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Does depression increase the risk of developing type 2 diabetes?

Martin P. Cosgrove[1], Lincoln A. Sargeant[2] and Simon J. Griffin[2]

Background Members of a scheme awarding injury pensions may allege that the onset of diabetes was precipitated or caused by depression induced by work in order to claim an injury award.

Aims To quantify the association between depression and subsequent development of type 2 diabetes in order to determine whether an individual in a pension scheme that awards injury pensions, who develops type 2 diabetes, should be awarded an injury pension, if the development of the diabetes followed a work-related depressive episode.

Methods Electronic and hand literature searches up to December 2006. Relative risk estimates from cohort studies of adults were pooled using fixed and random effects models. Attributable risk fraction was calculated using the Levin formula.

Results The presence of depression or depressive symptoms was associated with increased risk of subsequently developing type 2 diabetes. The pooled fully adjusted relative risk estimate from the three highest quality studies was 1.25 (95% CI: 1.02–1.48) and was homogenous. However, depression was no more frequent among those with and without prevalent, but previously undiagnosed, type 2 diabetes.

Conclusion Depression is associated with subsequent development of type 2 diabetes. However, the relative risk estimate is small and only 20% of cases of diabetes can be attributed to depression in people with both conditions. Further research is needed to determine possible causal mechanisms for the association and to ascertain whether depression and diabetes may have a common aetiology.

Key words Depression; diabetes; injury award; pension.

Introduction

Type 2 diabetes often runs in families and is more common with increasing age, weight, body mass index (BMI), sedentary lifestyle and certain dietary behaviours such as high fat intake [1]. In addition to these standard risk factors, it has long been suggested that risk of type 2 diabetes is increased by depression [2,3]. More recent reviews have continued to support this view [4–9]. A meta-analysis of nine longitudinal studies found that depressed adults had a 37% increased risk of type 2 diabetes [10].

Depression is common and a causal link with diabetes has implications for occupational health. However, the level of evidence for causation in epidemiology differs from the usual standard of proof required in occupational health practice, the balance of probabilities. This standard holds that at least 50% of cases of diabetes among people with depression should be attributable to depression.

The aims of this paper were to identify studies of the association between depression and type 2 diabetes and to quantify the strength of the association in order to assess the impact for occupational health practice. The objective was to determine whether an individual in a pension scheme that awards injury pensions, who develops type 2 diabetes, should be awarded an injury pension, if the development of the diabetes followed a work-related depressive episode. Two potential associations were investigated: does depression precipitate type 2 diabetes and does depression increase the subsequent risk of developing type 2 diabetes?

Methods

The following databases were searched: Allied and Comp Med, British Nursing Index 1994, CINAHL, DH data,

[1]Cherry Hinton Medical Centre, 34 Fishers Lane, Cambridge CB1 9HR, UK.

[2]MRC Epidemiology Unit, Strangeways Research Laboratory, Wort's Causeway, Cambridge CB1 8RN, UK.

Correspondence to: Martin Cosgrove, Cherry Hinton Medical Centre, 34 Fishers Lane, Cambridge CB1 9HR, UK. Tel: +44 1223 330315; fax: +44 1223 330316; e-mail: drmartincosgrove@yahoo.co.uk

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EMBASE, Kings Fund, MEDLINE, PsychInfo and PubMed up to December 2006. The following terms were used in a whole document search for papers: diabetes, blood glucose, depression, depressive symptoms, prospective, follow-up and longitudinal. From the list of papers, a manual search using the electronic abstract for potentially eligible papers was undertaken. This was supplemented by a hand search of references in identified reviews and original papers. A further hand search was undertaken of the major diabetes journals from January 1995 to December 2006.

We selected cohort, case control and cross-sectional studies of adult participants in community or occupational settings published in any language. Studies were required to include assessment of major depressive disorder or raised depression score on a validated scale at the time of screening for, or prior to, assessment of diabetes status. Studies which had an inadequate description of the method of depression assessment or featured type 1 diabetes, impaired glucose tolerance, insulin resistance or death as the outcome were excluded.

Two of the co-authors independently applied inclusion and exclusion criteria to potentially eligible papers and also extracted data from the selected papers onto standardized forms. Any disagreements were independently reviewed by the third co-author and then consensus was reached.

Quality markers were agreed a priori, based on SIGN methods (http://www.sign.ac.uk). They included the following study characteristics: the adequacy of the description of the source populations, the selection of participants and controls and description of withdrawals, adequacy of exclusion of individuals with diabetes at enrolment, quantitative assessment of blood glucose at the end of the study and a clear description of measurement and adjustment for confounding. The American College of Physicians Journal Club standard of 80% follow-up was applied. Assessment of the quality of the papers was undertaken independently by two authors. As with data extraction, the third author independently reviewed any disagreements and consensus was reached.

Where there were uncertainties concerning inclusion/exclusion criteria or data extraction, original authors were contacted by e-mail. Authors were also asked whether they were aware of other published or unpublished studies that might be included in the systematic review.

Crude or least-adjusted estimates of the risk ratio from each cohort study were pooled. This was not possible for one study [11] as these data were not reported. In contrast to the meta-analysis by Knol *et al.* [10], we included both studies using the NHANES I data [12,13] in the adjusted estimate because the studies were undertaken at different times, with different measures of depression, different duration of follow-up, different study groups, in different centres and reported different results. In the case of Kumari *et al.* study [26], the estimates for male and female were reported separately and this study was treated as two studies for the purpose of meta-analysis. The multivariable adjusted risk ratio estimates from each study were pooled. Both fixed and random effects models were used in pooling the risk estimates. Heterogeneity of studies was tested by means of the Cochran's Q test and quantified using the I-squared measure [14].

We undertook a sensitivity analysis to determine whether the results were influenced by particular studies. Publication bias was assessed by constructing a funnel plot of the relative risk estimate for each study against the corresponding standard error with asymmetry suggesting bias and by undertaking a Begg and Mazumdar adjusted rank correlation test [15]. Attributable risk fraction was calculated using the Levin formula [16].

All statistical analyses were performed using STATA, version 9.0 (Stata, College Station, TX, USA).

Results

The search strategy identified 2924 papers. These included two cross-sectional studies of the presence of depression at the time of screening for type 2 diabetes [17,18], four clinical depression or mental illness studies as measured by GP diagnosis/primary care database [19–22], one clinical paper using the Diagnostic Interview Schedule (DIS) as a depression assessment tool [23] and eight cohort studies using depression scales [11–13,24–28]. The study of the association between mental illness and diabetes in a primary care database [22] was excluded because conditions other than depression could be included. All nine prospective cohort papers [11–13,23–28] undertook some form of depression assessment and stratified the cohort into depressed/not depressed, low or high depression score and some undertook further division to investigate intermediate scores. The cohort study participants were followed up for a mean of 3–15.6 years.

Fourteen studies satisfied the inclusion criteria and a summary of these is given in Tables 1–3. All studies were assessed as being adequate with regards to three quality markers: description of selection of participants and controls, comparability of source populations and concealment of diabetes status. The findings for the other quality criteria are shown in Table 2. Confounding for age, sex and BMI/weight/obesity was considered necessary for adequate adjustment.

The two papers investigating the presence of depression at the time of screening for type 2 diabetes with an oral glucose tolerance test [17,18] showed no difference in the frequency of depression in those with or without prevalent, but previously undiagnosed, type 2 diabetes.

Three studies using general practitioner databases [19–21] had deficits in quality with regards to ascertainment of

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Table 1. Characteristics of included studies

Paper and year of publication	Setting	Size of study population	Type of study	Mean age ± SD (range)	Sex %, female	Number of cases of type 2 diabetes mellitus	Years of follow-up	Assessment of depression	% of population with depression	Assessment of diabetes status
Rajala *et al.* 1997 [17]	Finland community	734	Cross sectional	57 (57–57)	56	26[a]	Not applicable	Zung	12	Oral glucose tolerance test
Palinkas *et al.* 1991 [18]	USA community	1586	Cross sectional	69 ± 9	% not stated	209[a]	Not applicable	Beck	6	Oral glucose tolerance test
Nichols and Brown 2000 [19]	USA community	3360	Case control	63	46	1680	11	Clinical diagnosis	19	Medical record
Brown *et al.* 2005 [21]	Canada community	92 677	Case control	52 (20–95)	49	33 257	3	Clinical diagnosis	4	Medical record
van den Akker *et al.* 2004 [20]	Netherlands community	68 004	Historical cohort	38 ± 14	50	3245	15.6	Clinical diagnosis	2	Medical record
Eaton *et al.* 1996 [23]	USA community	1715	Prospective cohort	(≥18)	63	89	13	DIS	5	Self-report
Carnethon *et al.* 2003 [12]	USA community	6190	Prospective cohort	(25–74)	54	369	15.6	General well-being	9	Self-report
Saydah *et al.* 2003 [13]	USA community	8870	Prospective cohort	(32–86)	% not stated	465	9	CES-D	16%	Self-report
Arroyo *et al.* 2004 [28]	USA community	72 178	Prospective cohort	(45–72)	100	973	4	MHI-5 of the SF36	8	Self-report
Kawakami *et al.* 1999 [27]	Japan occupational	2764	Prospective cohort	(18–53)	0	43	8	Zung	12	Urinalysis then fasting plasma glucose, if positive, and then oral glucose tolerance test, if positive
Palinkas *et al.* 2004 [11]	USA community	2375	Prospective cohort	66 ± 8 (50–89)	57	79	8	Beck	8%	Self-report or oral glucose tolerance test
Kumari *et al.* 2004 [26]	UK occupational	10 138	Prospective cohort	(35–55)	30	130 in 1991–92, 361 in 1977–79	10.5	GHQ	31	Self-report or oral glucose tolerance test
Hill Golden *et al.* 2004 [24]	USA community	11 615	Prospective cohort	56 ± 6 (45–67)	% not stated	721	6	Vital exhaustion scale	Quartiles	Self-report or fasting or random plasma glucose
Everson-Rose *et al.* 2004 [25]	USA community	2662	Prospective cohort	46 ± 2 (42–52)	100	97	3	CES-D	23%	Self-report or fasting plasma glucose

[a]Newly diagnosed cases.

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Table 2. Quality assessment

Paper	Exclusion of individuals with diabetes at enrolment	Follow-up >80%	Description of withdrawals	Quantitative assessment of blood glucose at end of study	Confounding
Rajala *et al.* 1997 [17]	Adequate	Not applicable	Not applicable	Adequate	Inadequate
Palinkas *et al.* 1991 [18]	Adequate	Not applicable	Not applicable	Adequate	Inadequate
Nichols and Brown 2000 [19]	Inadequate	Not applicable	Not applicable	Inadequate	Inadequate
Brown *et al.* 2005 [21]	Inadequate	Not applicable	Not applicable	Inadequate	Inadequate
van den Akker *et al.* 2004 [20]	Inadequate	Adequate	Not applicable	Inadequate	Adequate
Eaton *et al.* 1996 [23]	Inadequate	Inadequate	Adequate	Inadequate	Adequate
Carnethon *et al.* 2003 [12]	Inadequate	Adequate	Adequate	Inadequate	Adequate
Saydah *et al.* 2003 [13]	Inadequate	Adequate	Adequate	Inadequate	Adequate
Arroyo 2004 *et al.* [28]	Inadequate	Adequate	Adequate	Inadequate	Adequate
Kawakami *et al.* 1999 [27]	Inadequate	Adequate	Adequate	Inadequate	Adequate
Palinkas *et al.* 2004 [11]	Adequate	Inadequate	Adequate	Adequate	Adequate
Kumari *et al.* 2004 [26]	Inadequate	Adequate	Adequate	Adequate	Adequate
Hill Golden *et al.* 2004 [24]	Adequate	Adequate	Adequate	Adequate	Adequate
Everson-Rose *et al.* 2004 [25]	Adequate	Adequate	Adequate	Adequate	Adequate

Table 3. Crude and adjusted relative risk of developing type 2 diabetes mellitus in people with depression

Study	Relative risk high score least-adjusted model (95% CI)	Variables in fully adjusted model	Relative risk high score fully adjusted model (95% CI)	Relative risk intermediate score fully adjusted model (95% CI)
Rajala *et al.* 1997 [17]	1.0 (0.3–2.9)	None	No adjusted model	Not assessed
Palinkas *et al.* 1991 [18]	Not given	GY	0.84(0.34–1.81)	Not assessed
Nichols and Brown 2000 [19]	1.23 (1.03–1.46)	None	No adjusted model	Not assessed
Brown *et al.* 2005 [21]	1.29 (1.2–1.37)	GYγ	Age 20–50, 1.23 (1.10–1.37); age 51 plus, 0.92 (0.84–1.00)	Not assessed
van den Akker *et al.* 2004 [20]	1.04 (0.84–1.28)	GWY	0.98 (0.79–1.21)	Not assessed
Eaton *et al.* 1996 [23]	1.58 (0.71–3.51)	BGRYβ	2.23 (0.90–5.55)	Not assessed
Carnethon *et al.* 2003 [12]	2.52 (1.73–3.67) GRY	ABEGPRTY	1.86 (1.27–2.71)	1.24 (0.91–1.70)
Saydah *et al.* 2003 [13]	1.39 (1.03–1.89)	BEGPRY	1.11 (0.79–1.56)	1.14 (0.90–1.45)
Arroyo *et al.* 2004 [28]	1.55 (1.27–1.9) GY	ABDGKLTY	1.22 (1.00–1.50)	Not assessed
Kawakami *et al.* 1999 [27]	2.32 (1.06–5.08) Y	AEJKNOPTUY	2.31 (1.03–5.20)	1.13 (0.56–2.28)
Palinkas *et al.* 2004 [11]	Not given	BGPY	2.5 (1.29–4.87)	Not assessed
Kumari *et al.* 2004 [26]	Males 1.17 (0.8–1.7), females 1.08 (0.6–1.9)	BGFIHOPQRTUVYα	1.17 males, (0.8–1.7); 1.03 females (0.6–1.8)	Not assessed
Hill Golden *et al.* 2004 [24]	1.63 (1.31–2.02) EGRSY	BCEGHIPRSTYZ	1.31 (1.01–1.64)	1.12 (0.90–1.39), Quartile 2; 1.03 (0.81–1.31), Quartile 3
Everson-Rose *et al.* 2004 [25]	1.66 (1.05–2.61) EMRY	EGMPRSWY	1.46 (0.90–2.36)	Not assessed

Key to adjustments in models: A, alcohol; B, BMI; C, caloric intake; D, diet; E, education; F, aspects of stress at work; G, sex; H, systolic BP; I, ECG abnormalities; J, shift work; K, chronic medical conditions (including hypertension); L, menopausal status; M, medication; N, obesity; O, occupation; P, physical activity; Q, length of follow-up; R, race; S, site of investigation; T, smoking; U, family history; V, height; W, weight; Y, age; Z, waist hip ratio; α, life events; β, health care in last 6 months and γ, physician visits in last year.

diabetes and only one [20] had a description of how the diagnosis of depression was made. One prospective cohort study [23] had a rigorous assessment of depression at baseline (DIS), but used self-report of diabetes to exclude individuals at baseline and as a mechanism of diabetes ascertainment at follow-up.

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Six of the prospective cohort studies using depression scales [11–13,26–28] had deficits in at least one aspect of quality. Only two cohort studies [24,25] undertook analysis of diabetes at the start to ensure exclusion of asymptomatic prevalent but undiagnosed diabetes. In one of the studies [26], assessment of glucose tolerance was undertaken at the mid-point of follow-up. Attrition bias was a significant problem in one of the studies [11]. Three of the studies relied on self-report of diabetes diagnosis [12,13,28].

The two cohort papers of adequate overall quality are those by Hill Golden [24] and Everson-Rose [25] which show, respectively, a 31 and 46% increase in risk of developing diabetes after a high depression score in a fully adjusted model. The combined estimate of the adjusted relative risk from these two studies was 1.34 (95% CI: 1.04–1.62) with no heterogeneity ($P = 0.71$, I-squared = 0%). Intermediate depression scores did not increase the risk in any of the papers using a depression scale (Table 3).

In the nine prospective papers using depression score or DIS as a diagnostic tool for depression, the pooled least-adjusted risk of developing type 2 diabetes associated with depression was 1.33 (95% CI: 1.19–1.46) in a fixed effects model. There was significant between study heterogeneity ($P = 0.02$, I-squared = 55%). The random effects models gave a pooled estimate of 1.42 (95% CI: 1.18–1.66). There was overall homogeneity in the results of the studies when the fully adjusted estimates were pooled ($P = 0.25$, I-squared = 20.4%). The fixed effects model gave a pooled estimate of 1.17 (95% CI: 1.05–1.29). Supplementary Figure 1 (available as Supplementary data at *Occupational Medicine* Online) gives the forest plot for the least adjusted risk estimates and Figure 2 the forest plot for the fully adjusted risk estimates.

There was no correlation between the number of years of follow-up in each study and the relative risk of developing type 2 diabetes ($r = 0.05$, $P = 0.89$) (Figure 3). The three prospective cohort studies using depression scales of best quality [24–26] were homogeneous in results. The pooled least-adjusted relative risk for these three studies was 1.42 (95% CI: 1.18–1.66) by the fixed effects model ($P = 0.27$ for heterogeneity and I-squared = 24%) and the fully adjusted estimate was 1.25 (95% CI: 1.02–1.48) ($P = 0.78$ for heterogeneity, I-squared = 0%).

Using the risk estimate of 1.25, in people with both depression and diabetes, 20% of the cases of diabetes could potentially be attributable to a depressive illness. The prevalence of depression was estimated in a recent systematic review to be 18% in people with diabetes [29]. Of the whole population of people with diabetes, the risk attributable to depression in our meta-analysis was 4%.

Given the good follow-up of the study population and careful consideration of those who were lost to follow-up,

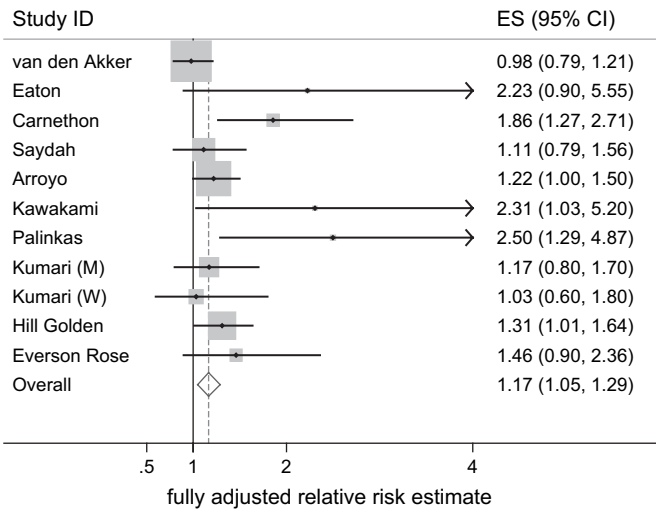

Figure 2. Forest plot for fully adjusted relative risk estimates (ES) in cohort studies (fixed effects model).

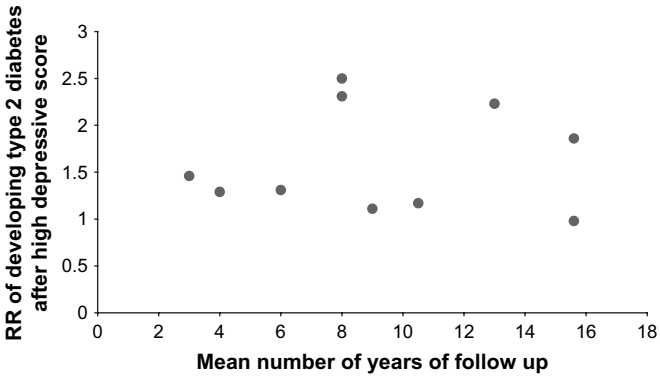

Figure 3. The association between the number of years of follow-up following depression score in cohort studies and the relative risk of developing type 2 diabetes using fully adjusted models.

we investigated whether inclusion or exclusion of the papers by Hill Golden [24] and Everson-Rose [25] would change the result. The pooled adjusted relative risk estimate fell slightly from 1.17 to 1.13, when these were excluded (fixed effects model). We also examined the potential for bias in Kumari's [26] paper because of the failure to measure glucose at the beginning of the study. The effect estimate was unchanged, when this study was excluded.

A funnel plot (Figure 4) suggested some evidence of publication bias against smaller cohort studies reporting no association or a negative association between depression and diabetes. However, the Begg and Mazumdar adjusted rank correlation test for publication bias was not statistically significant ($P = 0.10$).

Discussion

The results suggest that there may be a link between depressive symptoms and the subsequent development of

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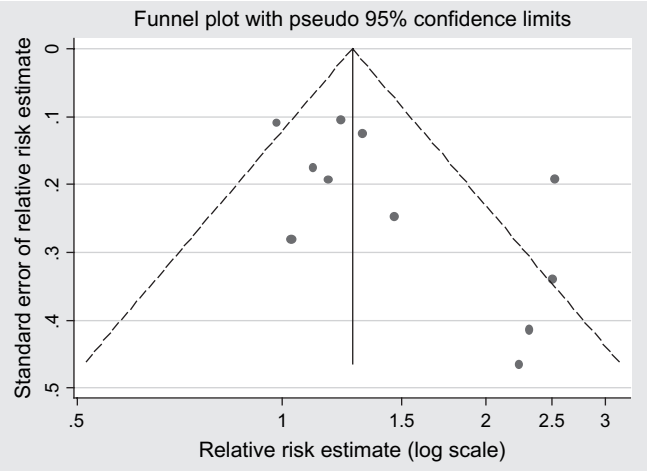

Figure 4. Funnel plot showing the relative risk of developing diabetes following a depressive episode in prospective studies using fully adjusted values.

type 2 diabetes. Our results are similar to those reported in a previous meta-analysis [10], despite some variation in the included studies. There does not appear to be, however, a dose–response relationship between the score on a depression scale and risk of diabetes. Only the high scores were associated with subsequent development of diabetes. Furthermore, there does not appear to be a relationship between the incidence of diabetes and time since a high depressive score in that the relative risk estimates did not vary with duration of follow-up.

Assuming that there is a true association between depression and subsequent development of type 2 diabetes, there are several possible explanations for this finding. First, it may be that depression is a direct cause of type 2 diabetes. The hypothalamo-pituitary adrenal (HPA) axis is abnormal during a major depressive episode due to increased hypothalamic levels of corticotropic-releasing hormone [30]. As a consequence, there are raised circulating plasma corticosteroid hormone levels and a blunted dexamethasone suppression test has been shown in subjects with major depressive disorder [30].

Bjorntorp has suggested that the link between stress and diabetes is central adiposity and proposes that stress causes a more central distribution of fat, which in turn causes diabetes [31]. The 'Bjorntorp hypothesis' first published in 1988 [32] is that the key to the metabolic syndrome, insulin resistance and type 2 diabetes is 'hypothalamic arousal,' that is excessive HPA axis activity and excessive sympathetic drive. As a consequence of the hypothalamic abnormality, there is increasing abdominal obesity, an increased free fatty acid concentration, increased heart rate, cardiac output and renin secretion, together with cortisol and androgen excess. Björntorp suggests that the original defect is due to 'poor coping' and 'environmental stress'.

A second explanation is that diabetes is not caused by depression, rather there is a common underlying aetiological mechanism to both conditions. For example, none of the studies controlled for birth weight and being small for dates at birth is known to increase the risk of developing both depression and diabetes. A potential mechanism is a defect in glucocorticoid sensitivity. A further explanation is that diabetes is preceded by symptoms such as tiredness and malaise that may be confused with depression when using a screening questionnaire. Finally, the development of diabetes in people with depression may be related to the behaviours associated with depression (inactivity, poor diet and obesity) or the drugs used to treat it rather than the depression itself.

The strengths of this meta-analysis are that we used a wide search strategy, using all languages and hand searching references in original articles. We incorporated independent assessment against inclusion criteria and for data extraction, quality assessment and sensitivity analyses. We are aware that other large-scale prospective research is being undertaken in this area but has not yet been reported. Other studies from general practice databases may have been undertaken, but not published for methodological reasons. We cannot rule out publication bias but every effort was made to find published and unpublished papers. Authors who responded to e-mails were not aware of other research in this field and the statistical test for publication bias was not significant.

There were a large number of participants in the included studies and quality assessment distinguished the better papers. The reason for heterogeneity in the results is likely to be related to the wide range of instruments used to measure depression symptoms, the different methods of assessment of the presence or absence of diabetes and the different baseline characteristics (for example mean age and BMI) of study participants. However, among the better papers, there is homogeneity of results.

There are four main limitations to this study: First, only two prospective cohort studies using depression scales of adequate quality were found. This limited the scope to examine a dose–response relationship between depressive symptoms and subsequent diabetes. Second, while depression scores are useful as a screening tool for depression and are correlated with major depressive disorder, they are not by themselves sufficient to make a diagnosis of major depressive disorder. Nevertheless, they are useful, reproducible methods of assessment with reasonable sensitivity and specificity. Third, some of the depression scales are not in widespread use in clinical or research practice and one of the tools (vital exhaustion) has never to our knowledge been validated against a gold standard criteria such as the Diagnostic and Statistical Manual. Finally, a depression score may vary with time. None of the studies repeated the depression scores.

Ascertainment bias, from participants with depression consulting practitioners more often and having more investigations, is likely to increase the prevalence of

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diabetes in people with depression. However, our sensitivity analysis demonstrated that the results were robust to inclusion or exclusion of studies in which the presence or absence of diabetes at baseline was rigorously assessed.

Our findings are similar to those of a recently published systematic review of depression and diabetes [10], but we have included a greater number and type of papers and have assessed the attributable risk of depression as a potential cause of diabetes. Our analysis provides the basis for the possible development of guidance by occupational health policy makers but also suggests that a common underlying aetiological mechanism may account for the findings.

What are the implications for occupational health practice? Based on our analysis, there is no evidence that the onset of type 2 diabetes is precipitated by depression (SIGN Grade B). There is insufficient justification to award an injury pension for diabetes to an employee who develops a work-related reactive depression and, within a period of weeks, is diagnosed with type 2 diabetes as well.

In those cases where an injury award is given based on the balance of probabilities, the following argument can be made. While, there is an increased risk of developing diabetes after a major depressive episode (as measured by a depression score), our findings suggest that the relative risk is <2 even without adjusting for the confounding effects of behaviours related to depression (SIGN Grade B). Thus on the balance of probabilities, we would state that type 2 diabetes is not caused by depression and an injury pension should therefore not be awarded. It is likely that further research will be undertaken in this field, the findings of which will need to be taken into account and are likely to alter the results of this review. This advice may need to be modified on the basis of further research.

In those cases where an injury award is given based on the attributable risk rather than the balance of probability, our meta-analysis estimates the attributable risk of developing diabetes following an episode of depression to be 20%. It is not possible to say in which person with both diabetes and preceding depression, the depression is the direct cause. An injury pension reflective of the attributable risk of 20% could therefore be awarded to each person making the claim, should the depression be directly attributable to work. However, it is possible that the association is not causal, but attributable to an underlying common aetiological mechanism. As before, the results of further research may alter this advice.

We believe that there are several potential explanations for the observed association between depression and type 2 diabetes, one of which is a shared aetiological pathway. Such a mechanism would be expected, on the basis of our results, to cause 4% of type 2 diabetes cases and 20% of the cases of type 2 diabetes and depression.

Key points

- There is good evidence that there is an association between depression and subsequently developing type 2 diabetes (possibly due to a common aetiological pathway); however, there is no evidence that depression precipitates the onset of type 2 diabetes.
- There is no reason to award an injury pension when the award is based on the balance of probabilities to an employee who alleges that their diabetes was caused by work-related depression.
- When the award is based on attributable risk, an award of 20% could be considered appropriate based on current evidence.

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Conflicts of interest

None declared.

References

1. Hu FB, Manson JE, Stampfer MJ *et al.* Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *N Engl J Med* 2001;**345:**790–797.
2. Menninger W. The inter-relationships of mental disorders and diabetes mellitus. *J Ment Sci* 1935;**81:**332–357.
3. Daniels G. Present trends in the evaluation of psychic factors in diabetes mellitus. *Psychosom Med* 1939;**1:**528–552.
4. Wales JK. Does psychological stress cause diabetes? *Diabet Med* 1995;**12:**109–112.
5. Jacobson AM. Depression and diabetes. *Diabetes Care* 1993;**16:**1621–1623.
6. Talbot F, Nouwen A. A review of the relationship between depression and diabetes in adults: is there a link? *Diabetes Care* 2000;**23:**1556–1562.
7. Rubin RR, Peyrot M. Was Willis right? Thoughts on the interaction of depression and diabetes. *Diabetes Metab Res Rev* 2002;**18:**173–175.
8. Musselman DL, Betan E, Larsen H, Phillips LS. Relationship of depression to diabetes types 1 and 2: epidemiology, biology, and treatment. *Biol Psychiatry* 2003;**54:**317–329.
9. Connolly V. "Sociotype": a key determinant of diabetes health. *Br J Diab Vasc Dis* 2004;**4:**141–143.
10. Knol MJ, Twisk JWR, Beekman ATF, Heine RJ, Snoek FK, Pouwer F. Depression as a risk factor for the onset of type 2 diabetes mellitus. A meta-analysis. *Diabetologia* 2006;**49:**837–845.
11. Palinkas LA, Lee PP, Barrett-Connor E. A prospective study of Type 2 diabetes and depressive symptoms in the

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elderly: the Rancho Bernardo Study. *Diabet Med* 2004;**21:**1185–1191.
12. Carnethon MR, Kinder LS, Fair JM, Stafford RS, Fortmann SP. Symptoms of depression as a risk factor for incident type 2 diabetes: findings from the National Health and Nutrition Examination Epidemiological Follow up Study, 1971–1991. *Am J Epidemiol* 2003;**158:**416–423.
13. Saydah SH, Brancati FL, Golden SH, Fradkin J, Harris MI. Depressive symptoms and the risk of type 2 diabetes mellitus in a US sample. *Diabetes Metab Res Rev* 2003;**19:** 202–208.
14. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *Br Med J* 2003;**327:** 557–560.
15. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics* 1994;**50:** 1088–1101.
16. Levin ML, Bertell R. Simple estimation of population attributable risk from case control studies. *Am J Epidemiol* 1978;**108:**78–79.
17. Rajala U, Keinanen-Kiukaanniemi S, Kivela SL. Non-insulin-dependent diabetes mellitus and depression in a middle-aged Finnish population. *Soc Psychiatry Psychiatr Epidemiol* 1997;**32:**363–367.
18. Palinkas L, Barrett-Connor E, Wingard D. Type 2 diabetes and depressive symptoms in older adults: a population based study. *Diabet Med* 1991;**8:**532–539.
19. Nichols GA, Brown JB. Does depression cause diabetes or diabetes cause depression. *Diabetes* 2000;**49(Suppl.):** 257-OR.
20. van den Akker M, Schuurman A, Metsemakers J, Buntinx F. Is depression related to subsequent diabetes mellitus? *Acta Psychiatr Scand* 2004;**110:**178–183.
21. Brown LC, Majumdar SR, Newman SC, Johnson JA. History of depression increases risk of type 2 diabetes in younger adults. *Diabetes Care* 2005;**28:**1063–1067.
22. Gulliford MC, Charlton J, Latinovic R. Increased utilization of primary care 5 years before diagnosis of type 2 diabetes: a matched cohort study. *Diabetes Care* 2005;**28:** 47–52.
23. Eaton WW, Armenian H, Gallo J, Pratt L, Ford DE. Depression and risk for onset of type II diabetes. A prospective population-based study. *Diabetes Care* 1996;**19:** 1097–1102.
24. Golden SH, Williams JE, Ford DE *et al.* Depressive symptoms and the risk of type 2 diabetes: the atherosclerosis risk in communities study. *Diabetes Care* 2004;**27:**429–435.
25. Everson-Rose SA, Meyer PM, Powell LH *et al.* Depressive symptoms, insulin resistance, and risk of diabetes in women at midlife. *Diabetes Care* 2004;**27:**2856–2862.
26. Kumari M, Head J, Marmot M. Prospective study of social and other risk factors for incidence of type 2 diabetes in the Whitehall II study. *Arch Intern Med* 2004;**164:**1873–1880.
27. Kawakami N, Takatsuka N, Shimizu H, Ishibashi H. Depressive symptoms and occurrence of type 2 diabetes among Japanese men. *Diabetes Care* 1999;**22:**1071–1076.
28. Arroyo C, Hu FB, Ryan LM *et al.* Depressive symptoms and risk of type 2 diabetes in women. *Diabetes Care* 2004;**27:**129–133.
29. Ali S, Stone MA, Peters JL, Davies MJ, Khunti K. The prevalence of co-morbid depression in adults with Type 2 diabetes: a systematic review and meta-analysis. *Diabet Med* 2006;**23:**1165–1173.
30. Pearson Murphy BE. Steroids and depression. *J Steroid Biochem Mol Biol* 1991;**38:**537–559.
31. Bjorntorp P. Visceral fat accumulation: the missing link between psychosocial factors and cardiovascular disease? *J Intern Med* 1991;**230:**195–201.
32. Bjorntorp P. Abdominal obesity and the development of noninsulin-dependent diabetes mellitus. *Diabetes Metab Rev* 1988;**4:**615–622.

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