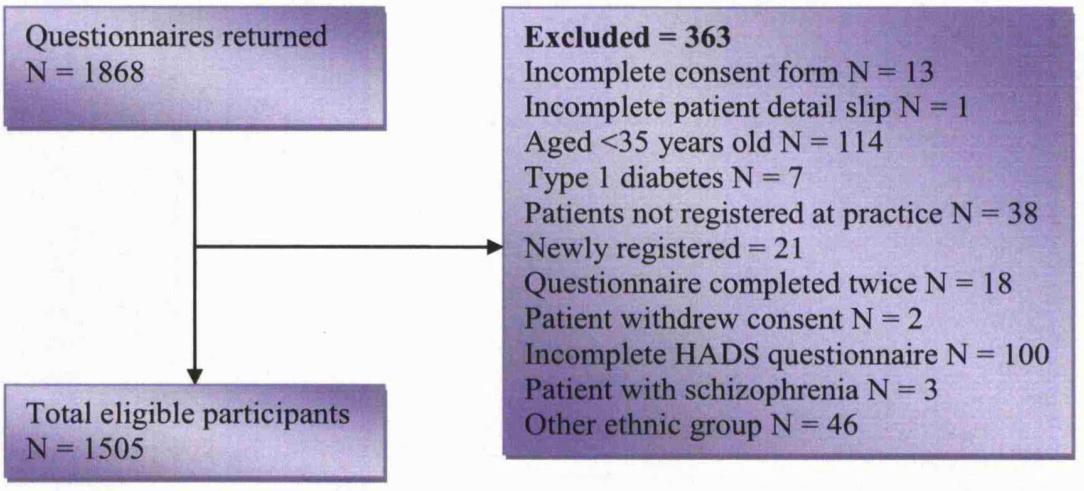
Questionnaires completed by individuals from other ethnic groups, including black African/ Caribbean, Chinese, Filipino and mixed backgrounds were excluded (N =

46) as there were too few to analyse as distinct groups and there is no theoretical justification for the combination of these groups into one category.

Incomplete data for self-reported smoking status were observed in 263 cases. For these cases, data were inferred from smoking status data available in GP notes.

Of 862 people with a diagnosis of type 2 diabetes, 855 had a HbA1c value recorded and of these 836 (97%) had a HbA1c value recorded within 12 months of completing the HADS questionnaire, 673 (78%) had a HbA1c recording in the last 180 days and 515 (60%) had HbA1c values within 90 days of completing the HADS. Finally missing data were observed for marital status and BMI for 109 and 115 cases respectively.

Figure 7.1. Participant recruitment



7.4.3 Sample characteristics

The demographic and medical characteristics of the population are summarized in Table 7.1. The total population included 862 individuals with type 2 diabetes and 643 without. Participants were aged between 35-97 years of age and had a mean age

of 56.8 years (SD 12.88). Sixty-five percent of participants were of South Asian origin and 35% were White European. The majority of South Asian participants were of Indian decent (91.2%) compared with 6.2% who were Pakistani and 1.9% who were Bangladeshi. Questionnaires were largely completed in English (84.1%). A large proportion of South Asian participants were able to complete questionnaires in English (75.5%) and 24.4% of questionnaires were completed using a translated version (81.2% in Gujarati, 9.6% in Urdu/ Hindi and 9.2% in Punjabi).

The majority of the sample was either married or cohabiting (72%). IMD ranks ranged from 187-31,774, with the mean IMD ranking of 9,456 (SD 7,652). Fifty-five percent of the sample had IMD scores indicating that they were in the lowest quartile of deprivation (the most deprived). Twelve percent of the sample were identified as current smokers, 19% as former smokers and 69% as non-smokers.
In terms of medical characteristics, 32% of the sample were classified as obese (BMI >30). The mean systolic blood pressure (SBP) was 130mmHg (SD 16) and mean diastolic blood pressure (DBP) was 76mmHg (SD 9). The mean values for total cholesterol and low and high density lipoproteins were 4.3mmol/L (SD 1.4), 2.3 (SD 0.9) and 1.2mmol/L (SD 0.32) respectively. One or more cardiovascular related comorbidity was present in 48% of the study population and non-cardiovascular related comorbidities in 31% of the population.

In total, 127 people were recognised as depressed based on the receipt of antidepressant medication or a recorded diagnosis. Of those recognised, 44 (34.6%) had a current diagnostic code for depression in their notes (in the 3 months prior to completing the questionnaire). Only 10 (7.9%) people had a current diagnosis of

depression (in the previous 3 months from completing the questionnaire) but were not currently on antidepressant medication.

7.4.4 Characteristics of sample by diabetes status and ethnic group

The characteristic of participants with and without type 2 diabetes by ethnic group are presented in Table 7.1.

Of those with type 2 diabetes, the mean duration of diabetes was 7.3 years (SD 6.14). The majority of these participants were treated with OAD medication only (64%) 9% were treated with insulin and 10% with a combination of insulin and OAD medication.

South Asian participants with type 2 diabetes were more likely to complete translated copies of the questionnaire (28.8%) in comparison to South Asians without type 2 diabetes (18.7%).

Regardless of ethnic group, participants with type 2 diabetes were more likely to be aged over 60 years (51% vs. 23% in those without diabetes) and included a larger proportion of males (48% vs. 38% females)

No significant differences were observed between people with and without diabetes for levels of deprivation, ethnicity, smoking or marital status. People with type 2 diabetes had higher rates of obesity than those without diabetes (42% vs. 24%) and had higher rates of cardiovascular related and non-cardiovascular related comorbidities (63% vs. 28% and 33 vs. 28%).

In both populations with type 2 diabetes and controls, a greater proportion of South Asians were aged <60 years, were married and fell within the lowest quartiles for IMD ranking (highest deprivation) in comparison to White Europeans,

In comparison to White Europeans, a smaller proportion of South Asians were current smokers, had a BMI >30 and had one or more cardiovascular and non-cardiovascular related comorbid condition (both in type 2 diabetes and controls).

No ethnic differences were observed between South Asian and White European participants in terms of the duration of diabetes. However, South Asians with diabetes were more likely to be treated with OAD medication only compared to White Europeans (68% vs. 57%) who were also more likely to be controlled using life style modification (25% vs. 14%). The mean HbA1c was 7.5% (SD 1.5) and was higher in South Asians in comparison to White Europeans (7.6% SD1.6 vs. 7.3% SD1.3). Although the proportion with poor control (defined as ≥7%) was slightly higher in South Asians in comparison to White Europeans (56% vs. 51%) no statistically significant difference was observed. Diabetes-related complications were present in 37% of the sample with a higher proportion of one or more complication observed in White Europeans in comparison to South Asians (40% vs. 35%)

Table 7.1. Demographic and medical characteristics of the total study population and by diabetes and ethnic status

		Total population N = 1505			South Asians vs. White Europeans with and without diabetes					
					Controls N = 643			Type 2 diabetes N = 862		
	Total N = 1505	Type 2 Diabetes N = 862	Controls N =643	P	South Asian N = 418	White European N = 225	P	South Asian N = 562	White European N = 300	P
Demographic variables										
Age										
< 59	918	425 (49.3)	493 (76.7)	.000	351 (84.0)	142 (63.1)	.000	339 (60.3)	86 (28.7)	.000
60 +	587	437 (50.7)	150 (23.3)		67 (16.0)	83 (36.9)		223 (39.7)	214 (71.3)	
Gender										
Female	847	451 (52.3)	396 (61.6)	.000	249 (59.6)	147 (65.3)	.178	291 (51.8)	160 (53.3)	.716
Male	658	411 (47.7)	247 (38.4)		169 (40.4)	78 (34.7)		271 (48.2)	140 (46.7)	
IMDR group										
1	830	480 (55)	350 (54.4)	.820	242 (57.9)	108 (48.0)	.000	328 (58.4)	152 (50.7)	.000
2	433	250 (29)	183 (28.5)		128 (30.6)	55 (24.4)		172 (30.6)	78 (26.0)	
3	114	63 (7.3)	51 (7.9)		25 (6.0)	26 (11.6)		26 (4.6)	37 (12.3)	
4	128	69 (8)	163 (9.2)		23 (5.5)	36 (16.0)		36 (6.4)	33 (11.0)	
Ethnicity										
White European	525	300 (34.8)	225(35.0)	.983	--	--	--	--	--	--
South Asian	980	562 (65.2)	418 (65.0)		--	--	--	--	--	--
Language										
English	1265	700 (81.2)	565 (87.9)	.001	340 (81.3)	--		400 (71.2)	--	.000
Translated	240	162 (18.8)	78 (12.1)		78 (18.7)	--		162 (28.8)	--	
Smoking status										
Never	1033	582 (67.5)	451 (70.1)	.474	347 (83.0)	104 (46.2)	.000	451 (80.2)	131 (43.7)	.000
Former	285	172 (20.0)	113 (17.6)		44 (10.5)	69 (30.7)		59 (10.5)	113 (37.7)	
Current	187	108 (12.5)	79 (12.3)		27 (6.5)	52 (23.1)		52 (9.3)	56 (18.7)	
Marital status										
Single	315	193 (24.2)	122 (20.4)	.144	48 (12.8)	74 (33.3)	.000	87 (17.3)	106 (35.7)	.000
Married	1081	606 (75.8)	475 (79.6)		327 (87.2)	148 (66.7)		415 (82.7)	191 64.3)	

Clinical variables										
BMI										
<29	905	496 (58.4)	409 (75.7)	.000	284 (78.7)	125 (69.8)	.032	366 (66.5)	130 (43.3)	.000
>30	485	354 (41.6)	131 (24.3)		77 (21.3)	54 (30.2)		184 (33.5)	170 (56.7)	
CV comorbidities										
0	782	322 (37.4)	460 (71.5)	.000	318 (76.1)	142 (63.1)	.001	247 (44.0)	75 (25.0)	.000
1	499	356 (41.3)	143 (22.2)		82 (19.6)	61 (27.1)		213 (37.9)	143 (47.7)	
2+	224	184 (21.3)	40 (6.2)		18 (4.3)	22 (9.8)		102 (18.1)	82 (27.3)	
Other comorbidities										
0	1042	578 (67.1)	464 (72.2)	.037	326 (78.0)	138 (61.3)	.000	412 (73.3)	166 (55.3)	
1	370	221 (25.6)	149 (23.2)		80 (19.1)	69 (30.7)		119 (21.2)	102 (34.0)	
2+	93	63 (7.3)	30 (4.7)		12 (2.9)	18 (8.0)		31 (5.5)	32 (10.7)	
Years of diabetes		--	--	--	--	--	--			
0-3	459	--	--	--	--	--	--	172 (57.3)	287 (51.1)	.213
4-14	312	--	--	--	--	--	--	99 (33.0)	213 (37.9)	
15+	91	--	--	--	--	--	--	29 (9.7)	62 (11.0)	
Treatment		--	--	--	--	--	--			
Lifestyle only	152	--	--	--	--	--	--	74 (24.7)	78 (13.9)	.001
OAD	553	--	--	--	--	--	--	172 (57.3)	381 (67.8)	
Insulin	74	--	--	--	--	--	--	27 (9.0)	47 (8.4)	
Both	83	--	--	--	--	--	--	27 (9.0)	56 (10.0)	
HbA1c		--	--	--	--	--	--			
<6.9	489	--	--	--	--	--	--	144 (48.8)	239 (44.2)	.225
>7	347	--	--	--	--	--	--	151 (51.2)	302 (55.8)	
Diabetes related complications		--	--	--	--	--	--			
0	544	--	--	--	--	--	--	181 (60.3)	363 (64.6)	.015
1	22	--	--	--	--	--	--	73 (24.3)	150 (26.7)	
2+	95	--	--	--	--	--	--	46 (15.3)	49 (8.7)	
Continuous variables										
Mean Age	57 (SD 13)	52 (SD 12.3)	61 (SD 12)	.000	50 (SD 11)	55 (SD 14)	.000	58 (SD 11)	66 (SD 12)	.000
Mean years of Diabetes	--	7.3 (SD 6.1)	--	--	--	--	--	7.0 (SD 5.8)	8.0 (SD 6.6)	.055
Mean HbA1c	--	7.5 (SD 1.5)	--	--	--	--	--	7.3 (SD1.3)	7.6 (SD 1.6)	.014*

*Difference compared using Mann-Whitney test, CV = cardiovascular

7.4.5 Prevalence of depression

The prevalence and severity of depression for both type 2 diabetes and controls is summarized in Figure 7.2. In group comparisons, no significant differences were observed between people type 2 diabetes and controls in terms of the prevalence of screen detected depression at each quartile of severity based on the HADS questionnaire (The term screen detected depression refers to all cases identified using the HADS during the study screening process). Furthermore no significant differences between cases with type 2 diabetes and controls were identified in the rates of diagnosed depression (patients identified via general practice records) or in the total estimate of depressive symptoms (combining those identified as depressed based on the HADS> 8 and those with a diagnosis recorded in the general practice records).

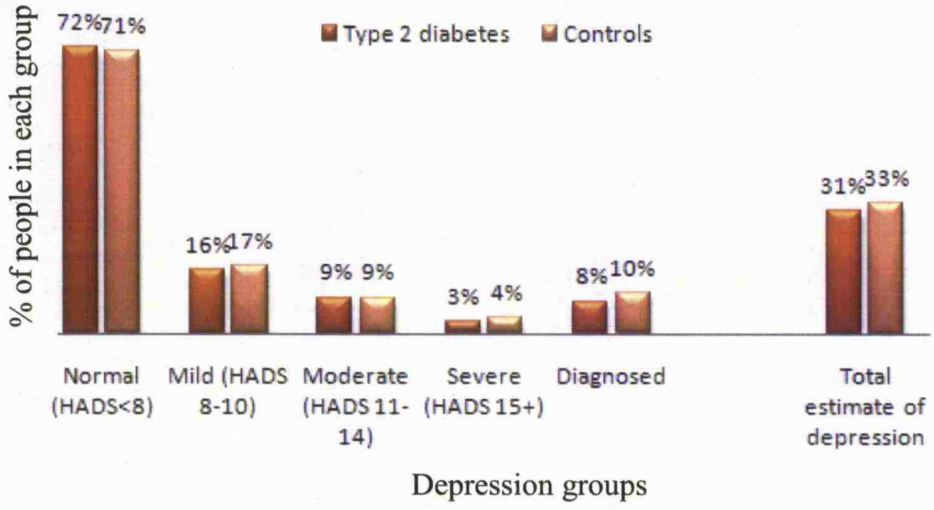


Figure 7.2. Prevalence of depression in type 2 diabetes and controls.

Mild to Severe depression (HADS≥ 8)

The prevalence of depression using a cut-point of ≥8 on the HADS (corresponding to mild-severe levels of depression) was 28% in people with type 2 diabetes and 29% in those without (p=0.679).

The characteristics of diabetes and control groups by depression status are shown in Table 7.2. In those with type 2 diabetes, higher rates of depression were observed in South Asians in comparison to White Europeans (31% vs. 22%, p = 0.007) and in those with cardiovascular related co-morbidities and non-cardiovascular related co-morbidities. The prevalence of depression also increased with increased duration of diabetes and in those with diabetes related complications. Higher rates of depressive symptoms were observed in South Asians who completed the questionnaire in a language other than English in comparison to questionnaires completed in English (40% vs. 28% p = 0.006)

In participants without diabetes, significantly higher rates of depression were observed only in females (33 vs.24% in males, p = 0.015) and those living within the lower and upper mid quartile ranges for deprivation (p = 0.039). No significant difference was observed between the rates of depressive symptoms when comparing South Asian participants completing questionnaires in English with those who completed a translated version (p =0.288). Figure 7.3 and figure 7.4 summarise the prevalence of depression by gender and ethnic group for both type 2 diabetes and controls and higher rates were observed in females in comparison to males, regardless of diabetes status.

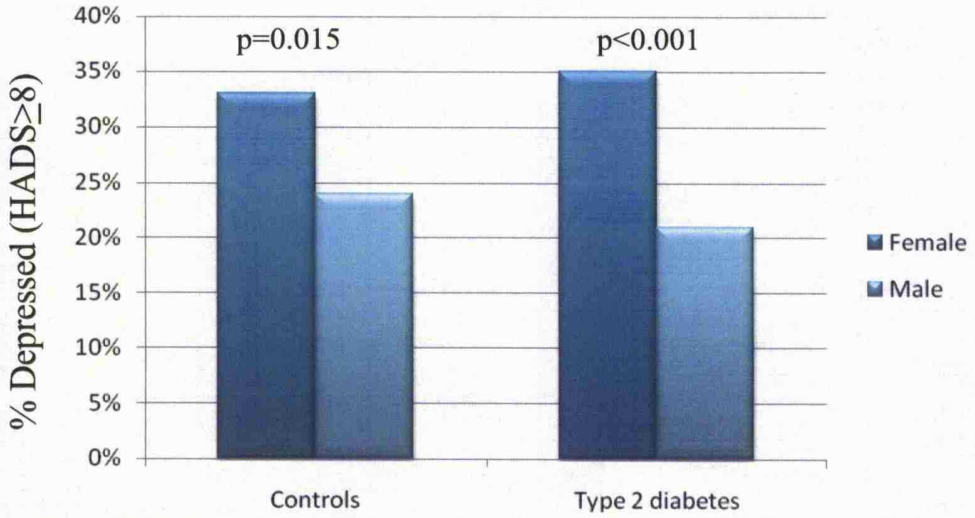


Figure 7.3. Prevalence of depression (Identified by HADS scores≥8) in type 2 diabetes and controls by gender.

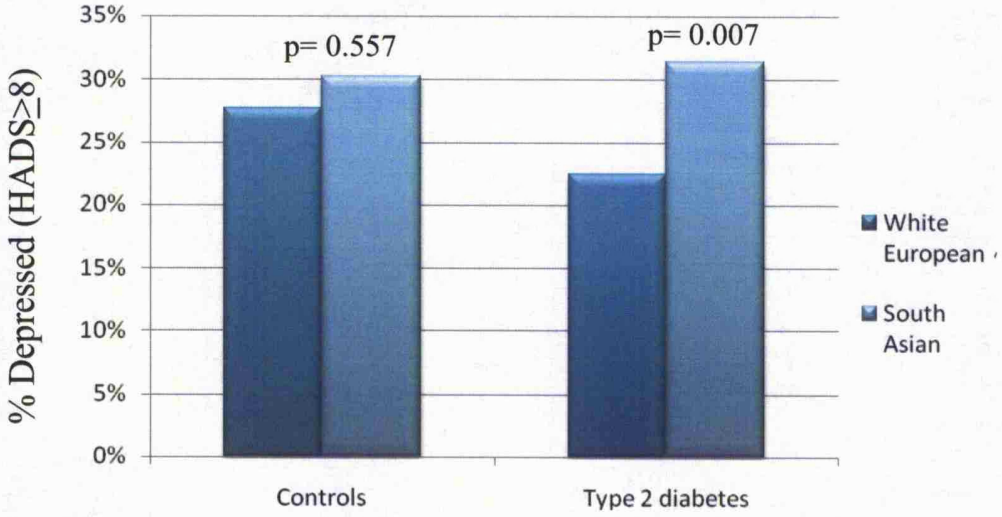


Figure 7.4. Prevalence of depression (Identified by HADS scores≥8) in type 2 diabetes and controls by ethnicity.

Table 7.2. Characteristics of people with and without diabetes by depression status (HADS≥8)

	Controls N = 634			Type 2 N = 854*		
	Non-depressed N =448	Depressed N =168	P	Non-depressed N = 613	Depressed N = 241	P
Age						
< 59	339 (69.5)	149 (30.5)	.269	290 (68.6)	133 (31.4)	.046
60 +	109 (74.7)	37 (25.3)		323 (74.9)	108 (25.1)	
Gender						
Female	263 (67.1)	129 (32.9)	.015	293 (65.4)	155 (34.6)	.000
Male	185 (76.4)	57 (23.6)		320 (78.8)	86 (21.2)	
IMDR group						
1	235 (67.9)	111 (32.1)	.039	327 (68.7)	149 (31.3)	.009
2	135 (75.8)	43 (24.2)		177 (71.7)	70 (28.3)	
3	31 (60.8)	20 (39.2)		53 (84.1)	10 (15.9)	
4	47 (79.7)	12 (20.3)		56 (82.4)	12 (17.6%)	
Ethnicity						
White European	162 (72.3)	62 (27.7)	.557	232 (77.)	67 (22.4)	.007
South Asian	286 (69.8)	124 (30.2)		381 (68.6)	174 (31.4)	
Smoking status						
Never	321 (72.3)	123 (27.7)	.260	406 (70.5)	170 (29.5)	.134
Former	72 (64.3)	40 (35.7)		133 (77.8)	38 (22.2)	
Current	55 (70.5)	23 (29.5)		74 (69.2)	33 (30.8)	
Marital status						
Single	78 (63.9)	44 (36.1)	.056	137 (71.7)	54 (28.3)	.733
Married	342 (73.2)	125 (26.8)		440 (73.3)	160 (26.7)	
BMI						
<29	289 (71.9)	113 (28.1)	.451	353 (71.9)	138 (28.1)	.842
>30	89 (67.9)	42 (32.1)		250 (71.0)	102 (29.0)	
CV comorbidities						
0	319 (70.0)	137 (30.0)	.545	221 (69.1)	99 (30.9)	.021
1	103 (74.1)	36 (25.9)		271 (76.8)	82 (23.2)	
2+	26 (66.7)	13 (33.3)		121 (66.9)	60 (33.1)	
Other comorbidities						
0	326 (71.3)	131 (28.7)	.438	426 (74.2)	148 (25.8)	.047
1	104 (70.7)	43 (29.3)		149 (68.3)	69 (31.7)	
2+	18 (60.0)	12 (40.0)		38 (61.3)	24 (38.7)	
Recognised depression						
No	423 (74.0)	149 (26.0)	.000	586 (74.2)	204 (25.8)	.000
Yes	25 (40.3)	37 (59.7)		27 (42.2)	37 (57.8)	
Years of diabetes	--	--	--			
0-3	--	--	--	340 (74.1)	119 (25.9)	.007
4-14	--	--	--	222 (72.5)	84 (27.5)	
15+	--	--	--	51 (57.3)	38 (42.7)	
Treatment	--	--	--			
Lifestyle	--	--	--	109 (72.2)	42 (27.8)	.271
OAD	--	--	--	403 (73.4)	146 (26.6)	
Insulin	--	--	--	49 (68.1)	23 (31.9)	
Both	--	--	--	52 (63.4)	30 (36.6)	
HbA1c	--	--	--			
<6.9	--	--	--	250 (72.5)	95 (27.5)	.754
>7	--	--	--	344 (71.2)	139 (28.8)	
Complications	--	--	--			
0	--	--	--	405 (75.1)	134 (24.9)	.009
1	--	--	--	150 (68.2)	70 (31.8)	
2+	--	--	--	58 (61.1)	37 (38.9)	

* Smaller figure due to missing cases of completed HADS

Moderate to severe depression (HAD≥ 11)

Levels of moderate to severe levels of depression (HADS≥11) were 17.4% in people with type 2 diabetes compared to 17.3% in those without diabetes (p = 0.999)

In those with type 2 diabetes, the prevalence of depression was greater in females (15 vs. 9%), in those aged <50 (15 vs. 9% in those aged 60+) and in those with non-cardiovascular related comorbidities (Table 7.3). In those without diabetes significantly higher rates of depression were observed in individuals who were not married/co-habiting compared to those who were married/co-habiting (19% vs. 10%) only. No significant difference was observed in the rates of moderate to severe depression between South Asian participants with or without type 2 diabetes, or in those who completed the questionnaire in English or a translated version (p= 0.444, p= 0.632). Figure 7.5 and Figure 7.6 show the prevalence of depression by gender and ethnic group for both type 2 diabetes and controls.

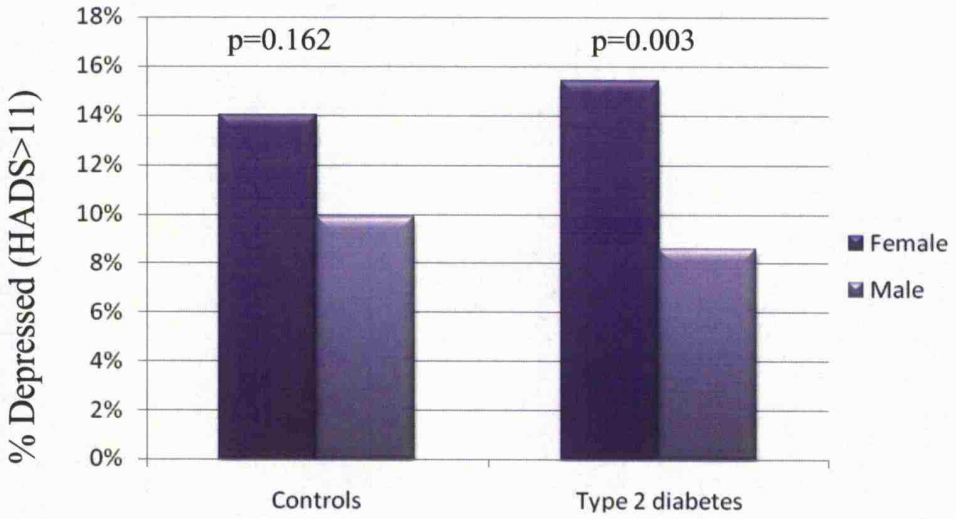


Figure 7.5. Prevalence of depression (HADS≥ 11) in type 2 diabetes and controls by gender

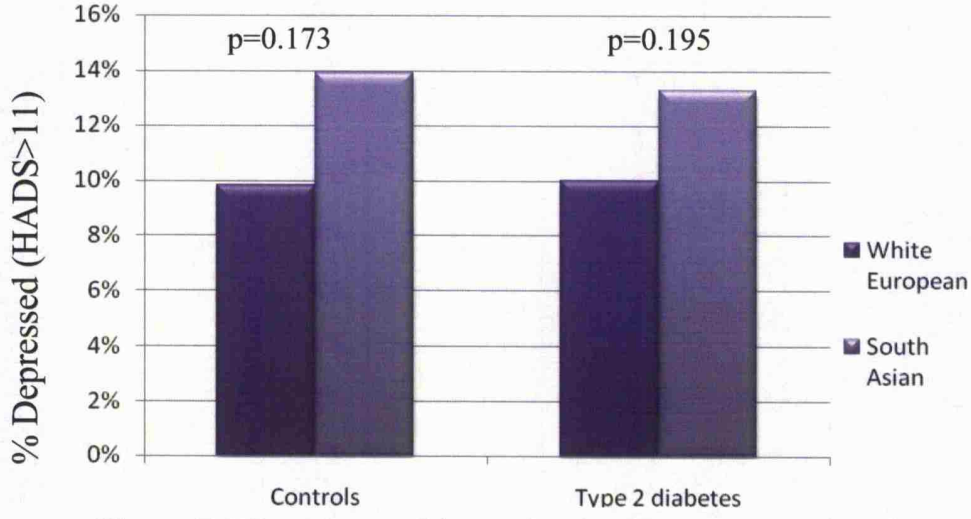


Figure 7.6. Prevalence of depression (HADS≥ 11) in type 2 diabetes and controls by ethnicity

Table 7.3. Characteristics of people with and without diabetes by depression status (HADS≥11)

	Controls N = 634			Type 2 N = 854*		
	Non-depressed N =555	Depressed N =79	P	Non-depressed N = 750	Depressed N = 104	P
Age						
< 59	421 (86.3)	67 (13.7)	.104	359 (84.9)	64 (15.1)	.012
60 +	134 (91.8)	12 (8.2)		391 (90.7)	40 (9.3)	
Gender						
Female	337 (86.0)	55 (14.0)	.162	379 (84.6)	69 (15.4)	.003
Male	218 (90.1)	24 (9.9)		371 (91.4)	35 (8.6)	
IMDR group						
1	298 (86.1)	48 (13.9)	.657	412 (86.6)	64 (13.4)	.554
2	160 (89.9)	18 (10.1)		219 (88.7)	28 (11.3)	
3	45 (88.2)	6 (11.8)		57 (90.5)	6 (9.5)	
4	52 (88.1)	7 (11.9)		62 (91.2)	6 (8.8)	
Ethnicity						
White European	202 (90.2)	22 (9.8)	.173	269 (90.0)	30 (10.0)	.195
South Asian	353 (86.1)	57 (13.9)		481 (86.7)	74 (13.3)	
Smoking status						
Never	389 (87.6)	55 (12.4)	.876	498 (86.5)	78 (13.5)	.142
Former	99 (88.4)	13 (11.6)		157 (91.8)	14 (8.2)	
Current	67 (85.9)	11 (14.1)		95 (88.8)	12 (11.2)	
Marital status						
Single	99 (81.1)	23 (18.9)	.023	167 (87.4)	24 (12.6)	.886
Married	417 (89.3)	50 (10.7)		529 (88.2)	71 (11.8)	
BMI						
<29	354 (88.1)	48 (11.9)	.696	433 (88.2)	58 (11.8)	.660
>30	113 (86.3)	18 (13.7)		306 (86.9)	46 (13.1)	
CV comorbidities						
0	394 (86.4)	62 (13.6)	.329	275 (85.9)	45 (14.1)	.366
1	125 (89.9)	14 (10.1)		316 (89.5)	37 (10.5)	
2+	36 (92.3)	3 (7.7)		159 (87.8)	22 (12.2)	
Other comorbidities						
0	401 (87.7)	56 (12.3)	.967	515 (89.7)	59 (10.3)	.010
1	128 (87.1)	19 (12.9)		188 (86.2)	30 (13.8)	
2+	26 (86.7)	4 (13.3)		47 (75.8)	15 (24.2)	
Years of diabetes				7.2 (SD 6.0)	7.5 (6.5)	.650
0-3	--	--	--	405 (88.2)	54 (11.8)	.578
4-14	--	--	--	270 (88.2)	36 (11.8)	
15+	--	--	--	75 (84.3)	14 (15.7)	
Treatment						
Lifestyle	--	--	--	132 (87.4)	19 (12.6)	.121
OAD	--	--	--	488 (88.9)	61 (11.1)	
Insulin	--	--	--	65 (90.3)	7 (9.7)	
Both	--	--	--	65 (79.3)	17 (20.7)	
HbA1c						
<6.9	--	--	--	300 (87.0)	45 (13.0)	.735
>7	--	--	--	425 (88.0)	58 (12.0)	
Complications						
0	--	--	--	476 (88.3)	63 (11.7)	.543
1	--	--	--	194 (88.2)	26 (11.8)	
2+	--	--	--	80 (84.2)	15 (15.8)	

* Smaller figure due to missing cases of completed HADS, CV = cardiovascular

Diagnosed depression

In total, 127 people were recognised as depressed based on the receipt of antidepressant medication or a recorded diagnosis. Of those recognised, 44 (34.6%) had a current diagnostic code for depression in their notes (in the 3 months prior to completing the questionnaire). Only 10 (7.9%) people had a current diagnosis of depression (in the previous 3 months from completing the questionnaire) but were not currently on antidepressant medication.

The rate of diagnosed depression was 7% in people with diabetes compared to 10% in those without (p =0.175).

In people with type 2 diabetes, the levels of diagnosed depression were increased with higher levels of deprivation, in White Europeans compared to South Asians (11 vs. 6%, p = 0.016) and in current smokers as opposed to former and never smokers (16% vs. 8.1 and 5.8%, p = 0.005), A higher prevalence of depression was also observed in those with non-cardiovascular related comorbidities and in those treated with a combination of OAD medication and insulin.

Participants without diabetes and with diagnosed depression were more likely to be White European (16% vs. 6%), to be current smokers (19% vs. 11 % former smoker and 7% in non-smokers) and to be unmarried and not living with a partner (19 vs. 7.4% married or living with a partner). Higher rates of diagnosed depression were also observed in those with non-cardiovascular related comorbidities (Table 7.4). No significant difference was observed in the rates of diagnosed depression between South Asian participants with or without type 2 diabetes, who completed the

questionnaire in English compared to those who completed a translated version (P = 1.69 and P =0.688) .Figure 7.7 and Figure 7.8. Show the prevalence of depression by gender and ethnic group for both type 2 diabetes and controls.

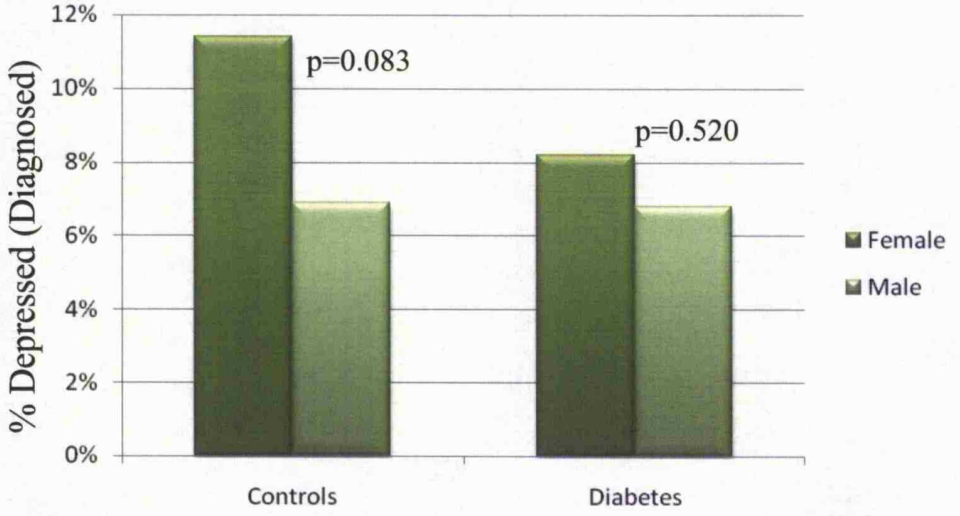


Figure 7.7. Prevalence of depression in type 2 diabetes and controls by gender

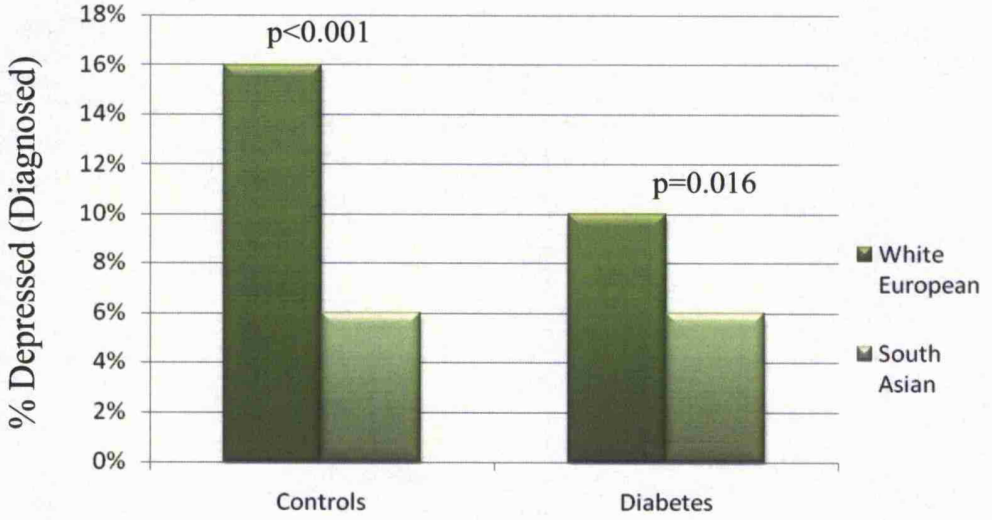


Figure 7.8. Prevalence of depression in type 2 diabetes and controls by ethnicity

Table 7.4. Characteristics of diabetes and control groups by depression status (Diagnosed depression)

	Controls N = 634			Type 2 N = 854*		
	Non-depressed N =581	Depressed N =62	P	Non-depressed N = 797	Depressed N = 65	P
Age						
< 59	443 (89.9)	50 (10.1)	.535	386 (90.8)	39 (9.2)	.096
60 +	138 (92.0)	12 (8.0)		411 (94.1)	26 (5.9)	
Gender						
Female	351 (88.6)	45 (11.4)	.083	414 (91.8)	37 (8.2)	.520
Male	230 (93.1)	17 (6.9)		383 (93.2)	28 (6.8)	
IMDR group						
1	309 (88.3)	41 (11.7)	.246	433 (90.2)	47 (9.8)	.027
2	170 (92.9)	13 (7.1)		238 (95.2)	12 (4.8)	
3	48 (94.1)	3 (5.9)		59 (93.7)	4 (6.3)	
4	54 (91.5)	5 (8.5)		67 (97.1)	2 (2.9)	
Ethnicity						
White European	189 (84.0)	36 (16.0)	.000	268 (89.3)	32 (10.7)	.016
South Asian	392 (93.8)	26 (6.2)		529 (94.1)	33 (5.9)	
Smoking status						
Never	417 (92.5)	34 (7.5)	.010	548 (94.2)	34 (5.8)	.005
Former	100 (88.5)	13 (11.5)		158 (91.9)	14 (8.1)	
Current	64 (81.0)	15 (19.0)		91 (84.3)	17 (15.7)	
Marital status						
Single	99 (81.1)	23 (18.9)	.000	172 (89.1)	21 (10.9)	.125
Married	440 (92.6)	35 (7.4)		563 (92.9)	43 (7.1)	
BMI						
<29	373 (91.2)	36 (8.8)	.465	466 (94.0)	30 (6.0)	.071
>30	116 (88.5)	15 (11.5)		320 (90.4)	34 (9.6)	
CV comorbidities						
0	417 (90.7)	43 (9.3)	.820	300 (93.2)	22 (6.8)	.824
1	129 (90.2)	14 (9.8)		328 (92.1)	28 (7.9)	
2+	35 (87.5)	5 (12.5)		169 (91.8)	15 (8.2)	
Other comorbidities						
0	426 (91.8)	38 (8.2)	.039	546 (94.5)	32 (5.5)	.007
1	132 (88.6)	17 (11.4)		197 (89.1)	24 (10.9)	
2+	23 (76.7)	7 (23.3)		54 (85.7)	9 (14.3)	
Years of diabetes						
0-3	--	--	--	420 (91.5)	39 (8.5)	.318
4-14	--	--	--	294 (94.2)	18 (5.8)	
15+	--	--	--	83 (91.2)	8 (8.8)	
Treatment						
Lifestyle	--	--	--	138 (90.8)	14 (9.2)	.031
OAD	--	--	--	519 (93.9)	34 (6.1)	
Insulin	--	--	--	70 (94.6)	4 (5.4)	
Both	--	--	--	70 (84.3)	13 (15.7)	
HbA1c						
<6.9	--	--	--	320 (92.2)	27 (7.8)	1.00
>7	--	--	--	452 (92.4)	37 (7.6)	
Complications						
0	--	--	--	511 (93.9)	33 (6.1)	.091
1	--	--	--	202 (90.6)	21 (9.4)	
2+	--	--	--	84 (88.4)	11 (11.6)	

* Smaller figure due to missing cases of completed HADS, CV = cardiovascular

7.4.6 The association between type 2 diabetes and screen detected depression

Mild to severe depression (HADS≥8)

Table 7.5. presents the results from unadjusted and adjusted logistic regression models. In unadjusted models the odds of depression were higher in the younger age group (<59 years of age), in females, in those with higher levels of deprivation (lower IMDS quartiles), in South Asians, in those with Cardiovascular related-comorbidities and in those with 2 or more non-cardiovascular related comorbidities. No significant difference in the odds of depression was observed between participants with and without type 2 diabetes.

A significant association between depression and type 2 diabetes also failed to be demonstrated in adjusted models, although female gender, South Asian ethnicity, higher deprivation and presence of cardiovascular and non-cardiovascular related comorbidities remained strong predictors.

No association was observed between depression and type 2 diabetes in the separate models conducted in South Asian and White Europeans and the interactions examined between type 2 diabetes and ethnicity, age or gender each proved to be statistically non-significant.

Moderate to severe depression (HADS≥11)

In models using a higher cut-off for depression (HADS≥11), no increased risk for depression was observed in those with type 2 diabetes, in either adjusted or unadjusted analyses (Table 7.6). An association between the prevalence of

depression and type 2 diabetes also failed to be demonstrated in models conducted separately in South Asians and White Europeans. Furthermore no statistically significant interactions between type 2 diabetes and ethnicity, age and gender were observed.

In unadjusted analyses, the odds of depression were increased in those aged <59 years, in females, South Asians, and in those with cardiovascular and non-cardiovascular related comorbidities. In adjusted analyses, younger age group, female gender and the presence of cardiovascular and non-cardiovascular related comorbidities remained significantly associated with an increased risk for depression.

Diagnosed depression.

No association was observed between type 2 diabetes and the risk of depression defined by physician diagnosis. Again this association failed to be demonstrated in adjusted and unadjusted analyses as well as separate analyses by ethnic group. Furthermore the findings were not modified by ethnicity, age or gender (Table 7.7).

The risk of a diagnosis of depression was increased in younger people (<59 years), in females, those with higher levels of deprivation and in those with non-cardiovascular related comorbidities, in both adjusted and unadjusted analyses. In contrast to depression identified via the HADS, the odds of a depression diagnosis were increased in White Europeans in comparison to South Asians.

Table 7.5. Unadjusted and adjusted odds of depression (based on HADS ≥8) in people with diabetes vs. those without

	Total population N = 1376				Models conducted separately by ethnicity: White European N = 478		South Asian N = 898	
	Unadjusted	P	Adjusted	p	Adjusted	p	Adjusted	p
Type 2 diabetes vs. without	**0.947(0.755-1.188)**	**.638**	**1.070(0.81-1.400)**	**.625**	**0.879 (0.529-1.459)**	**.617**	**1.158 (0.840-1.597)**	**.371**
Age <59 vs. 60+	0.749 (0.592-0.947)	.016	1.327 (0.992-1.775)	.057	1.667 (1.000-2.779)	.050	1.140 (0.801-1.622	.466
Female vs. Male	1.804 (1.427-2.280)	.000	1.766 (1.370-2.276)	.000	1.372 (0.864-2.178)	.180	1.988 (1.459-2.708)	.000
IMD 1	r	.015	r	.084	r	.024	r	.618
2 vs. 1	0.783(0.603-1.016)	.066	0.848(0.643-1.119)	.244	0.615 (0.354-1.067)	.084	0.939 (0.679-1.299)	.705
3 vs. 1	0.772 (0.496-1.201)	.251	0.971(0.612-1.539)	.900	0.709 (0.348-1.445)	.344	1.28 (0.691-2.374)	.432
4 vs. 1	0.504 (0.315-0.804)	.004	0.541(0.332-.884)	.014	0.326 (0.1490.711)	.005	0.733 (0.384-1.399)	.346
SA vs. WE[1]	1.365 (1.072-1.737)	.012	1.365 (1.032-1.806)	.029	--		--	
CV related comorbidity 0	r	.014	r	.013	r	.106	r	.034
1 vs. 0	0.722 (0.558-0.934)	.013	0.824(0.614-1.105)	.196	0.631 (0.366-1.090)	.099	.903 (0.636-1.282)	.568
2 vs. 0	1.136 (0.825-1.564)	.433	1.426 (0.975-2.088)	.068	1.114 (0.581-2.135)	.745	1.681 (1.043-2.711)	.033
Non-CV related comorbidity 0	r	.032	r	.022	r	.013	r	.411
1 vs. 0	1.193 (0.919-1.550)	.185	1.212 (0.915-1.605)	.179	1.205(0.748-1.940)	.444	1.246 (0.875-1.773)	.222
2 vs. 0	1.733 (1.115-2.692)	.014	1.859(1.170-2.955)	.009	2.797 (1.408-5.556)	.003	1.259 (0.653-2.428)	.491
BMI> 30 vs. <29	1.086 (0.852-1.386)	.504	0.971 (0.744-1.267)	.827	1.071 (0.672-1.706)	.773	.889 (0.636-1.243)	.492
Interaction Models[2]								
Type 2 diabetes * Ethnicity			1.487 (0.877-2.519)	0.140				
Type 2 diabetes * Age			1.325(0.754-2.329)	0.328				
Type 2 diabetes * Gender			1.489 (0.892-2.485)	0.128				

r Reference category,[1] SA = South Asian. WE = White European, CV = cardiovascular [2]Interaction models adjusting for age, gender, ethnicity (as appropriate) , cardiovascular-related comorbidities, other comorbidities and BMI

Table 7.6 Unadjusted and adjusted odds of depression (based on HADS ≥11) in people with diabetes vs. those without

	Total population N = 1376				Models conducted separately by ethnicity: White European N = 478		South Asian N = 898	
	Unadjusted	P	Adjusted	p	Adjusted	p	Adjusted	p
Type 2 diabetes vs. without	**0.974 (0.713-1.331)**	**.870**	**1.192(0.826-1.720)**	**.347**	**1.468 (0.692-3.113)**	**.317**	**1.101(0.719-1.686)**	**.657**
Age <59 vs. 60+	1.696 (1.207-2.382)	.002	1.694 (1.124-2.554)	.012	2.619(1.231-5.571)	.012	1.371(0.842-2.231)	.205
Female vs. Male	1.729 (1.245-2.401)	.001	1.661(1.165-2.368)	.005	0.931 (0.478-1.813)	.833	2.093(1.366-3.205)	.001
IMD 1	r	.389	r	.789	r	.039	r	.705
2 vs. 1	0.769 (0.534-1.109)	.159	0.846 (0.577-1.241)	.392	0.397(0.165-0.955)	.039	1.052(0.680-1.627)	.820
3 vs. 1	0.746 (0.397-1.401)	.362	0.955(0.498-1.830)	.889	0.388(0.112-1.344)	.135	1.478(0.674-3.241)	.329
4 vs. 1	0.723 (0.394-1.327)	.295	0.792 (0.415-1.509)	.478	0.280 (0.081-.970)	.045	1.351(0.626-2.914)	.443
SA vs. WE[1]	1.423 (1.012-2.000)	.042	1.445(0.976-2.140)	.066	--	.111	--	.978
CV related comorbidity 0	r	.177	r	.622	r	.145	r	.925
1 vs. 0	0.723 (0.507-1.031)	.073	0.862(9.579-1.285)	.466	0.549 (0.245-1.231)	.496	1.022(0.646-1.617)	.884
2 vs. 0	0.802 (0.504-1.274)	.350	1.087(0.634-1.863)	.762	1.374(0.550-3.428)	.172	.950(0.478-1.890)	.068
Non-CV related comorbidity 0	r	.025	r	.016	r	.658	r	.137
1 vs. 0	1.235 (0.863-1.767)	.248	1.310(0.896-)1.918	.164	1.171(0.582-2.357)	.061	1.415(0.896-2.235)	.046
2 vs. 0	2.073(1.207-3.560)	.008	2.243(1.265-3.979)	.006	2.428(0.959-6.151)	.817	2.180(1.014-4.690)	.715
BMI> 30 vs. <29	1.134 (0.814-1.581)	.458	1.026(0.716-)1.471	.889	1.084(0.548-2.143)	.317	0.921(0.593-1.431)	.657
Interaction Models[2]								
Type 2 diabetes * Ethnicity			0.788 (0.369-1.681)	.537				
Type 2 diabetes * Age			0.972(0.412-2.293)	.948				
Type 2 diabetes * Gender			1.601(0.786-3.260)	.195				

r Reference category,[1] SA = South Asian. WE = White European, CV = cardiovascular, [2]Interaction models adjusting for age, gender, ethnicity (as appropriate) , CV-related comorbidities, other comorbidities and BMI

Table 7.7. Unadjusted and adjusted odds of depression (based diagnosis in patient records) in people with diabetes vs. those without

	Total population N = 1390				Models conducted separately by ethnicity: White European N = 479		South Asian N = 911	
	Unadjusted	P	Adjusted	p	Adjusted	p	Adjusted	p
Type 2 diabetes vs. without	**0.764 (0.531-1.10)**	**.148**	**0.785 (0.508-1.213)**	**.276**	**0.826 (0.431-1.583)**	**.564**	**0.759 (0.417-1.383)**	**.368**
Age <59 vs. 60+	1.551 (1.045-2.302)	.029	2.021 (1.240-3.296)	.005	2.442 (1.245-4.790)	.009	1.600 (0.800-3.201)	.184
Female vs. Male	1.460 (1.000-2.133)	.050	1.198 (0.789-1.819)	.396	1.657 (0.872-3.148)	.123	0.881 (0.494-1.568)	.666
IMD 1	r	.012	r	.006	r	.003	r	.631
2 vs. 1	0.517 (0.326-0.819)	.005	0.535 (0.328-.875)	.013	0.283 (0.120-0.665)	.004	0.847 (0.458-1.566)	.597
3 vs. 1	0.552 (0.249-1.223)	.143	0.431 (0.180-1.030)	.058	0.383 (0.129-1.137)	.084	0.506 (0.116-2.202)	.363
4 vs. 1	0.488 (0.221-1.078)	.076	0.348 (0.145-.831)	.018	0.269 (0.090-0.798)	.018	0.493 (0.115-2.125)	.343
SA vs. WE[1]	0.431 (0.298-0.621)	.000	0.422 (0.276-.647)	.000	--	.882	--	.329
CV related comorbidity 0	r	.958	r	.420	r	.621	r	.380
1 vs. 0	1.014 (0.676-1.521)	.947	1.272 (0.793-2.040)	.319	1.191 (0.596-2.379)	.763	1.340 (0.697-2.57)	.144
2 vs. 0	1.081 (0.640-1.828)	.770	1.487 (0.786 2.810)	.222	1.154 (0.455-2.925)	.124	1.910(0.802 4.547)	.055
Non-CV related comorbidity 0	r	.000	r	.007	r	.341	r	.061
1 vs. 0	1.730 (1.154-2.595)	.008	1.571 (1.014-2.434)	.043	1.356 (0.725-2.537)	.044	1.800 (0.973-3.330)	.062
2 vs. 0	2.885 (1.598-5.208)	.000	2.544 (1.345-4.812)	.004	2.405 (1.026-5.639)	.872	2.643 (0.954-7.324)	.569
BMI> 30 vs. <29	1.429 (0.970-2.104)	.071	1.089 (0.711 1.667)	.696	0.950 (0.512-1.765)	.000	1.198(0.643 2.231)	.368
Interaction Models[2]								
Type 2 diabetes * Ethnicity			1.257 (0.569-2.781)	.571				
Type 2 diabetes * Age			1.365 (0.556-3.351)	.498				
Type 2 diabetes * Gender			0.751 (0.323-1.743)	.504				

r Reference category,[1] SA = South Asian. WE = White European, CV = cardiovascular, [2]Interaction models adjusting for age, gender, ethnicity (as appropriate) , CV-related comorbidities, other comorbidities and BMI

7.4.7 Ethnic differences in the prevalence of depression in type 2 diabetes

Mild to severe depression

In unadjusted models (Table 7.8), a higher risk for depression was associated with South Asian ethnicity, younger age group (<59 vs. ≥60), female gender and having a diagnosis of diabetes for 15+ years in comparison to 0-5 years. The odds of depression were lowest in the highest quartile for IMD (representing the least deprived group) in comparison to the lowest quartile (the most deprived group).

In multiple logistic regression analysis South Asian ethnicity was a significant independent risk factor for depression. The odds were also increased in those aged <59 years, in females, in those with high levels of deprivation, those with 2 or more non-cardiovascular related comorbidities, those with 2 or more diabetes related complications and in those with diabetes for a duration of 15+ years.

In models conducted separately by ethnicity (Table 7.9), only female gender was associated with an increased risk of depression in South Asian participants with type 2 diabetes. In White Europeans, the odds of depression were increased in those aged <59 years old, in females and in those with 2 or more non-cardiovascular related co-morbidities and diabetes related complications.

Interaction analyses revealed that the association between ethnicity and depression was moderated by age and the presence of 2 or more non-cardiovascular related

comorbidities. The interactions were examined by conducting Chi-squares comparisons between the prevalence of depression in South Asian and White European groups separately for those aged <59 years and ≥60 years of age. No significant difference in the prevalence of depression was observed between South Asians and White Europeans aged < 59 years old (32.2% in South Asians vs. 32.6% in White Europeans, p = 0.905); however in those aged ≥60 the prevalence of depression was significantly higher in South Asians in comparison to White Europeans (31.7% vs. 18.3% p = 0.02). Odds ratios for depression in South Asians vs. White Europeans were also estimated separately for those aged <59 and ≥60. No differences in the odds for depression were observed between South Asians and White Europeans aged <59 years of age (OR 0.938 95% CI 0.565-1.556, p= .803), however in those aged ≥60, the odds of depression were twice as high in South Asian participants compared to White Europeans (OR 2.066 95%CI 1.318-3.239, p =.002), suggesting that the odds of depression are increased in South Asians with type 2 diabetes aged ≥60 but not in those aged <59 years.

Chi squared comparisons were also examined separately by the number of non-cardiovascular related co-morbidities (0, 1 or 2+). The findings showed that in those with no comorbidities or one comorbidity, the prevalence of depression was significantly higher in South Asians in comparison to White Europeans (29.4% vs. 16.9%, p=0.003 and 37.9% vs. 24.5%, p=0.048). A higher rate of depression was observed in White Europeans with 2 or more complications, but no significant difference was observed in comparison to South Asians with 2 or more comorbidities

(45.2% in White Europeans vs. 32.3% in South Asians, p= 0.434). Similarly, the odds of depression were significantly higher in South Asians in comparison to White Europeans in those with one cardiovascular related co-morbidity vs. none (OR 2.054 95%CI 1.298-3.249, p=0.002 and OR 1.882, 95%CI 1.047-3.384, p= 0.0345). No significant difference in the odds of depression was observed between South Asians and White Europeans with 2 or more non cardiovascular related co-morbidity vs. none (OR 0.578, 95% CI 0.206-1.625, p= 0.299).

Table 7.8. Unadjusted and adjusted odds of depression in South Asians vs. White Europeans (HADS ≥8)

	Total population type 2 diabetes N = 817			
	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	p
SA vs. WE[1]	1.581(1.142-2.190)	.006	1.462 (0.997-2.144)	.052
Age <59 vs. 60+	1.372 (1.017-1.850)	.039	1.528 (1.056-2.211)	.025
Female vs. Male	1.968 (1.447-2.677	.000	2.054 (1.464-2.881)	.000
IMDR 1[2]	r	.110	r	.069
2 vs. 1	0.881(0 .587-1.322)	.539	0.840 (0.584-1.209)	.348
3 vs. 1	0.798 (0.529-1.202)	.280	0.491 (0.232-1.036)	.062
4 vs. 1	0.591(0 .384-0.909)	.017	0.492 (0.249-0.970)	.041
CV comorbidity 0	r	.022	r	.110
1 vs. 0	0.675(0.480-0.951)	.025	0.758 (0.519-1.108)	.153
2+ vs. 0	1.107(0.750-1.635)	.609	1.175 (0.735-1.8780	.500
Other comorbidity 0	r	.044	r	.026
1 vs. 0	1.333 (0.948-1.875)	.099	1.368 (0.945-1.981)	.097
2 +vs. 0	1.818 (1.055-3.133)	.031	2.073 (1.153-3.728)	.015
Complications 0	r	.008	r	.046
1 vs. 0	1.410 (0.999-1.990)	.050	1.310 (0.902-1.901)	.156
2+ vs. 0	1.928 (1.222-3.043)	.005	1.878 (1.111-3.175)	.019
Duration 0-5	r	.006	r	.035
5-14	1.081 (0.780-1.499)	.640	0.973 (0.670-1.413)	.887
15+	2.129 (1.332-3.403)	.002	1.980 (1.114-3.519)	.020
Treatment, lifestyle	r	.260	r	.861
OAD	0.940 (0.628-1.407)	.764	1.044 (0.653-1.6680	.858
Insulin alone	1.218 (0.662-2.242)	.526	0.927 (0.439-1.957)	.842
Insulin and OAD	1.497 (0.844-2.656)	.168	1.262 (0.617-2.579)	.524
BMI>30	1.044 (0.771-1.413)	.782	0.891 (0.627-1.265)	.518
HbA1c >7	1.063 (0.782-1.446)	.696	0.869 (0.607-1.244)	.443

[1]SA= South Asian, WE= White European, CV = cardiovascular,[2]Indices of multiple deprivation rank, r = Reference category, OAD = Oral Anti-diabetic Medication

Table 7.9. Factors associated with depression (HADS≥8) in South Asian and White Europeans with type 2 diabetes.

	Type 2 diabetes N = 817				
	SA N = 523 OR (95% CI)	P	WE N = 294 OR (95% CI)	P	Ethnicity* variable P
Age <59 vs. 60+	1.140 (0.762-1.705)	.525	2.155 (1.132-4.104)	.019	.043
Female vs. Male	2.091 (1.43503.046)	.000	1.849 (1.014-3.369)	.045	.667
IMD 1	r	.346	r	.469	.992
2 vs. 1	0.925 (0.612-1.398)	.712	0.976 (0.480-1.986)	.947	.775
3 vs. 1	0.560 (0.200-1.564)	.269	0.591 (0.204-1.712)	.333	.916
4 vs. 1	0.507 (0.210-1.223)	.131	0.483 (0.166-1.411)	.183	.854
CV comorbidity 0	r	.032	r	.261	.170
1 vs. 0	0.769 (0.500-1.180)	.229	0.558 (0.272-1.144)	.111	.294
2+ vs. 0	1.547 (0.911-2.627)	.106	0.789 (0.352-1.768)	.566	.061
Other comorbidity 0	r	.394	r	.006	.057
1 vs. 0	1.360 (0.871-2.123)	.177	1.261 (0.667-2.385)	.475	.912
2+ vs. 0	0.994 (0.441-2.238)	.988	4.111 (1.725-9.795)	.001	.022
Complications 0	r	.152	r	.029	.827
1 vs. 0	1.267(0.830-	.273	1.884 (0.946-	.072	.568
2+ vs. 0	1.811 (0.951-	.071	2.623 (1.209-	.015	.706
Duration 0-5	r	.152	r	.138	.869
5-14	0.990 (0.655-1.497)	.962	0.877 (0.441-1.745)	.709	.610
15+	1.772 (0.951-3.302)	.071	2.293 (0.899-5.849)	.082	.996
Treatment, lifestyle	r	.553	r	.487	.355
OAD	0.697 (0.409-1.189)	.186	1.477 (0.692-3.152)	.313	.128
Insulin alone	0.683 (0.304-1.536)	.357	1.324 (0.414-4.233)	.636	.441
Insulin and OAD	0.867 (0.407-1.847)	.712	2.296 (0.792-6.654)	.126	.105
BMI>30	0.782 (0.514-1.189)	.250	1.068 (0.581-1.962)	.833	.368
HbA1c >7	0.797 (0.541-1.175)	.252	1.260 (0.676-2.350)	.467	.143

r = Reference category, CV = cardiovascular, SA = South Asian, WE = White European, OAD = Oral Anti-diabetic Medication

Moderate to severe depression

In both adjusted and unadjusted logistic regression models (Table 7.10), an increased risk of depression was observed in females, those aged <59 years of age and in those with 2 or more non-Cardiovascular related comorbidities.

In models conducted separately by ethnicity (Table 7.11), the odds of depression in South Asians was doubled in females compared to males. In White Europeans, the odds of depression were higher in those aged <59 years of age and with 2 or more non-cardiovascular related comorbidities. Interactions analyses revealed no significant

effects of any of the independent variables examined and the relationship between ethnicity and depression.

Table 7.10. Unadjusted and adjusted odds of depression in South Asians vs. White Europeans (HADS ≥11)

	Total population type 2 diabetes N = 817			
	Unadjusted OR (95%CI)	P	Adjusted OR (95%CI)	p
SA vs. WE	1.379 (0.880-2.163)	.161	1.355 (0.804-2.282)	.254
Age <59 vs. 60+	1.743 (1.145-2.653)	.010	1.847 (1.115-3.058)	.017
Female vs. Male	1.930 (1.254-2.970)	.003	2.053 (1.289-3.269	.002
IMD 1		.574		.835
2 vs. 1	0.823 (0.513-1.321)	.420	0.880 (0.536-1.445)	.614
3 vs. 1	0.678 (0.281-1.636)	.387	0.790 (0.308-2.024)	.623
4 vs. 1	0.623 (0.259-1.500)	.291	0.701 (0.284-1.728)	.440
CV comobidity vs. none		.368		.673
1 vs. 0	0.716 (0.450-1.138)	.157	0.880 (0.531-1.460)	.622
2+ vs. 0	0.846 (0.490-1.460)	.547	1.149(0.610-2.164)	.667
Other comorbidity vs. none		.006		.004
1 vs. 0	1.393 (0.870-2.229)	.167	1.391(0.847-2.285)	.193
2+ vs. 0	2.786 (1.468-5.286)	.002	3.123 (1.579-6.176)	.001
Complications 0		.523		.517
1 vs. 0	1.013 (0.623-1.647)	.960	.968 (0.577-1.623)	.901
2+ vs. 0	1.417 (0.769-2.610)	.264	1.450 (0.730-2.881)	.288
Duration 0-5		.559		.387
5-14	1.000 (0.638-1.567)	1.000	.943 (0.568-1.567)	.821
15+	1.400 (0.740-2.648)	.301	1.575 (0.728-3.408)	.248
Treatment, lifestyle	r	.094	R	.133
OAD	0.868 (0.501-1.505)	.615	1.004 (0.539-1.869)	.990
Insulin alone	0.748 (0.299-1.870)	.535	0.682 (0.235-1.979)	.481
Insulin and OAD	1.817 (0.886-3.728)	.103	1.986 (0.810-4.873)	.134
BMI>30 vs. <29	1.122 (0.742-1.697)	.585	0.861 (0.540-1.373)	.529
HbA1c >7 vs. <6.9	0.910 (0.600-1.3800	.656	0.728 (0.451-1.176)	.195

r = Reference category, CV = cardiovascular, SA = South Asian, WE = White European

Table 7.11 Factors associated with depression (HADS≥11) in South Asian and White Europeans with type 2 diabetes

	Total population type 2 diabetes N = 817				
	SA N =523 OR (95% CI)	P	WE N = 294 OR (95% CI)	P	Ethnicity* variable P
Age <59 vs. 60+	1.436 (0.824-2.501)	.201	2.891 (1.218-6.857)	.016	.193
Female vs. Male	2.141 (1.269-3.614)	.004	1.543 (0.679-3.506)	.300	.414
IMD 1	r	.972	R	.263	.249
2 vs. 1	1.075 (0.614-1.882)	.800	0.486 (0.164-1.440)	.193	.168
3 vs. 1	1.045 (0.292-3.735)	.946	0.678 (0.179-2.573)	.568	.703
4 vs. 1	1.265 (0.458-3.494)	.651	0.171 (0.021-1.374)	.097	.099
CV comobidity 0	r	.990	R	.324	.428
1 vs. 0	0.962 (0.545-1.697)	.892	0.583 (0.218-1.555)	.281	.221
2+ vs. 0	0.966 (0.458-2.038)	.928	1.188 (0.410-3.443)	.751	.882
Other comorbidity 0	r	.102	R	.019	.518
1 vs. 0	1.544 (0.863-2.761)	.143	1.104 (0.444-2.743)	.831	.617
2+ vs. 0	2.341 (0.928-5.906)	.071	4.165 (1.469-11.804)	.007	.407
Complications 0	r	.806	R	.547	.877
1 vs. 0	1.057 (0.593-1.884)	.852	0.982 (0.356-2.707)	.972	.752
2+ vs. 0	1.334 (0.564-3.154)	.512	1.722 (0.623-4.759)	.295	.755
Duration 0-5	r	.391	R	.296	.322
5-14	1.243 (0.714-2.164)	.442	0.507 (0.180-1.426)	.198	.132
15+	1.764 (0.768-4.049)	.181	1.365 (0.376-4.961)	.636	.704
Treatment, lifestyle	r	.294	R	.700	.851
OAD	0.806 (0.390-1.665)	.560	1.004 (0.376-2.681)	.993	.815
Insulin alone	0.584 (0.180-1.898)	.371	0.750 (0.137-4.117)	.740	.813
Insulin and OAD	1.511 (0.591-3.864)	.389	1.865 (0.507-6.863)	.349	.851
BMI>30 vs. <29	0.858 (0.495-1.490)	.588	1.054 (0.456-2.437)	.902	.643
HbA1c >7 vs. <6.9	0.819 (0.489-1.372)	.448	0.785 (0.337-1.829)	.575	.934

r = Reference category, CV = cardiovascular, SA = South Asian, WE = White European

7.4.8 The prevalence of recognised and unrecognised depression

In people with mild to severe depression (HADS≥8) no significant difference was observed in rates of undiagnosed depression between those with and without type 2 diabetes (Table 7.12) However rates of undiagnosed depression were significantly higher in South Asians compared to White Europeans, both in those with type 2 diabetes (90% vs. 63%, p=0.018) and in those without (77.2% vs. 50%, p=0.01).

However in addition, of those with type 2 diabetes 27 (4.4%) participants scoring below the threshold for mild to severe depression (HADS<8) were also recognised as depressed in the general practice records (5.2% in White Europeans vs. 3.9% in South Asians).

Twenty-five (5.6%) of participants without type 2 diabetes scored below the threshold for mild to severe symptoms of depression and were also recognised as depressed in general practice records (9.3% in White Europeans vs. 3.4% in South Asian).

In those with moderate to severe symptoms of depression (HADS≥11) (Table 7.12), rates of undiagnosed depression were higher in those with diabetes compared to those without (82.7% vs. 69.6%, p=0.037) and were significantly higher in South Asians in comparison to White Europeans, both in those with type 2 diabetes (90.5% vs. 63.3%, p=0.018) and in controls (77.2 vs. 50%, p=0.02).

Forty-six (6.1%) participants scoring below the threshold for moderate to severe depression (HADS<11) were recognised as depressed according to their general practice records (7.8% in White Europeans vs. 5.2% in South Asians, P<0.05).

Thirty-eight (6.8%) of control participants below the threshold for moderate to severe symptoms of depression and were also recognised as depressed in general practice records (12.4% in White Europeans vs. 3.7% in South Asians, P<0.05).

Table 7.12 Prevalence of recognised and unrecognised depression by HADS cut-off

	Total with Depression (HAD> 8) N = 427 (5)			Total with Depression (HADS≥11) N = 183		
	Unrecognised	Recognised	P	Unrecognised	Recognised	P
Type 2 diabetes	204 (84.6)	37 (15.4)	.219	86 (82.7)	18 (17.3)	.037
Controls	149 (80.1)	37 (19.9)		55 (69.6)	24 (30.4)	
Type 2 diabetes						
South Asians	67 (90.5)	7 (9.5)	.018	67 (90.5)	7 (9.5)	.018
White Europeans	19(63.3)	11 (36.7)		19 (63.3)	11 (36.7)	
Controls						
South Asians	44 (77.2)	13 (22.8)	.001	44 (77.2)	13 (22.8)	.002
White Europeans	11 (50.0)	11 (50.0%)		11 (50.0)	11 (50.0)	

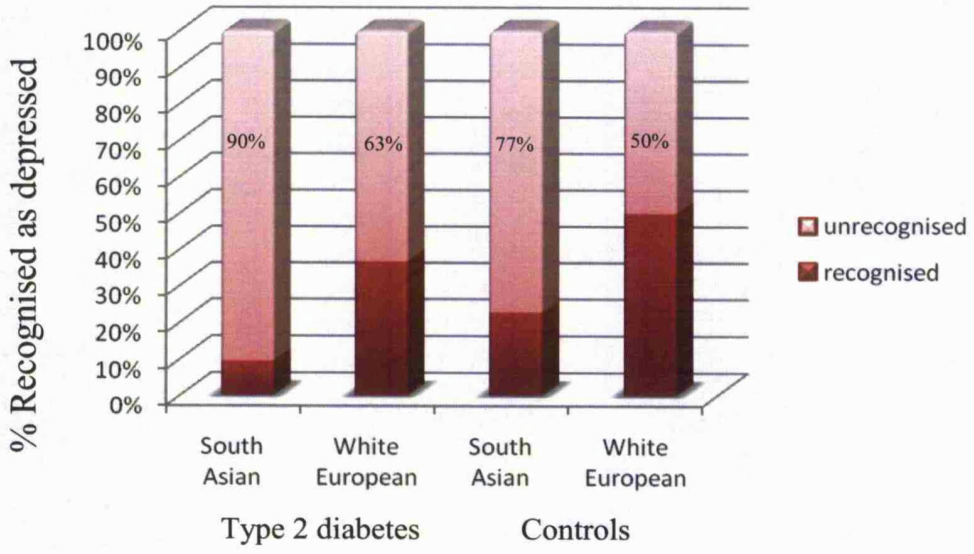


Figure 7.9. Rates of unrecognised depression in South Asians vs. White Europeans with moderate-severe symptoms of depression (HADS≥11)

Chapter 8

Depression in people with type 2 diabetes in primary care: Discussion

8.1 The prevalence of depression in people with type 2 diabetes in comparison to people without diabetes

The findings from the present study are in line with previous research which suggests that people with type 2 diabetes frequently suffer with comorbid depression [75, 195]. The findings demonstrate that 28% of general practice attenders with type 2 diabetes had at least mild symptoms of depression, with 17.4% suffering from moderate to severe symptoms.

Although it is recognised that rates of depression may vary as a function of the psychometric properties of the screening tool selected and the selected cut-off point for depression [334], rates of mild to severe depression reported in this study are within the ranges of 11-60% reported by previous studies utilising self-report assessments of depression in people with diabetes[75] . Furthermore the prevalence of depression using a higher cut- off point on the HADS, corresponding to moderate to severe levels of depression is strikingly similar to a prevalence of 17.6% reported in the meta-analysis of controlled studies of people with type 2 diabetes presented in Chapter 2 [195].

Overall the prevalence figures are higher in comparison to findings from two recent studies using the Hospital Anxiety and Depression scale in the UK and Ireland. Holt et al (2009) [356] reported a fairly low prevalence rate of 2.3% (moderate to severe depression) in 431 people with both established and screen detected type 2 diabetes in the UK. As acknowledged by the authors, the lower levels of depression may have been

attributable to methodological factors including a 'healthy responder' bias during the study recruitment[356]. Collins et al also (2009)[357] examined the prevalence of depression in 1038 people with type 2 diabetes attending primary and secondary care services in Ireland and reported rates of mild to severe depression in 22.4% of participants and rates of moderate to severe depression in 10%. As discussed in Chapter 2, prevalence estimates of depression may also vary according to a number of factors, including the medical and demographic characteristics of the population under investigation [75, 195]. The findings of the present study are unique in comparison to previous estimates, in that they represent the first reports of screen detected depression in consecutive South Asian and White European general practice attenders with type 2 diabetes in the UK. Examining the prevalence figures of White European participants only, the estimates of depression are comparable to the findings of Collins et al[357] (mild to severe depression = 22% and moderate to severe depression = 10%), suggesting that a higher overall rate of depressive symptoms in the present study is largely due to ethnic variation.

Although there is no precise estimate of the prevalence of depression in the current UK general population, previous estimates have suggested rates of approximately 5% [72]. Furthermore prevalence estimates of depression using a cut-off of 8 and above on the HADS, range between 10.4-11% in general population samples [357-360]. While the present study identified higher rates of depression in those with type 2 diabetes, the findings do not support the results from the meta-analysis described in Chapter 2, which concludes that the odds of depression are almost twice as likely in those with

diabetes in comparison to those without [195]. In contrast the present findings revealed no significant difference in either the prevalence or the odds for depression between these two groups suggesting that the association between depression and diabetes may be less robust than previously acknowledged.

There may be various explanations for the discrepancy between previous reports and the findings from the present study. Firstly, in contrast to much of the previous literature described in Chapter 2 [75, 195], the present findings are strengthened by the controlling for a number of potentially confounding factors including both clinical as well as demographic covariates. As discussed in Chapter 2 previous studies examining the cross-sectional association between depression and type 2 diabetes have failed to adequately control for possible confounding factors; including age and the presence of comorbid conditions which in turn may have inflated the difference in depression rates between those with type 2 diabetes and comparison control groups in previous studies. The impact of potentially confounding factors is demonstrated, by a recent population based study of common mental disorders (including depression, anxiety and mixed anxiety and depression) in those with diabetes in the UK [361]. The authors concluded that people with both type 1 and type 2 diabetes were at a 50% increased risk of common mental disorders. However, after adjustment for other comorbid physical illness the magnitude of the association between depression and diabetes was largely diminished [361]. Furthermore when controlling for the effects of impairments to activities in daily living, no significant association was observed, suggesting that psychological distress may result from the burden associated with chronic illness [361].

There is also suggestion that the prevalence of depression may have been over estimated in previous studies in people with diabetes due to depression screening using questionnaires which have not specifically been developed for people with diabetes and which also include items measuring the somatic symptoms of uncontrolled diabetes [300, 362, 363]. The HADS scale on the other hand was specifically selected for use in the present study, due to its explicit omission of somatic items of depression [341] (Chapter 6). As a result of this potentially increased specificity, it may be argued that the magnitude of difference between rates of depression in those with and without type 2 diabetes may have been less pronounced. Alternatively, it may be argued, that there have been few head to head comparisons of the psychometric properties of the HADS with other commonly used depression screening instruments specifically in a population with diabetes, although one recent study has suggested that the HADS may be no more superior in terms of its specificity for depression in comparison to screening tools which do not solely focus on the cognitive symptoms of depression, for example the CES-D [364]. Furthermore it was suggested that the exclusion of somatic symptoms may in fact be related to under recognition of depressed cases [364].

An alternative explanation may be in relation to possible variations in the people classified as depressed using different assessment methods. For example the findings from Anderson et al's meta-analyses of the prevalence of depression in patients with both type 1 and type 2 diabetes concluded that prevalence estimates of depression vary as a function of the method used to assess depression, with rates up to three times

higher observed in studies using self-report symptom checklists compared to those using diagnostic interviews [75]. The authors highlight the possibility that the two approaches identify different, yet overlapping samples of depressed individuals. Whereas diagnostic interviews specifically identify major depressive disorder and exclude other clinically relevant presentations, self-report measures identify a broader spectrum of disorders (e.g. dysthymic disorder, or minor or subsyndromal depression) or symptoms that may reflect other co morbid psychiatric illness (e.g. anxiety or general distress) [75, 365]. In addition, evidence is also accumulating to suggest that many self-report tools which have often been used in studies of depression in people with diabetes may also tap into the symptoms of diabetes related emotional distress, which include feeling such as anxiety related to diabetes management as well as and fears and concerns about hypoglycaemia and the development of complications [365]. For example Hermanns et al (2006) examined the performance of the commonly used BDI and CES-D depression scales against the PAID (problem areas in diabetes) scale [334]. Findings revealed that when evaluated against diagnostic interview and the PAID, both the BDI and CES-D showed sensitivity towards the negative affectivity associated with depression and the negative affect associated with diabetes-related distress[334]. Fisher et al (2007) [365] also examined differences between a structured diagnostic interview and a commonly used self report depression assessment questionnaire, the CES-D in a population with type 2 diabetes. Their results concluded that the rate of depression based on the CES-D was twice as high as the rate of major depression identified by the structured interview. Furthermore 70% of those scoring above the cut-off point defined for likely depression ($\geq$ 16 or $\geq$22) were not considered

to be clinically depressed according to clinical interview, whereas approximately a third of patients with a diagnosis of depression based on the clinical interview did not score above the cut-off for depression based on the CESD. A further finding revealed a higher correlation between measures of diabetes-specific distress and the intensity of depressive symptoms as identified by the CES-D, than the correlation between diabetes-related distress and major depression identified by clinical interview. Together these findings suggest that subclinical depression as classified by the some self-report depression tools may be more reflective of general emotional and diabetes-specific distress rather than major depression specifically. Considering that symptoms of diabetes related distress are common in people with diabetes [366], the fact that these tools identify increased levels of psychological morbidity in people with diabetes may therefore be considered unsurprising. There may also be variations in the people classified as depressed using different self-report tools [365]. Differences may be due to the different cut-points for symptoms scores for depression or the time period over which symptoms occur. They may also be due the wide variation in the inclusion of different symptoms of depression, some of which may be more likely to tap into symptoms of emotional distress. The fact that increased levels of depression were not observed in people with diabetes in the present study may be related to fact that in contrast to other previously used measures of depression, the depression subscale of the HADS largely focuses on anhedonia (the inability to experience joy from normally enjoyable life events or activities). The focus of the HADS-D on what may be considered to be the core symptoms of depression and their separation from symptoms of anxiety may explain a lack of elevated symptom scores in people with diabetes. It is

important to recognise that there has been no research to evaluate the sensitivity of the HADS-D for diabetes related distress and that further psychometric testing is clearly necessary to support such rationalisation.

Alternatively, these findings may point to important cultural differences in the association between depression and type 2 diabetes. The majority of studies identified in the meta-analysis presented in Chapter 2 were conducted in the USA [195]. The prevalence rates of diabetes are reported to be twice as high in the UK in comparison to the USA [367], in addition there are considerable differences in the organisation of the healthcare system, access to this healthcare, as well as the potential economic burden associated with diabetes [367]. For example, contrary to the UK, publicly funded health care is not available to all residents in the USA and many may not be privately insured for various reasons, as a result there may be greater out of pocket expenditure in many with chronic disease, particularly diabetes. These differences considered, it is likely that the psychosocial impact of type 2 diabetes would differ cross-culturally. Although a study into cross-cultural differences has suggested higher rates of rates of anxiety and depression among people with type 1 diabetes in the UK in comparison to the USA, the study did not include a non-diabetic comparison group in either country and therefore the possible interaction between the organisational or cultural environments with comorbid depression in those diabetes is unknown [302].

The higher prevalence rates in those without type 2 diabetes may also explained by limitations inherent to the methodological design and conduct of the study. Firstly it is

recognised that a high response rate was achieved among participants with type 2 diabetes. Although this was attained due to longer waiting times for those with diabetes, many of those with diabetes reported a keen interest to participate in the study describing how it was the first opportunity they had been given to discuss emotional issues without their diabetes taking precedence. For those without diabetes, although it was not possible to keep a record of the precise response rate, it was noted that the response rate was lower in comparison to those with type 2 diabetes, the majority of who agreed to participate it the study. It is possible that control participants with high levels of emotional disturbance may have perceived a greater personal relevance of the study and may have been more willing to take part, thus introducing a responder bias. However reasons for refusal provided by those without type 2 diabetes were generally attributed to a lack of time, a particular problem for the control participants due to the shorter length of waiting time before general practice appointments. In addition, it was not possible to collect demographic or medical information from non-responders and therefore the extent to which a response bias may have favoured participation by depressed controls is difficult to estimate.

Causal hypotheses for the increased prevalence of depression in people with diabetes relative to those without, remains poorly understood, although it is acknowledged that a number of bi-directional pathways are likely to be at play (Chapter 1 section 1.12) [368, 369]. Importantly, results from meta-analyses suggest that depression is associated with a 37% increased risk for the development of type 2 diabetes [29]. Furthermore recent data in the UK have demonstrated that depression may be associated with both

recognised and unrecognised diabetes [356] suggesting that depression may not simply be a consequence of the burden of the disease or its treatment but that there may also be an organic pathway underlying the comorbidity[370, 371]. The proposed biological pathways linking depression and diabetes could have implications for interpreting the lack of association demonstrated between depression and diabetes in the present study, as it is recognised that as many as 25% of people with diabetes may be undiagnosed [32]. It is therefore possible that any association between depression and type 2 diabetes may have been weakened due to increased levels of depression in those with unrecognised diabetes in the comparison control group. However it should also be recognised that research regarding the association between depression and undiagnosed diabetes is inconsistent. For example Knol et al [372] reported elevated rates of depression in a large population sample with type 2 diabetes in the Netherlands even when controlling for demographic and lifestyle variables, however no association was demonstrated between depression and either impaired fasting glucose ($\geq$5.6 and <7) or undiagnosed type 2 diabetes. Furthermore research examining the association between depression and insulin resistance, a major risk precursor for type 2 diabetes, have shown mixed results [373-379]. Cross sectional studies have demonstrated both positive[373-376] and negative[377] relationships between depression and insulin resistance, whereas retrospective [378] and prospective [379] studies have demonstrated no association. A number of factors may account for the discrepancies between study findings including failure in many studies to account for a number of covariates which may influence both depression and diabetes and thus complicate true estimates of risk in either direction [380]. Further carefully designed longitudinal

studies are still required to disentangle the complex causal relationship between depression and diabetes and to identify possible moderating factors. In the meantime the prevalence of undiagnosed type 2 diabetes and the extent to which it may be associated with depression in the present study population is unknown.

The possibility that all participants with type 2 diabetes were not identified using the Read codes specified in the study protocol cannot be ruled out. It is possible that misclassification occurred, in that some people were diagnosed type 2 diabetes but were not coded as such, and were thus included in the comparison control group. One study examining the validity of diabetes Read codes in primary care concluded that only 63% of patients known to have diabetes were identified [381]. Since this study and the introduction of the Quality and Outcomes Framework for General Practice in 2004, changes in the recording of diabetes were introduced which involved a more specific set of Read codes for both type 1 and type 2 diabetes. There is also evidence that the use of these newer Read codes may result in fewer patients recorded with diabetes, although this may only effect those in extreme age groups (<5 years and 90+) [382]. The possibility of misclassification of those with type 2 diabetes in the present study is reduced by the cross-examination of records with highly accurate prescription records and other diabetes related codes. In addition participants' diabetic status was often confirmed during discussions at study recruitment and thus cases of misclassified diabetes are likely to be small.

8.2 Comparison of the prevalence of depression in South Asian and White European people with type 2 diabetes.

In those with type 2 diabetes, factors associated with depression are consistent with previous reports which suggest that increased odds for depression are associated with younger age, female gender, increased deprivation, the presence of comorbidities and diabetes related complications as well as increasing duration of diabetes [75, 126, 156, 213, 257, 258, 260].

In addition the present study offers new contributions, in that it is the first to examine ethnic differences in the prevalence of screen detected depression between South Asian and White European people with type 2 diabetes in the UK. The findings show that in comparison to White Europeans, South Asians with type 2 diabetes are at increased risk for depression based on a HADS cut-off of >8 but not >11 suggesting an increased risk for milder symptoms of depression. These findings confirm previous reports from studies in the USA which have suggested an increased risk for depression among ethnic minority groups with diabetes [126, 230, 257, 258, 260].

The available data do not make it possible to draw inferences regarding exact causes for these disparities although it can be seen that factors associated with depression varied between South Asians and White Europeans. Further analyses revealed no ethnic differences in the risk for depression in those with two or more comorbid conditions. Whereas the odds of depression were associated with a greater number of comorbidities in White Europeans, South Asians with no or one non cardiovascular related co-

morbidity were at increased risk for depression in comparison to White Europeans. A plethora of studies have identified multiple risk factors associated with depression in people with type 2 diabetes and the most consistent is arguably in relation to the increased odds of depression in those with a greater number of coexisting comorbidities. It is plausible that these conditions are related to an increased psychosocial burden associated with diabetes which in turn may lead to psychological distress and depression, although it is important to consider that the number of comorbidities is not necessarily a surrogate for the severity of perceived burden of illness. Whilst findings in White Europeans with type 2 diabetes are in line with previous reports, the lack of association in South Asians may indicate that comorbid conditions may not be as detrimental to psychological health in South Asians with type 2 diabetes.

Studies of risk factors for depression in people with diabetes also suggest higher rates of depression in the younger years of life and lower rates in the older aged adults [156, 213, 306, 383] . This may possibly reflect a greater disparity between perceptions of functional status and expectations in younger adults with diabetes, although there may also be issues of measurement error due to difficulties in detecting depression in older adults [384]. In the present study, although the prevalence of depression declined with older age in White Europeans with type 2 diabetes, the protective effect of older age was not evident in South Asians aged 60 years and above, with this group demonstrating higher levels of depression (HADS$\geq$8) in comparison to White Europeans. Again, the present data are not sufficient to elucidate the possible mediators of this association, although the findings do echo suggestions of a higher rate of

depressive symptoms in older South Asian adults in the UK in general [385-387]. Reasons for high rates of depression in South Asian elderly may be attributable to a multitude of factors such as social disadvantage, migration and levels of acculturation. It can be seen that many older South Asians are often first generation migrants and the hardships associated with a dramatic change in circumstance may render them to be particularly susceptible to mental health problems including depression [388]. It is also suggested that first generation South Asians may have particular challenges or lower degrees of willingness to assimilate to the host culture in comparison to subsequent generations. This may have a number of implications for the mental health of older adults when attitudes or expectations differ from those of more assimilated family members creating family conflicts and tensions which in turn may promote and maintain depressive affect [388, 389]. Additionally first-generation migrants may be more vulnerable to discrimination and racist attitudes in comparison to more assimilated South Asians due a greater perceived difference from the host culture, which again may be associated with detriments to mental health [388, 390].

It is important to note that there is variation between studies which compare prevalence rates of depression in South Asians in the UK, with some evidence also suggesting that certain characteristics such as close social groups, may in fact have a protective effect on mental distress [81]. Alternatively, these findings may also be related to the use of inappropriate screening instruments with very little research focusing on the resilience and protection against mental distress afforded by aspects of South Asian culture [82].

In the context of diabetes, there are likely to be differences in the health beliefs of South Asians and White Europeans in regards to the causes and consequences of a diagnosis of type 2 diabetes, as well divergence in the meaning ascribed to living with the condition and its treatment. Differentiating attitudes may be influenced by the combination of cultural norms, religious beliefs as well as factors associated with socioeconomic deprivation and discrimination, with many of these issues being predominantly salient in the generally older first generation South Asians. This group may face particular challenges with integrating diabetes recommendations with traditional South Asian lifestyle, for example the belief that diabetes should be associated with a transition from traditional dietary habits in some South Asians may evoke a strong set of emotions, particularly when such behaviour change can often result in a perceived sense of social exclusion. South Asians, particularly older adults, may also face barriers in terms of access to services and appropriate diabetes-related educational support [391, 392]. In turn this may be associated with lower levels of understanding and knowledge about diabetes, both of which have previously been associated with depression in those with diabetes [213]. Lower levels of knowledge and erroneous beliefs about diabetes and its management may also impair efforts to self-care which in turn may cause feelings of guilt, anger and hopelessness and eventually depression. The fact that ethnic differences were observed in the prevalence of mild-moderate symptoms of depression but not moderate to severe levels may be attributable to a lack of statistical power as a result of the smaller sample of participants scoring >11 on the HADS. Structured education and self-management programmes which target health beliefs and facilitate behavior change have shown promising results in

terms of reducing symptoms of depression in people with type 2 diabetes [393], although it is yet to be seen whether similar improvements may be achieved in South Asian groups.

The findings from the present study also identified an increased prevalence of depression in non-English speaking South Asians in comparison to English speakers. As with old age, proficiency in English may also represent a proxy for a lower level of acculturation and the psychological conflict associated with integration of diabetes health beliefs and behaviours with aspects of South Asian life. Indeed, acculturation through the process of acquiring the dominant cultures language (i.e. English) is likely to expose individuals through both media outlets (including newspaper, television and radio programmes) as well as interactions with members of the dominant culture, to greater skills in health literacy and access to diabetes-related healthcare information. These findings support recent reports of an increased prevalence of depression in non-English speaking people with type 2 diabetes in Australia [394], although in the present study it is important to acknowledge that proficiency in English was not formally assessed. Instead participants were given the opportunity to complete the assessments in the language of their preference, which may not be as strongly associated to levels of acculturation as English proficiency in itself.

8.3 Recognition of depression

The findings from the present study also demonstrated that in those with type 2 diabetes, 85% of people with mild to severe symptoms and 83% of those with moderate to severe symptoms of depression may be un-recognised in primary care.

The finding that depression goes undetected in primary care patients is not a new one, as research has shown that general practitioners in the UK fail to diagnose depression in up to 50% of cases [395]. In addition the findings revealed that in those with type 2 diabetes the rates of unrecognised moderate to severe symptoms of depression were significantly higher among those with type 2 diabetes in comparison to non-diabetic controls. These findings are consistent with studies which demonstrate high levels of under detection and under treatment of depression in primary care patients with diabetes in the USA [172, 257] and are the first to suggest that similar difficulties are faced in primary care in the UK.

Of those scoring <8 and <11 on the HADS-D, 4.4% and 6.1% respectively were also currently recognised as depressed according to their medical records. It is not known whether these participants represent successful or maintenance of treatment, or inappropriate prescribing or antidepressant medication.

Factors associated with a greater likelihood of diagnosed depression included variables known to be associated risk factors, including higher levels of deprivation, current smoking status, a greater number of comorbidities and increased complexity of diabetes

treatment. However the higher rate of diagnosed depression in White Europeans in comparison to South Asians contrasts with the increased prevalence of depression observed in South Asians when comparing ethnic differences in the prevalence of screen detected depression (HADS≥8). Furthermore in comparisons of diagnosed cases of depression with those identified using the HADS it was apparent that rates of under detection were significantly greater in South Asians in comparison to White Europeans both with and without type 2 diabetes. In addition the rates of under-recognition were higher in South Asians with diabetes in comparison to those without.

A variety of factors are known to contribute to the recognition and treatment of depression in primary care, including issues related to patients, health care professionals and problems associated with the financing as well as the organisation and delivery of mental health services in primary care[396]. Similarly reasons for under-recognition in the present study are likely to be multi-factorial, although there has been limited study into barriers to effective recognition in those with diabetes, particularly in the UK. Despite the inclusion of an indicator to screen for depression as part of the QOF[133], it is important to consider that during the study data collection, national guidelines for depression management failed to specifically make reference to diabetes, although new recommendations for the treatment of depression in chronic medical conditions has since rectified this[129]. Such omissions and lack of consensus may have perpetuated a 'normalising' attitude among health care professionals who may view symptoms of depression to be a natural response to the burden associated with any challenging physical illness and thus may consider the independent treatment

for depression to be unnecessary [71, 95, 318, 397]. Furthermore the time constraints within primary care consultations may perpetuate an increased focus on physical conditions such as diabetes and treatment for a 'secondary' diagnosis such as depression may be deferred [318, 398]. Alternatively there may be diagnostic uncertainties, when symptoms of depression such as insomnia, fatigue and appetite disturbances overlap with symptoms of hyperglycaemia [71, 97, 313, 318]. There may also be a lack of confidence, or perceived lack of skill among primary care providers to screen for depression in people with diabetes. Although there are a number of tools available, research has failed to examine provider attitudes towards the use of such screening methods and beliefs about the appropriateness and acceptability of their use with people with diabetes as well as different cultural and ethnic groups. Finally there may be concerns about lack of guidance regarding the appropriate treatment and care pathways for those identified with depression in primary care as well as confusion regarding possible drug interactions, both of which may pose a barrier in terms screening for fear of 'opening a can of worms'.

The recognition of depression may also be hampered by the unwillingness of many people with diabetes to seek help for depression for various reasons. As with health care professionals, patients may also view their psychological symptoms as secondary to their diabetes care [95]. Normalisation i.e. feelings that symptoms of depression are to be expected given the context of their diabetes may also prevent patients from seeking help, particularly if they perceive primary care providers to have a somatic mindset.

Lower rates of recognised depression, particularly in South Asians with diabetes may reflect the additive difficulties health care professionals face when diagnosing depression in transcultural settings. Although language and cultural barriers between patients and health care professionals may partly explain these differences [399], disparities may also be present when the patient and treating clinician belong to the same ethnic group [263]. Diagnostic challenges in South Asian groups may also occur due to variations in explanatory models for depression between patients and health care professionals, although currently, there is little evidence to support this theory. Earlier research has suggested that when the perceptions and conceptualisations of depression held by Punjabi South Asians do not match the medical model held by their treating physicians, patients are less likely to have their depression recognised [263]. However later research comparing the care pathways in both South Asian and White European groups with depressive disorders revealed no ethnic differences between participants in terms of both their explanations for their symptoms as well as their beliefs regarding causal pathways [400]. In addition, although diagnostic criteria for depression (DSM-IV) apply to people of all backgrounds, it has been argued that the cultural context in which the condition occurs may mould its clinical presentation. Again earlier studies have suggested that the diagnosis of depression may be complicated due to differences in the idioms of distress, particularly the somatisation of depressive symptoms which appears to be common in minority ethnic groups [401] For example South Asian women in London identified somatic idioms such as 'a sinking heart', 'feeling hot' and symptoms of 'gas' [402]. It is argued that these idioms may reflect the 'hot and cold'

models of the traditional Indian Ayurvedic system which also incorporates a combined physical and mental approach to medicine in contrast to the dualism which appears to dominate western practice [403]. However later research has demonstrated that psychological explanations for depression in primary care were common in both White groups and Punjabi South Asians and in fact few Punjabis provided somatic/medical explanations for their depressive symptoms [265]. There may be various explanations for the inconsistencies for the data regarding the somatisation theory to explain the under recognition of depression in South Asians with depression. Firstly it is argued that that may be selective reporting of symptoms as South Asians may be more likely to resist disclosure of depressive symptoms [404]. It is also important to consider that due to the limited research conducted it is not possible to consider the diversity of sub-cultures within the 'South Asian group' which may contribute to the discordance in the data. For example differences in idioms of distress may vary between religious, cultural and language subgroups. Differences in levels of acculturation are also likely to play a part as it also noted that minority groups appear to experience increasing levels of affective and fewer somatic symptoms of depression with increasing levels of acculturation [401].

Help-seeking behaviour in South Asians may also be hampered by issues relating to social stigma, although there is preliminary evidence to suggest that levels of stigma attached to depression may change due to acculturation[401, 405]. It has also been suggested that minority ethnic groups may seek help from traditional healers, family members or other personal contacts [401, 406] although again in contrast to this

explanation, research examining care pathways in South Asians and White Europeans in the UK, suggest that South Asians do not report an increased tendency to seek support from lay or traditional healers[400].

8.4 Overall strengths and limitations

8.4.1 Strengths

The present research has a number of strengths. Firstly, the sample size was large and thus sufficient to test the study hypotheses, however most notably the study involved a sample of subjects attending inner-city practices including a large proportion of South Asians, many of whom were older and also did not speak English. The recruitment of non-English speaking participants meant that the study was less vulnerable to recruitment bias, a particular concern in observational studies of this nature. The generalisability of the findings is further enhanced as the data were not limited to a single practice. In addition a high response rate was achieved, particularly in those with diabetes and therefore it is unlikely that recruitment favoured those without depression or English speakers only.

8.4.2 Study limitations

A number of limitations in the present study warrant consideration. Firstly regarding the rate of depression it is important to be aware that although there is evidence that the HADS performs well in identifying cases of depression in people with medical illness including diabetes [339, 364]it does not provide a diagnosis of depression ; in clinical practice it is advised that those who screen positive on such instruments should receive

further diagnostic assessment in order to ascertain the presence and severity of depressive disorder. The results from these analyses should thus be interpreted with caution and further study involving the use of gold standard criteria for determining the presence of depression is warranted.

The rate of recognised depression in the present analyses may have been under estimated. The recognition of depression was ascertained from general practice records and the validity of this method is unknown and therefore maybe subject to question. For example there may be diversity in the way in which primary care health professionals code the presence of depression and depressive symptoms. Although the identification of diagnosed cases in the present study involved the use of multiple EMIS and Read codes for depression in combination with prescription data, it is important to be aware that although many patients with depression may not be coded as such in primary care records, many that are recognised also do not receive treatment for it [269] and thus the present data cannot account for cases in which depression was both uncharted in medical records and untreated with antidepressant medication.

It is also acknowledged that it was not possible to account for all potentially confounding factors, particularly in relation to comorbid conditions. For example arthritis is a common chronic condition which may be more prevalent in those with diabetes. Due to issues relating to inaccuracies in the coding of the condition in general practice records it was not possible to extract information relating to the presence of this condition. However considering the higher level of depression in those without

type 2 diabetes, it is unlikely that the omission of arthritis would account for this finding.

A number of issues may also have implications for considering the generalisability of these findings. Firstly the findings are limited to those practices which agreed to take part in the present study. It is possible that there may have been differences between practices which agreed to participate in the research and those that did not, for example differences in the attitudes, beliefs and management strategies for depression may all influence the recognition of depression as well as the willingness of practices to participate in a study of this nature. In addition it was beyond the scope of the present study to examine differential rates in the recognition of depression by practice characteristics. For example, there is evidence to suggest that general practitioners are more likely to identify depression in people who they know [407]. Although the present study included both single GP practices as well as group practices, the majority of participants were recruited from practices with larger list sizes. As a result of the high population turnover in such practices, it may be that general practitioners are less likely to develop an ongoing relationship with their patients as opposed to smaller practices, which may in turn be associated with lower levels of identification. As the present study did not assess the primary care provider- patient relationship or continuity, future which studies which incorporate such measures into the analyses are necessary.

Despite the incentive to screen those with diabetes (and ischaemic heart disease)for depression[31], it is not known whether or not practices were actively involved with

routinely screening participants for depression, although there is currently little evidence to suggest that the screening according to the QOF leads to improvements in the identification or treatment of depression.

As with many studies identifying low rates in the detection of depression in primary care settings, the study presents cross-sectional data [408]. Higher rates in the detection of depression have been reported in longitudinal studies, with one in seven cases remaining undetected at three year follow up as opposed to one in two in cross-sectional studies [395]. This also represents a limitation in that it is not possible to comment on the clinical importance of undetected cases of depression, that is whether they are associated with disability, impairments in self care activities, or adverse diabetes related outcomes. It is also not possible to comment on whether cases are likely to be diagnosed at a later date, how many may recover without a diagnosis or how many will remain depressed and untreated. Again these details have important implications in terms of furthering understanding of both the identification and treatment of depression in primary care and future longitudinal studies which distinguish between new cases of depression, ongoing cases and those that relapse are necessary.

The present study may be criticised for the use of broad ethnic categories. For example it can seen that 'South Asians' represent a heterogeneous group who are diverse in terms of country of origin as well as culture, language spoken and religion and thus to assume that their experiences of health and interaction with health care professionals

are the same may be misleading. Although the examination of ethnic/ cultural subgroups (i.e. based on religion or language) may aid in furthering understanding towards cultural specific models of illness, the definition of various subdivisions amongst South Asians may also be problematic. For example even when examining groups by country of origin, additional differences such as language, religion, generational status and level acculturation also warrant consideration, therefore the quantitative pursuit of comparing ethnic subdivisions may not be worthwhile. Furthermore it is important to note that such a strategy would also result in small samples and consequently insufficient numbers to conduct subgroup analyses.

A large proportion of participants with diabetes were recruited via retinal screening services in general practice. Although participating general practices maintained that the uptake of these services were high, precise attendance figures were not collected. The potential bias which may have resulted as a consequence of differential rates of uptake by depression status or ethnicity is therefore unknown although the recruitment of consecutive general practice attenders and as well as patients from diabetes clinics may have minimised this.

Although problems with validity are not uncommon in epidemiological research , such difficulties are particularly likely to occur when concepts are examined cross culturally [322] . The present study adopted an Etic approach to the assessment of depression, that is, the HADS which was originally developed and validated in English was translated for use in non-English speaking South Asians. This approach was considered necessary

due to the need to make comparisons between South Asian and White European participants (Chapter 6, section 6.2.1). It has already been argued that traditional westernised methods of depression assessment may not identify cases of depression in some South Asians if there are cultural differences in the manifestation and expression of depression [168, 263, 264] and the question of whether directly translated questionnaires encapsulate the same meaning as the original has been widely debated [409-411]. For example there may be a mismatch between the cultural context in which an instrument was developed and the culture of the participant. In the case of the HADS this may include questions such as those relating to watching television or listening to the radio which may not be common pastime in some subgroups of South Asians. As such, it is important to recognise a level of standard which should be considered when applying instruments that have been developed in one culture (i.e. the west) and applying them in other communities. For example it is argued that instruments should ideally be validated in community populations, compared with a gold standard and have acceptable levels of sensitivity and specificity [412]. Although the HADS has been shown to be a reliable and valid measure of depression and anxiety for Urdu speaking South Asians in Pakistan [331], it has had very little detailed linguistic and conceptual validation for use in South Asians in the UK and so confidence in the use of this tool to identify depression in this population, as well as the appropriateness of comparing English and translated versions of the questionnaire may be questionable. This is not to discourage the use of the HADS in UK South Asians, but to highlight the need for further linguistic and conceptual validation. Furthermore in order to overcome the drawbacks associated with the Emic and Etic approaches to assessment of depression in

different communities, one suggestion includes the inclusion of a qualitative evaluation of the research instrument into the in the research design and thus allowing local descriptions and explanatory models of depression to be explored [406].

Psychometric concerns relating to the HADS may potentially undermine the appropriateness of comparing groups with diabetes and those without. Although, the HADS has been used to screen for depression in a number of studies involving people with diabetes, the specific psychometric properties of the questionnaire in this population has also received very little attention. Although a recent study comparing the HADS with a clinical interview in an Australian population with type 2 diabetes has shown that the HADS may reliably predict depression [364], optimal cut-offs have also been shown to vary across different populations as well as across primary care populations [339]. Although the present study adopted the recommended instrument scores generally assumed for the HADS, it may be argued that it is necessary to ascertain cut-off values for depressive caseness individually in different populations prior to study. Psychometric anomalies in the factor structure of the HADS have also been noted in a number of clinical populations, including coronary heart disease[413], end-stage renal disease[414] and chronic fatigue syndrome[415]; therefore further structural evaluation of the HADS in people with diabetes also represents an important avenue for future research.

8.5 Implications

The Quality and Outcomes Framework (QOF), introduced into the general practice contract in 2004[131], provides financial incentives to improve the quality of chronic conditions including diabetes in primary care. Based on the findings of several studies which suggested higher rates of depression in people with diabetes in comparison to those without [75, 416, 417], an indicator to screen for depression in people with diabetes was added to the QOF in 2006[31]. However it is important to consider that the majority, if not all the evidence to support the inclusion of this indicator is based on studies conducted outside of the UK. While there is some evidence to suggest that people with diabetes in the UK often suffer with comorbid depression[300, 418], these are the first data to examine the prevalence of depression in a large UK primary care population with type 2 diabetes in comparison to a non-diabetic control group recruited from similar settings. The present findings suggest that regardless of ethnicity, the prevalence of depression is not increased in people with type 2 diabetes in comparison to non-diabetics in primary care, however before considering the clinical implications of these findings, future studies in the UK are needed to replicate these findings and to identify potentially moderating factors which may account for the discrepancies between the present findings and previous research. In addition considering the possibility that depression is a risk factor for the development of type 2 diabetes and the questionable validity of identifying all cases using diagnostic Read codes, future studies investigating this association should systematically screen for diabetes to ensure that all cases are identified. In addition measures that accurately measure differentiate between

the continuum of psychological problems observed in multi-ethnic groups with type 2 diabetes are clearly needed.

Increased levels of mild-moderate symptoms of depression in South Asians with diabetes are clinically relevant. Although mild episode of depression in primary care may often remit, it is recognised that such symptoms have been demonstrated to impede efforts to self manage and are associated with adverse diabetes related outcomes [93, 157, 239]. Furthermore mild episodes of depression may also predispose to an increased vulnerability towards the development of more severe illness when individuals are exposed to additional life stress[419]. With the steady increase in the prevalence of type 2 diabetes in the South Asian population [55, 420, 421]and the potential physical and economic burden associated with comorbid depression [422], it is timely for further research to examine additional factors beyond those recorded in routine general practice records, which may include differences in illness representations or even diabetes related distress, as possible explanations for the disproportionate rates of mild-severe levels of depression observed in this group. Further research should also to examine the utility of language preference as a marker for acculturation and the interaction with health literacy and diabetes education on the pathogenesis of depressive affect in South Asian people with type 2 diabetes. The identification of such risk factors may in inform the development of preventative and management strategies for multicultural populations with depression with or without type 2 diabetes.

A number of solutions have been explored in terms of improving recognition and help seeking for depression in cross-cultural settings, for example increasing cultural competency (i.e skills and practices which promote culturally appropriate services) at both a provider and institutional level may be one strategy [401]. Furthermore, in order to facilitate the diagnosis of depression in cross-cultural settings, the DSM-IV [401] also includes a specific model for cultural assessment, which is designed to supplement standard clinical assessments by incorporating an evaluation of patients' cultural specific experiences, such as explanatory models of illness, help seeking preferences and symptoms. Preliminary research also suggests that educational material on depression targeted at specific South Asian communities may be successful in terms of improving help seeking attitudes [423]. However if efforts to develop effective strategies to dispel the observed disparities in the recognition of depression in those with type 2 diabetes are to be successful, further research into understanding the barriers to effective recognition in both South Asian and White Europeans is paramount. Importantly there is a need to explore the perspectives from patients as well as health care providers, which in turn can inform appropriate training for healthcare professionals as well as interventions aimed at the patient level.

Regardless of whether rates of depression are any higher in people with diabetes compared to those without, the recognition and effective treatment of psychological and emotional problems such as depression represent a fundamental aspect of diabetes management, particularly due to associations with maladaptive and impaired self-management behaviours, the use of poor coping strategies as well as elevated blood

glucose levels [85, 424, 425]. Furthermore depression is associated with an increased risk of mortality in people with diabetes [98, 238]. Considering the elevated rates of type 2 diabetes in South Asians and a higher probability of adverse diabetes related outcomes, increased levels of unrecognised depression in this group may have important public health implications. Further research is therefore warranted in order to understand the underlying reasons increased levels of depression in all people with diabetes for as well as developing effective interventions to recognise depression reduce inequalities in depression care for multiethnic groups with diabetes.

Chapter 9

Overall thesis discussion

9.1 Summary of findings

Both type 2 diabetes and depression are common chronic disorder effecting people worldwide [30]. Type 2 Diabetes is characterised as a complex metabolic disorder, often involving laborious self-management, reduced health related quality of life and often the prospect of diabetes related complications [30]. The number of people with type 2 diabetes in the UK is substantial and predicted to rise to approximately four million by 2025[31]. Depression on the other hand is a mood disorder associated with high levels of personal disability, lost quality of life, multiple morbidity and an increased risk of mortality [71, 79]. Depression also poses significant concerns for public health in that 5% of the UK population are estimated to suffer from the disorder at any point in time [72].

Despite representing distinctly burdensome disorders in their own right, a link between the two conditions was first suggested as early as the 1600's when the British physician, Thomas Willis noted that diabetes appeared to result from 'Sadness or long sorrow' [426]. In recent times there has been growing concern into the links between the comorbidity as results from meta-analyses now support these early theories and conclude that depression may be associated with a 60% increased risk for the development of type 2 diabetes [29, 369]. Furthermore the adverse effects associated with depression may be particularly detrimental in those with type 2 diabetes, with adverse consequences including an increased risk for micro and macro-vascular

complications [427], increased functional impairment [428] and higher rates of mortality in comparison to people with diabetes alone [98, 99, 238].

Despite recognition of the growing diversity of cultures in the UK, there are marked disparities in the health of many minority ethnic groups including South Asians [11, 60]. South Asians with diabetes in the UK represent a particularly relevant group to study in light of their increased risk for developing type 2 diabetes [21, 245] as well as increased likelihood for inadequate control and the subsequent development of a number of potentially preventable diabetes related complications [20, 21].

In light of these findings, the present thesis aimed to contribute to the broader literature pertaining to the association between depression and diabetes by describing a series of studies including systematic reviews and observational studies which examine this comorbidity, specifically in the context of a multi-ethnic UK population.

Chapter 2 presents the results of a systematic literature review and meta-analysis of studies examining the prevalence of depression in people with type 2 diabetes in comparison to those without. The findings of the meta-analysis revealed that the prevalence of depression was almost twice as high in people with type 2 diabetes in comparison to those without. However the review also identified a number of limitations and gaps in the current research knowledge. Firstly the paucity of well controlled studies was highlighted. In addition many studies failed to control for potentially confounding factors which may have inflated rates of depression in people

with type 2 diabetes. Finally no data were available in regards to the prevalence of depression in people with and without type 2 diabetes in the UK.

As well as examining ethnic differences in the association between depression and type 2 diabetes, the present thesis also sought to determine the association between depression and health-related quality of life (HRQOL). As an awareness grows of the decrement to health-related quality of life in people with diabetes and its adverse clinical consequences, investigators have become increasingly interested in measuring HRQOL in clinical trials. Given that psychological factors such as depression may contribute to diminished HRQOL, Chapter 3 sought to conduct a systematic literature review in order to scrutinise the association between depression and HRQOL in people with type 2 diabetes. Overall the results indicated that self-reported depressive symptoms were associated with decrements in both generic and diabetes specific aspects of health related quality of life and on multiple domains. Due to the cross sectional nature of the studies, it was not possible to determine the direction of causation and therefore future prospective evaluations are still needed in order to elucidate this. Understanding the direction of the relationship may help to develop interventions which aim to improve HRQOL via targeting of depressive symptoms or vice versa and thus improve the psychological well-being and overall quality of life in people with type 2 diabetes.

The findings from the review presented in Chapter 2 provided rationale for further research into the prevalence of depression in people with type 2 diabetes in both primary and secondary care services in the UK.

The second stage of this research involved two studies which were conducted using the routine database of a secondary care diabetes clinic (Chapter 4 and Chapter 5). The first of these studies examined differential rates of diagnosed depression in sample of 6230 individuals who were of either South Asians or White Europeans origin and with either type 1 or type 2 diabetes (Chapter 4). The results identified the first estimate of depression in a multiethnic UK population with diabetes with overall prevalence figures of diagnosed depression of 8% in people with type 1 diabetes and 10% in those with type 2 diabetes. Most importantly however, the study identified ethnic differences in the prevalence of diagnosed depression between South Asian and White Europeans. White Europeans were more likely to have a diagnosis of depression in comparison to South Asians.

Landmark studies have shown that improving glycaemic control in those with type 1 and type 2 diabetes markedly reduces the development of diabetes related complications [63]. In clinical practice however, many patients face problems with self-management and thus remain in poor glycaemic control. South Asians with type 2 diabetes in the UK are at increased risk of elevated HbA1c, as well as micro- and macro-vascular complications in comparison to White Europeans [21, 33, 245]. A multitude of studies have demonstrated an association between depression and HbA1c

[85] although it is important to recognise that the findings have not been consistent [85]. Due to a paucity of data from the UK and no data regarding the association in South Asians with diabetes, the second of the studies conducted using the secondary care dataset (as described in Chapter 4) aimed to determine whether the association between depression and HbA1c was observable in a multiethnic secondary care population with type 1 and type 2 diabetes. In addition, the study aimed to determine whether the association between depression and poor glycaemic control was moderated by ethnicity. The findings presented in Chapter 5 revealed no association between diagnosed depression and HbA1c in type 1 diabetes, however surprisingly revealed that those with type 2 diabetes who were achieving optimal glycaemic targets were more likely to have a diagnosis of depression. Finally the study showed that depression did not explain ethnic differences in glycaemic control between South Asian and White Europeans with type 1 or type 2 diabetes.

Although the results from Chapter 4 and 5 do not make it possible to determine the reasons for ethnic differences in the rates of depression as well as the lack of observed association between depression and HbA1c, it was speculated that the differences in the rates of diagnosed depression at least may be due to variations in the presentation or identification of depression between these two ethnic groups. For example there has been some suggestion from previous research that the diagnosis of depression may be particularly problematic in South Asians without diabetes (Chapter 4, section 4.4). Similarly the hypothesised high rates of undiagnosed depression in people with diabetes in this dataset may explain the somewhat unexpected findings in regards to

higher HbA1c levels in those without diagnosed depression, i.e. the methodological limitations in the identification of depressed cases using routine data may have undermined the notion of a non-depressed comparison group.

These speculations were further investigated during the third stage of the research which involved examining rates of depression in primary care attendees, utilising both screening methods for depression assessment as well as identifying cases diagnosed in patient records.

When selecting the methodology for addressing these questions, it was necessary to consider issues relating to the most appropriate method of screening for depression in the population of interest. The arguments for selecting the Hospital Anxiety and Depression scale are presented in chapter 6. The chapter considered how issues relating to validity may call into question the underlying construct that self-report symptom questionnaires tap into. The possibilities for inaccuracies may largely occur on two levels. Issues which are of primary concern include the validity of the tool in patients with diabetes and other illnesses likely to be encountered in general practice settings, as well as the tool's validity for use in different ethnic groups and in its linguistically translated versions. The HADS was identified as the most appropriate tool for this purpose as it was developed for use in clinical settings (Chapter 7). Particularly, the scale excludes somatic items which may otherwise have compromised validity due to the potential overlap with the physical symptoms of diabetes. In addition the tool provides separate scores for anxiety and depression. A review of the validity of the

HADS demonstrated that the tool shows good sensitivity and specificity for depression in people with a range of comorbid conditions, although it is recognised that the studies did not include people with diabetes. However considering the lack of research examining the psychometric properties of depression screening tools in people with diabetes and no evidence to suggest that the HADS performs less accurately particularly in people with diabetes, this tool was considered to be the most appropriate for the research question. In addition, the tool had the added advantage in that it was available in the main South Asian languages (Urdu, Gujerati, Punjabi and Bengali) and therefore it would not be necessary to exclude a large proportion of the South Asian population on the basis of limited English literacy.

The results from this research are presented in Chapter 7 which specifically aimed to examine the following questions in a multiethnic primary care population; (1) what is the prevalence of depression in people with type 2 diabetes relative to those without, (2) are there ethnic differences in the rates of depression between South Asian and White European people with type 2 diabetes and (3) are there differences in the rates of recognised depression by diabetes and ethnic status. Overall the results in Chapter 7 concluded that in contrast to the studies included in the review in Chapter 2, although high levels of depression where identified in people with type 2 diabetes, there was no significant difference in the risk for depression between those with type 2 diabetes compared to those without. Further analyses in those with type 2 diabetes revealed that South Asians had increased rates of mild to severe depression in comparison to White Europeans. Again this finding appears to contrast with those reported in Chapter 4 in

which White Europeans had an increased risk for a diagnosis of depression in their secondary care medical records. It was speculated that the results presented in Chapter 4 and 5 may reflect the under-diagnosis of depression in South Asians and people with type 2 diabetes, and indeed the results presented in Chapter 7 would support this notion as 90% of South Asians who were identified as moderately to severely depressed according to the HADS screening instrument were not currently recognised as depressed according to practice records. In comparison 63% of White Europeans scoring in the range for moderate to severe symptoms of depression were currently recognised as depressed. The data also demonstrated that rates of un-recognised depression were higher in those with type 2 diabetes in comparison to those without diabetes (83% vs. 70%).

9.2 Implications for research and clinical practice

The findings from the present thesis conclude that rates of depression are not increased in primary care attendees with type 2 diabetes in comparison to those without. In addition an association between depression and HbA1c was not demonstrated in either White Europeans or South Asians with either type 1 or type 2 diabetes. However these findings are not to suggest that depression is not a relevant comorbidity in people with type 2 diabetes in the UK.

Depression is a well established cause of disability and disease burden worldwide [429]. Furthermore there is a wealth of evidence to suggest that depression may exert negative consequences in those with type 2 diabetes via a decrease in self- care

activities including regular exercise, adherence to medication recommendations and dietary habits [91, 430, 431]. The detrimental effects of depression are not limited to major depressive disorder as even sub-threshold depression has been associated with impoverished self care and mortality [238, 430].

The cost of comorbid depression in people with diabetes to the NHS is likely to be substantial. Although there is a paucity of data from the UK, a US based study comparing 4398 depressed and non-depressed people with diabetes revealed total health care costs up to 70% higher in individuals with diabetes and depression in comparison to diabetes alone [422].

Although South Asians represent approximately 4% of population [4], they also constitute a larger proportion of those with type 2 diabetes, with rates of up to 6 times higher in comparison to White Europeans [16, 17]. In addition there is ample evidence to suggest ethnic disparities in the rate of a number of diabetes related complications in this group [20, 21, 432]. The higher rates of mild to severe depression identified in South Asians with type 2 diabetes in comparison to White Europeans (Chapter 7) therefore represents an additional public health concern in relation to this comorbidity.

However, depression is a treatable condition and evidence from a number of randomised controlled trials suggest that it can be successfully treated using psychological therapies, antidepressant medication as well as a combination of both [127]. However a necessary precursor to successful treatment is the identification of

depression in people with diabetes. Unfortunately the findings from the present thesis suggest that the recognition of depression in people with type 2 diabetes and in particular South Asian people with type 2 diabetes is challenging (Chapter 4 and Chapter 7).

Screening has been shown to improve the recognition of depression [433] and as such a number of national as well as international guidelines and recommendations for diabetes care recommend screening for depression in people with diabetes [129, 133, 273, 434]. In order to facilitate this in busy clinical settings a number of depression screening tools are available. Their main advantages include that they are generally not time consuming and thus helpful when time constraints are present. In addition they can be used to assess the severity of depression allowing a stepped-care approach to depression management as well as the monitoring of depressive symptoms over time [31, 129]. NICE guidance and the British Medical associations Quality and Outcomes Framework (QOF), advocate the use of the PHQ-2 as an initial screener followed by severity assessment in positive cases using either the PHQ-9, BDI or the HADS (Chapter 1) [31, 133]. However, despite the incentivisation and recommendations from NICE, there are arguments against the use of such screening protocols.

Firstly it is important to recognise that these tools were not designed for use in people with diabetes specifically and as such there has been recent discussion regarding the appropriateness of their use in this population [364]. Although recent studies have demonstrated the usefulness of the HADS [364] and BDI [334], there is currently no

data regarding the psychometric properties of the PHQ-9 in people with diabetes. Preliminary data regarding these tools in primary care populations in the UK have also demonstrated a lack of concordance between the measures' categorisation of depression severity [435]. Furthermore it is important to recognise that there is currently no data regarding the validity of these tools in South Asians with diabetes in the UK (Chapter 6). Further research examining the psychometric properties of these tools in multiethnic populations in the UK with diabetes is therefore essential in order support their case finding and severity rating capabilities in this population.

The under-recognition of depression in people with diabetes, and in particular, the ethnic disparities observed may not simply be a consequence of the potential failure of current screening tools to identify depression. Barriers to detection may also result from whether tools are actually used and also the manner in which they are used in clinical practice. The primary care consultation is in no doubt a complex interaction between patients and the treating health care professional, and so sophisticated consultation skills should be an essential component in creating both a context of trust between practitioner and patients, as well as improving the accuracy in distinguishing depressive symptoms from the symptoms associated with type 2 diabetes. Unfortunately, the barriers in detecting cases of depression in multiethnic populations with type 2 diabetes in the UK remain speculative and thus if efforts are to be made in order to reduce ethnic inequalities in the detection of depression as well as improve detection rates in people with diabetes, further qualitative research is warranted in order to understand not only issues relating to the practices and beliefs of health care professionals, but also barriers

related to the disclosure of psychological symptoms on the part of presenting patients (Chapter 8).

In the mean time health care professionals should be aware that there may be limitations in the use of screening instruments in people with diabetes and in particular in South Asian groups and therefore be willing to probe for symptoms of depression or at least follow up responses on self report questionnaire with a discussion of the patients' responses.

It is also important to note that there also arguments which call into question the effectiveness screening for depression in people with type 2 diabetes. For example, since the introduction of the QOF depression screening indicator in 2006, studies have yet to show whether improvements in both the detection and treatment for depression have been made. The results from one audit into whether screening for depression in accordance to the QOF recommendations actually improved detection and treatment of depression in people with diabetes showed little evidence of benefit during the first year of QOF implementation [436]. However this data was collected from a single rurally located primary care practice with a small list size and therefore the results may not be generalisable to general practices elsewhere in the UK. Despite this, the finding do echo the conclusions reached by a number of studies conducted in non-diabetic populations [437] in primary care, which is where most people with diabetes in the UK are managed. Gilbody et al (2008) [437] conducted a review of randomised controlled trials which examined the effectiveness of using screening instruments for detecting

depression. The review incorporating over 75'000 patients, revealed that routinely administered depression screening had little influence on either the recognition of depression, its management or whether screening improved mental health in primary care [437].

Although screening for depression may not lead to improvements in depression outcomes on its own, there is evidence to suggest that when such screening is employed within an organised system of depression management, depression outcomes can be vastly improved [437, 438]. Gilbody et al (2006) conducted a meta-analysis of 37 randomised controlled trials which examined collaborative care (a popular approach in the USA) for depression, in comparison to usual primary care [438]. The findings of the review demonstrated that collaborative care was associated with a two-fold increase in adherence to antidepressant medication as well as improvements in depression which lasted up to five years [438]. The findings of the review also highlighted specific features of the most successful collaborative care interventions. These included 1) a depression care manager who was responsible for patient education as well as the monitoring of depression treatment. And 2) supervision of the case manager by a psychiatrist or psychologist who is able to recommend evidenced based recommendations for antidepressant therapy or psychotherapy [439, 440].

Katon et al (2004) demonstrated the effectiveness of this approach in people with diabetes enrolled onto the Pathways study [128]. The Pathways randomised controlled trial aimed to determine whether enhanced quality of depression care in primary care

settings would be associated with improvements in both depression and diabetes related outcomes. The first step of the pathways study involved screening patients for depression. Those screening positive for major depression and or dysthymia (N= 329) were then randomised to either a stepped care case management intervention or usual care. Participants in the intervention group received enhanced education of and support for antidepressant medication treatment prescribed by the primary care health care professional or problem-solving therapy based on their preferences. In cases with persistent depression, treatment was adjusted [128].

The results of the trial showed that at 6 and 12 months, in comparison to those receiving usual care patients in the intervention group showed greater improvements in the adequacy of the dose of antidepressant medication treatment, reduced severity of depression, a higher rating of patient-rated global improvement and higher satisfaction with care [128]. Benefits in terms of cost-effectiveness were also demonstrated, with a net benefit of approximately US$1000 per patient treated [441].

In the US, socio-culturally adapted models of collaborative care for depression have also shown promising results in terms of reducing ethnic disparities in depression care outcomes among Hispanic people with diabetes [442]. The culturally sensitive collaborative care intervention which involved facilitated access to socioeconomic resources as well as incorporating linguistic and cultural factors was associated with significant reductions in depressive symptoms as well as improvements in emotional and physical functioning [442].

Thus culturally adapted models collaborative care for depression may offer a promising avenue for reducing the ethnic disparities in depression observed between south Asians and White Europeans with type 2 diabetes in the present study. Further research is therefore needed in the UK to examine the feasibility of such an approach in primary care as well as the specific cultural barriers to be addressed.

It is noteworthy that neither the pathways study nor the culturally adapted collaborative care model for Hispanics with diabetes showed improvements in diabetes related outcomes, specifically HbA1c [128, 442]. A recent systematic review of published randomised controlled trials which evaluated the treatments of depression in people with diabetes [127] concluded that although well-established treatments for depression appear to be effective in terms of improving mood in people with diabetes, there was no indication of beneficial effects on glycaemic control. Furthermore although there is evidence that combined interventions may improve depression in people with diabetes[127], it is important to consider that further research into improving depression outcomes is still warranted as many people with depression and diabetes do not respond to treatment[128, 366]. For example at 12 month follow-up of the pathways study, up to 46% of patients either did not respond to treatment or experienced a re-lapse of depression [128].

It is important to consider that people with diabetes may experience a range of emotional of psychological problems which may interfere with the self-management of

their condition as well as perpetuate symptoms of depression. These issues can range from general anxiety and diabetes-related distress to the more clinical symptoms of depression[443]. More recently there has been increased attention towards the prevalence of diabetes-related distress, which appears to be particularly elevated in those with depression [444].

Diabetes-related distress differs from clinical depression in that it focuses on the feelings related to the demands associated with diabetes and it's management, including worries about the future and the prospect of diabetes related complications, as well as feelings of guilt and anxiety when falling off track with diabetes management [366]. In recent years measurement inconsistencies between different self-report tools for depression assessment have called into question the underlying construct which these tools tap into, with particular focus on the specificity of 'depression' and how it differs from diabetes-related distress' [334, 365] (Chapter 8). It has been argued that sub-threshold scores for depression on some depression screening instruments may be more reflective of general or diabetes specific distress [365].

Fisher et al examined independent measures of both depression and diabetes-related distress in 506 people with diabetes. when examining associations with adverse diabetes related outcomes (including physical activity and HbA1c), both general and diabetes-related distress were related to behavioural as well as biological outcomes, whereas no associations were observed with those diagnosed with major depressive disorder [365]. Similarly, Gonalez et al (2008) [445] examined the independent

associations between depression and diabetes related distress and measures of self-care in people with 484 US primary care patients with type 2 diabetes. In contrast to the findings of Fisher et al [335], specific symptoms of depression showed a greater negative impact with diabetes self-care behaviours than diabetes related distress.

Thus both depression and diabetes-related distress may have independent effects on diabetes related outcomes. The findings presented in Chapter 7 conclude that the prevalence of mild to severe levels of depression are increased in South Asians with type 2 diabetes in comparison to White Europeans. Although an association between depression and HbA1c was absent in the analysis presented in Chapter 5 as well as Chapter 7, levels of diabetes-related distress in this population and the extent to which they may explain the findings are unknown. Diabetes related distress is prevalent in diabetes[366] and may have independent associations with HbA1c[365, 366]. Furthermore levels of diabetes related distress are known to be associated with poor knowledge of diabetes[112, 446], which may be particularly problematic in South Asian groups who generally have inadequate access to diabetes self-management education[391, 447]. Further evidence to support this theory is available from diabetes educational interventions which equip individuals with knowledge to better cope with diabetes-related challenges. Results from a number of studies demonstrate a decline in subthreshold levels of depression following diabetes education [96, 393, 448]

Further research is therefore needed to examine the extent to which ethnic differences in the rates of depression (including both subclinical depression and depressive

disorder) are confounded by diabetes-specific emotional problems, as this may have implications for the effective management of both depression and diabetes related outcomes. This may include longitudinal epidemiological studies which involve measure of diabetes, depression and diabetes-specific distress in order to elucidate causality and their inter-relations. In addition research is needed to examine whether interventions aimed the effective recognition and management of depression or more general diabetes related distress can be effective in terms of improving both psychological as well as diabetes related outcomes.

9.3 Conclusion

The first step in addressing ethnic inequalities in diabetes care requires an understanding of the level of need. The present thesis identified a higher prevalence of depression in South Asian people with type 2 diabetes in comparison to White Europeans. Furthermore rates of under-recognition of depression were higher in people with type 2 diabetes and even more so in South Asian people with type 2 diabetes.

The under recognition of depression in people with type 2 diabetes and particularly the ethnic inequalities observed in the present thesis, represent a significant public health concern, with potentially high costs in terms of disability, morbidity, mortality [93, 98, 272, 441].

With a growing BME population in the UK and the rising prevalence of type 2 diabetes, particularly in South Asian groups, it is timely to build on the research

evidence and to develop culturally appropriate and sensitive mental health services for all people with diabetes.

As the majority of people with type 2 diabetes are managed in primary care, routine diabetes appointments represent a valuable opportunity for primary care health care professionals to identify depression and provide treatment.

Further research is warranted in order to disentangle the various psychological presentations which may manifest in people with type 2 diabetes. In particular there is a need for research to examine the screening accuracy of commonly used depression assessment tools in both people with type 2 diabetes as well as different ethnic and cultural groups. In addition there is a need to explore barriers faced by health care professionals in relation to screening and recognition of depression in multiethnic populations in with diabetes in the UK. However while this knowledge can be used to improve rates of detection, further empirical testing of the effects of case finding of depression on both psychological as well as behavioural outcomes is warranted.

It is also important to consider that a diagnosis of depression without effective treatment may lead to stigma and discrimination[449] and thus raise ethical questions in regards to screening for depression in people with diabetes. Thus RCT's are urgently required to examine embedding screening interventions within a system of collaborative care. Studying the help-seeking behaviours of South Asian people with diabetes and depression can inform the development of ethnic and culturally

appropriate interventions. These should aim to not only improve rates of recognition but also increase service use, adherence to treatments, and treatment effectiveness. Finally it is important for future research to widen the focus from measures of depression only and also consider general as well as diabetes-specific distress.

Appendices

I, II, III, IV, V, VI & VII

Appendix I

Hospital Anxiety and Depression Scale (HADS)

Clinicians are aware that emotions play an important part in most illnesses. If your clinician knows about these feelings he or she will be able to help you more. This questionnaire is designed to help your clinician to know how you feel. Read each item below and **underline the reply** which comes closest to how you have been feeling in the past week. Don't take too long over your replies; your immediate reaction to each item will probably be more accurate than a long, thought-out response.

I feel tense or 'wound up'
Most of the time
A lot of the time
From time to time, occasionally
Not at all

I still enjoy the things I used to enjoy
Definitely as much
Not quite so much
Only a little
Hardly at all

I get a sort of frightened feeling as if something awful is about to happen
Very definitely and quite badly
Yes, but not too badly
A little, but it doesn't worry me
Not at all

I can laugh and see the funny side of things
As much as I always could
Not quite so much now
Definitely not so much now
Not at all

Worrying thoughts go through my mind
A great deal of the time
A lot of the time
Not too often
Very little

I feel cheerful
Never
Not often
Sometimes
Most of the time

I can sit at ease and feel relaxed
Definitely
Usually
Not often
Not at all

I feel as if I am slowed down
Nearly all the time
Very often
Sometimes
Not at all

I get a sort of frightened feeling like 'butterflies' in the stomach
Not at all
Occasionally
Quite often
Very often

I have lost interest in my appearance
Definitely
I don't take as much care as I should
I may not take quite as much care
I take just as much care as ever

I feel restless as if I have to be on the move
Very much indeed
Quite a lot
Not very much
Not at all

I look forward with enjoyment to things
As much as I ever did
Rather less than I used to
Definitely less than I used to
Hardly at all

I get sudden feelings of panic
Very often indeed
Quite often
Not very often
Not at all

I can enjoy a good book or radio or television programme
Often
Sometimes
Not often
Very seldom

Finally a few questions about yourself:

1. Are you male or female? Male ☐ Female ☐ **2. Occupation** ***(please print in capitals)*** _____

3. Are you: Single ☐ Married/living with partner ☐ Divorced/separated ☐ Widowed ☐

4 Please tell us to which grouping you feel you belong.

White English, Scottish, Welsh, Irish	☐	White other	☐	Black Carribean	☐
Black African	☐	Indian	☐	Pakistani	☐
Bangladeshi	☐	Chinese	☐	Other (Please specify)	☐ _____

5. Do you smoke tobacco? Yes☐ No, quit in the past year☐ No, quit over a year ago☐ No, Never☐

Please check that you have answered all the questions, Thank you very much.

Appendix II

University of Leicester
Department of Health Sciences (General Practice and Primary Health Care), University of Leicester, Leicester General Hospital, Gwendolen Road, Leicester LE5 4PW.

The Prevalence of Depression in Diabetes: A primary care study.
Principal Investigator: Saima Ali

Date

Practice Address

Dear…

I am writing to invite your practice to take part in a study investigating the prevalence, impact and identification of depression in patients with type 2 diabetes.

Enclosed is an information sheet which will explain the purpose of the study and what will be required from your practice if you agree to take part (*DepressionanddiabetesPracticeInformationsheetMarch06/V1*). If after having read this information, you would like to take part in this study please complete the reply slip enclosed with this letter. The reply slip also asks for some additional information about your practice. This is to allow us to assess your practice's suitability for being part of this study.

Yours sincerely

Saima Ali, (Postgraduate Research Student)

Kamlesh Khunti (Research Supervisor)

University of Leicester

Appendix III

Department of Health Sciences (General Practice and Primary Health Care), University of Leicester, Leicester General Hospital, Gwendolen Road, Leicester LE5 4PW.

The Prevalence of Depression in Diabetes: A primary care study.
Principal Investigator: Saima Ali

STUDY INFORMATION SHEET

Why is this research being done?
Evidence suggests that depression in patients with diabetes may be linked to poorer diabetes related health outcomes. However, it is possible that through correctly identifying and treating depression in these patients, glycaemic control and possibly the risks of diabetes related complications may be improved. Unfortunately few large scale studies examining the relationship between depression and diabetes have been conducted in the UK. Such research is necessary in order to plan and estimate the level of need for health services aimed at improving care for those with diabetes. In addition no research has examined whether the identification and rates of depression in patients with diabetes is any different in South Asians patients, despite their increased risk of diabetes and diabetes related complications.
This research therefore aims to examine the prevalence, impact and identification of depression in patients with type 2 diabetes, in a multi-ethnic general practice population.

What will it involve for the practice?
We aim to conduct this research using a self-report questionnaire and data from GP records. Patients with and without type 2 diabetes will be recruited from your practice and will be asked to complete a short questionnaire. In order to do this will require members of practice staff to distribute information packs to patients attending routine appointments. Information packs will contain an information sheet for patients, a consent form and the questionnaire which will assess levels of anxiety and depression. Your practice's participation will involve allowing a researcher to collect the questionnaires from consenting patients and also extract data from their patient notes. We hope to collect completed questionnaires and examine the notes for approximately 100 patients from your practice. All work will take place at the practice and we envisage it will take approximately 2-4 weeks to complete. Completed questionnaires will be temporarily stored at the practice for a period of 1 week, safe storage of questionnaires will therefore need to be negotiated. Data will be extracted from patient notes by a researcher with an honorary NHS contract with the PCT. A payment to cover staff time will be negotiated with participating practices

What to do next
If you agree for your practice to participate in this study please complete the reply slip attached. A reply paid envelope is enclosed. If you have any concerns or queries about this study, please contact Saima Ali by telephone (0116 258 4437) or via email (Sa81@le.ac.uk)

University of Leicester

Appendix IV

Department of Health Sciences (General Practice and Primary Health Care), University of Leicester, Leicester General Hospital, Gwendolen Road, Leicester LE5 4PW.

REPLY SLIP

I would be willing for my practice to volunteer to take part in the above study as described in the study information sheet (DepressionanddiabetesPracticeInformationSheetMarch06/V1).

I understand that this will involve recruiting general practice attenders to complete a short questionnaire at the practice and examining their GP notes.

I understand that practice staff will be required to provide information packs to patients and that all data collection will be carried out by a researcher from the University of Leicester

Name _____ Role in Practice _____

(please sign) _____ (Date) _____

Please could you provide the following information. This information will help us to select practices which are suitable for taking part in the research.

The patient list size of the practice _____

The number of GPs working at the practice _____

Number of patients with a recorded diagnosis of depression. _____

Are you a teaching practice? Yes/ No

How patient data is recorded, including computer system used_____

_____

Thank you very much.

Please return this form in the envelope provided which does not need a stamp.

Appendix V

To be printed on general practice headed paper

Date

Dear Patient

The prevalence and impact of co-morbid depression with type 2 diabetes in primary care.

This general practice has agreed to take part in a study with researchers at the University of Leicester. The purpose of this research is to examine whether there is a link between depression and diabetes in adults and also to investigate whether there is a relationship between having depression with diabetes and poorer heath.

Enclosed is an information sheet which will explain more about the study and what will happen if agree to take part. Please take some time to read this carefully. If you agree to take part please sign the consent form enclosed with this letter and return it to the researcher who is available at the practice today. Contact details are also provided on the information sheet if you require any more information or further assistance.

Yours sincerely

(Practice Manager)

University of Leicester

Appendix VI

Department of Health Sciences (General Practice and Primary Health Care), University of Leicester, Leicester General Hospital, Gwendolen Road, Leicester, LE5 4PW

The prevalence of depression in diabetes: A primary care study

Principal investigator: Miss Saima Ali

For telephone enquiries please ring Saima Ali on 0116 258 4437 between 10am and 4pm.

We would like to invite you to take part in some research being carried out by researchers at the University of Leicester. Before you decide, it is important for you to understand why the research is being done and what it involves. Please take time to read the following information and feel free to ask or discuss anything with the researcher who is present at the practice today or to contact her later on the number shown above.

Why is this research being done?
We know that quite a lot of people have symptoms of depression. This is sometimes described as 'feeling low' or 'feeling blue' and is something that doctors can help with. We would like to know whether people with diabetes are more likely to be depressed than people without diabetes. Depression in people with diabetes may be related to other problems such as difficulties in controlling blood sugar and we would like to see if this is true in a mixed ethnic population in Leicester.

Why have I been invited?
You have been selected because you attended your GP surgery today. Not everyone who is invited to take part in this research will have depression or diabetes. Therefore even if you do not have these conditions, we still need your help. It is entirely up to you to decide if you want to take part and you can change your mind at any time with no questions asked.

What would my participation in the study involve?
To participate in this study you will need to complete a short questionnaire, which will take about 5 minutes. This questionnaire will involve some questions about how you feel as well as some background information about yourself.

With your permission, we would also like to look at your GP medical records. All information that you share with us will remain completely confidential. Your name will be recorded on a consent form so that we can access information in your records but after that point your name or any other identifying information will not be used. This study will not affect your medical treatment in any way.

If you agree, we would also like your permission to use the information from your questionnaire for future research. If we use this information in the future, we will not link it to your name.

What information is held in my GP records?
General practice records contain information about visits to your GP surgery, your hospital visits, medication prescribed and medical history from the time you were born to the present time. Information may be held on computer or in paper files. Although we may be able to see other information about you, we will collect only the information we need for our research.

Will my information be kept confidential?
All the information that is examined will be treated as confidential. The details we collect will be anonymised which means your name, address or any other information which could be used to identify you will not be used in this research or any future research which may be conducted using this data. Your doctor will not know what you have said in the questionnaire. However, if you agree we will inform yourself and/ or your GP if we feel that you may be suffering from high levels of anxiety or depression.

Do I have to take part?
It is your right to decide whether or not you would like to take part in this study. You do not have to complete the questionnaire or allow us to have access to your medical records, or give a reason if you choose not to. Your medical care will not be affected by whether or not you take part. The principal investigator will not examine any of the questionnaires for a period of one week. If you complete the questionnaire today and decide within one week that you no longer with to take part you may withdraw from the study by contacting the principal investigators using the details provided above. The principal investigator will not collect your questionnaire from your general practice and will ensure that it is carefully destroyed. You can also withdraw from this research at any time later on with no questions asked, again by contacting the principal investigator and both your questionnaire and any data we collect from your records will be deleted from our database.

Could I be harmed in any way?
Some questions may ask you about matters that may be private but it is highly unlikely that you would be harmed in any way by this research. Therefore no automatic compensation arrangements have been made. The research is indemnified by the University of Leicester. If you were to be harmed by someone's negligence, there may be grounds for legal action but you may have to pay for it.

What should I do now?
Having read this information we hope that you are willing to complete the questionnaire and will allow researchers to have access to your GP record. If you agree, please sign and date the consent form enclosed and return it to the researcher that is available at the practice. If you still have any questions about the study please feel free to ask the researcher.

This study has been reviewed by the Leicestershire, Northamptonshire & Rutland Research Ethics Committee 2.

Thank you very much for taking the time to consider taking part in this study.

University of Leicester

Appendix VII

Department of Health Sciences (General Practice and Primary Health Care), University of Leicester, Leicester General Hospital, Gwendolen Road, Leicester LE5 4PW.

Centre Number:
Patient Identification Number for this study:

CONSENT FORM

Title of Project: The Prevalence of Depression in Diabetes: A primary care study

Name of Researcher: Saima Ali

I confirm that I have read and understand the information sheet dated June 2006 (version 2) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
I agree to be contacted by letter if the results from the questionnaire indicate that I may be suffering from high levels of depression and/ or anxiety, and for my GP to also be informed

I agree to take part in the above study.

_____	_____	_____
Name of Patient	Date	Signature

Patient ID number ☐☐☐☐

Practice ID number _____
(We will fill these in)

IMPORTANT

Please also note that if you have any of the following, you can not complete this questionnaire:

- Type 1 diabetes
- Gestational diabetes
- Type 2 diabetes diagnosed less than 3 months ago

Please enter your full name and date of birth on this slip. This slip will be removed once we have allocated your questionnaire with a study ID number.

Full name (please complete in block capitals): _____
Date of birth (Day/Month/Year): _____

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