



Comorbid elevated symptoms of anxiety and depression in adults with type 1 or type 2 diabetes: Results from the International Diabetes MILES Study

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ARTICLE INFO

Article history:

Received 22 February 2019

Received in revised form 5 April 2019

Accepted 22 April 2019

Available online 28 April 2019

Keywords:

Anxiety

Depression

Comorbidity

Self-care

Health behavior

ABSTRACT

Aims: We examined: (a) the prevalence of comorbid elevated symptoms of anxiety/depression; (b) its demographic/clinical correlates; (c) associations with self-care behaviors, by diabetes type.

Methods: Cross-sectional self-report data of 6590 adults with diabetes (42% type 1; 58% type 2) from the Australian and Dutch Diabetes MILES studies were used. Elevated symptoms of anxiety/depression were defined as GAD-7 \geq 10/PHQ-9 \geq 10.

Results: In both diabetes types, comorbid elevated symptoms of anxiety/depression were present in 9% and symptoms of anxiety alone in 2%; symptoms of depression alone were present in 8% of adults with type 1 diabetes and 11% with type 2 diabetes. Shorter diabetes duration (type 1 only) was the only characteristic that distinguished those with comorbid elevated symptoms of anxiety/depression but not those with symptoms of anxiety/depression alone from the reference group (no/minimal symptoms of anxiety/depression). Those with comorbid elevated symptoms of anxiety/depression had increased odds of sub-optimal diabetes self-care behaviors compared with the reference group, with higher odds than those with symptoms of anxiety or depression alone.

Conclusions: Comorbid elevated symptoms of anxiety/depression affected one in ten respondents, who also had increased odds of suboptimal diabetes self-care. Those with shorter type 1 diabetes duration may be at increased risk.

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1. Introduction

The prevalence of depression – defined as major depressive disorder or elevated symptoms of depression based on questionnaires – is nearly double in adults with diabetes compared to those without this chronic

metabolic condition, affecting approximately one in five individuals.^{1,2} Depression has been associated with worsened health outcomes for people across the diabetes spectrum, including persistent hyperglycemia, a higher risk for diabetes-related vascular complications, worse intervention outcomes and higher mortality rates in longitudinal studies.^{3–7} It is also associated with increased healthcare utilization and costs.⁸ Much less is known about the health effects of anxiety in this group. Diabetes has been associated with 1.25-fold increased odds of anxiety disorders and elevated symptoms, with pooled prevalence rates ranging from 14% for any anxiety disorder, 27% for anxiety disorder not otherwise specified,

Declarations of interest: none.

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and 40% for elevated symptoms of anxiety based on questionnaires.^{9,10} In 2002, a meta-analysis found that anxiety disorders, but not elevated symptoms of anxiety, were associated with hyperglycemia.¹¹ Studies that have focused on longer-term outcomes are inconclusive, with some finding an increased risk of cardiovascular events and mortality and others noting a protective role for anxiety, potentially explained by increased attention to health status and self-care.^{12–15}

A recent narrative review of emotional problems in adults with diabetes encouraged better understanding of the co-occurrence and interaction among psychological conditions.¹⁶ As the specifier “with anxious distress” has been added to the diagnosis of major depressive disorder in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), the comorbidity of depression and anxiety is especially relevant. A large Canadian population-based study found that diabetes was associated with almost double the odds of having comorbid major depression disorder and generalized anxiety disorder.¹⁷ However, three longitudinal studies examining the health effects of comorbid depression and anxiety among people with type 2 diabetes again have inconclusive results. Iversen et al. found that elevated symptoms of depression were only associated with increased all-cause mortality risk in individuals without elevated symptoms of anxiety, while Naicker et al. suggested the increased risk of all-cause mortality for comorbid symptoms was comparable to the risk for elevated symptoms of depression overall.^{13,15} Bruce et al. studied the associations of both a questionnaire-based construct of anxious depression and the DSM-5 categories on all-cause mortality and incident cardiovascular events and deaths.¹² They found that anxious depression predicted incident cardiovascular events and cardiovascular mortality with similar hazard ratios to major depression, while the combination of major depression and generalized anxiety disorder was only associated with cardiovascular mortality.¹²

To better understand the effect of comorbid anxiety and depression on health outcomes, studies are needed examining potential mediators of this relationship. Smith et al. investigated the association of co-existing elevated symptoms of anxiety and depression with self-care in a community sample of adults with type 2 diabetes, and found that elevated symptoms of anxiety and depression (both alone and in combination) were associated with suboptimal self-reported self-care.¹⁸ However, their study did not include adults with type 1 diabetes and only included four indicators of self-care (blood glucose monitoring, eating habits, physical activity, and smoking). The characteristics of people with diabetes who experience comorbid anxiety and depression remain unclear, but reports suggest that this combined comorbidity may be associated with having complications. For example, a higher rate of diabetes-related eye problems has been reported in those with comorbid elevated symptoms of anxiety and depression than in those with neither or only one.¹³

Therefore, the aims of the present study are to examine, in two national cross-sectional samples of adults with type 1 and type 2 diabetes: (a) the prevalence of elevated symptoms of anxiety alone, elevated symptoms of depression alone, and comorbid elevated symptoms of anxiety/depression; (b) the characteristics of adults with diabetes with elevated symptoms of anxiety/depression alone and comorbid elevated symptoms of anxiety/depression on a range of socio-demographic and clinical factors; and (c) the associations of elevated symptoms of anxiety alone, elevated symptoms of depression alone and comorbid elevated symptoms of anxiety/depression with a range of self-care and health behaviors.

2. Subjects, materials and methods

2.1. Participants and procedure

The current study used data from the Australian and Dutch Diabetes MILES (Management and Impact for Long-term Empowerment and Success) studies. A detailed description of the design and sample

characteristics of these studies has been published elsewhere.^{19,20} Briefly, both studies examined the psychosocial and behavioral aspects of living with diabetes using self-report surveys. For Diabetes MILES – Australia, 15,000 of the approximately one million registrants of the National Diabetes Services Scheme were randomly selected and contacted. To be eligible they had to be between 18 and 70 years with type 1 or type 2 diabetes. There was an over-sampling of adults with type 1 diabetes to ensure large sufficient numbers for sub-group analyses. Diabetes MILES – The Netherlands used a convenience sample of people with any type of diabetes aged 19+ years, without an upper age limit. The study was advertised through Dutch health websites, the digital newsletter of the Dutch Diabetes Research Foundation, and the magazine, twitter account and digital newsletter of the Dutch Diabetes Association.

All participants provided informed consent, either on paper or digitally, and both studies received ethical approval from the relevant ethical committees (Deakin University Human Research Ethics Committee reference number 2011-046; Tilburg University Psychological Research Ethics Committee reference number EC-2011 5).

In total, 3338 and 3960 eligible respondents took part in the Australian and Dutch studies, respectively. Data from the two studies needed to be merged in order to look at the four anxiety/depression subgroups across both diabetes types with adequate power. Where there were significant differences between Australian and Dutch participants in terms of demographic or clinical characteristics, these were minimal in size or could be explained by differences in sampling procedure (data not shown), and were considered unlikely to have a concerning influence on the results. For the present analyses, we used the cross-sectional data from participants with type 1 or type 2 diabetes with valid data on the questionnaires measuring anxiety and depressive symptoms ($n = 6590$; 50% Australian; 42% type 1 diabetes). There was a significant difference in the prevalence of elevated symptoms of anxiety/depression across both groups (Australia versus The Netherlands: 72% versus 87% for no/minimal symptoms of anxiety/depression; 3% versus 1% for elevated symptoms of anxiety only; 12% versus 7% for elevated symptoms of depression only; and 13% versus 5% for comorbid elevated symptoms of anxiety/depression; $p < 0.001$). However, it is unlikely that these differences in prevalence lead to different associations with socio-demographic, clinical and behavioral factors. Therefore, the results section reports estimates for the combined group only.

2.2. Questionnaires

2.2.1. Anxiety and depression

Symptoms of anxiety during the past two weeks were measured with the 7-item Generalized Anxiety Disorder questionnaire (GAD-7).²¹ Each item is scored on a four-point Likert scale, with the summed total score ranging from 0 to 21 and higher scores indicating more anxiety symptoms. A cut-off of ≥ 10 is commonly used to indicate elevated anxiety symptoms.²¹ Symptoms of depression during the past two weeks were measured with the 9-item Patient Health Questionnaire.²² Each item is scored on a four-point Likert scale, with the summed total score ranging from 0 to 27 and higher scores indicating more depressive symptoms. A cut-off of ≥ 10 is commonly used to indicate elevated depressive symptoms (PHQ-9).²² For both questionnaires, when one item value was missing it was substituted with the mean of the remaining items to calculate the total score. Symptoms of anxiety/depression comorbidity status was defined as: (a) no/minimal symptoms of anxiety/depression (GAD-7 < 10 and PHQ-9 < 10); (b) elevated symptoms of anxiety alone (GAD-7 ≥ 10 and PHQ-9 < 10); (c) elevated symptoms of depression alone (GAD-7 < 10 and PHQ-9 ≥ 10); and (d) comorbid elevated symptoms of symptoms of anxiety and depression (GAD-7 ≥ 10 and PHQ-9 ≥ 10).

2.2.2. Self-care behaviors

A revised version of the Diabetes Self-Care Inventory²³ assessed the frequency of performing self-care activities with scores ranging from 1

“never” to 5 “(almost) always”: taking the required number of insulin injections each day, adjusting insulin dosage, taking the prescribed number of tablets to lower blood glucose level, taking the prescribed cholesterol/blood pressure lowering medication, following a healthy diet, and meeting the norm for healthy exercise. Two additional items enquired about the number of blood glucose measurements and the number of foot inspections per week (continuous variables). A separate item was added to measure current smoking, inspired by the Smoking and Health Survey 2010 of Cancer Council Victoria. The items on insulin adjustment and self-monitoring of blood glucose were not used for participants with type 2 diabetes, as their responses may reflect not being trained or advised to adjust their insulin, and/or lack of knowledge, skills or self-efficacy, rather than being an indicator that they are not following recommendations. Also, the recommended number of daily insulin injections and SMBG frequency can vary significantly between individuals with type 2 diabetes.

For ease of interpretation, scores on each self-care item were dichotomized into optimal and suboptimal self-care. For all medication-taking items, suboptimal self-care was defined as any response lower than “(almost) always”. For diet and exercise, suboptimal self-care was defined as any response frequency less than “regularly”. Suboptimal self-monitoring of blood glucose (SMBG) was defined as <28 measurements per week (i.e. <4/day on average). Suboptimal foot care was defined as less than one inspection per week. For the smoking item, suboptimal self-care was defined as current daily smoking of cigarettes, cigars, pipes or other tobacco products.

2.2.3. Sociodemographic and clinical characteristics

Participants self-reported their gender, age, educational level, primary diabetes treatment, diabetes duration, diagnosed depression and anxiety, and comorbid conditions that were potentially micro- and macrovascular complications.

2.3. Statistical analyses

All analyses were conducted separately by diabetes type, using IBM SPSS Statistics v22. A *p*-value of <0.05 was considered to indicate statistical significance. Comparisons of anxiety/depression symptom variables across diabetes types were made using independent samples *t*-tests and χ^2 tests, as appropriate. Comparisons of anxiety and depression symptom severity across anxiety/depression symptom comorbidity status were made using ANOVAs. Cohen’s *d* was calculated as a measure of effect size (subtracting the means of both groups and then dividing by

the standard deviation of the two groups combined), with 0.20, 0.50 and 0.80 representing a small, moderate and large effect, respectively.

To examine demographic and clinical correlates of elevated symptoms of anxiety alone, elevated symptoms of depression alone, and comorbid elevated symptoms of anxiety/depression, compared to no/minimal symptoms of anxiety and depression (reference group), a multinomial logistic regression analysis was run for type 1 and type 2 diabetes separately. To avoid problems with overfitting, we followed the guideline of including one independent variable per 10+ events for the smallest group of the dependent variable²⁴ and selected the six allowed variables based on previous literature. These were gender, age, education, diabetes duration, comorbid vascular conditions, and insulin treatment (type 2 diabetes only).

To examine the relation of elevated symptoms of anxiety alone, elevated symptoms of depression alone and the elevated symptoms of anxiety/depression comorbidity with suboptimal self-care, logistic regression analyses were run with the dichotomized self-care behaviors as dependent variables. Comorbidity status was entered as an independent variable, with no/minimal anxiety/depression symptoms as reference group. All analyses adjusted for gender, age, education, diabetes duration, insulin use (type 2 diabetes only), and the presence of comorbid vascular conditions. Results of elevated symptoms of anxiety alone and some of the suboptimal behaviors need to be interpreted with caution, as the frequencies were low.

3. Results

Characteristics of the sample are provided in Table 1, stratified by diabetes type. Participants with type 1 diabetes were, on average, 15 years younger, and significantly less likely to report having had a diagnosis of anxiety or depression now or in the past (12% versus 15%, *p* < 0.001 and 17% versus 20%, *p* = 0.005, respectively) compared to those with type 2 diabetes.

With respect to symptoms of depression and anxiety, those with type 1 diabetes had slightly lower PHQ-9 total scores than those with type 2 diabetes (5.2 ± 5.1 [median 4.0, interquartile range 1.0–7.9] versus 5.5 ± 5.5 [4.0, 1.0–8.0], *p* = 0.03). The two groups did not differ with respect to GAD-7 total score (3.9 ± 4.3 [3.0, 1.0–6.0] versus 3.7 ± 4.5 [2.0, 0.0–6.0], *p* = 0.08). As shown in Fig. 1, comorbid elevated symptoms of anxiety/depression were present in 9% of the participants (regardless of diabetes type). Elevated symptoms of anxiety alone (elevated anxiety symptoms without elevated depression symptoms) was reported by 2% in each sample, and elevated symptoms of depression alone (elevated depression symptoms without elevated anxiety

Table 1
Demographics and clinical characteristics of the sample, stratified by diabetes type.

	Type 1 diabetes (<i>n</i> = 2782)	Missing values	Type 2 diabetes (<i>n</i> = 3808)	Missing values
Demographics				
Female	60% (1669)	12	49% (1850)	20
Age, years	45 ± 15 (45, 33–56)	20	60 ± 10 (61, 54–67)	45
Low educational level	11% (310)	54	22% (797)	129
Australian	49% (1365)	0	50% (1920)	0
Clinical characteristics				
Main treatment		7		24
Insulin pump	36% (1010)		3% (116)	
Insulin injections	64% (1765)		42% (1576)	
GLP-1 injections	NA		1% (55)	
Blood glucose lowering tablets	NA		43% (1632)	
Lifestyle only	NA		11% (405)	
Diabetes duration, years	19 ± 14 (16, 8–30)	17	10 ± 8 (9, 4–14)	30
Macrovascular disease ^a	10% (272)	0	23% (892)	0
Microvascular disease ^b	23% (644)	0	23% (891)	0

Numbers reported are mean ± SD (median, interquartile range) or % (*n*).

NA: not applicable.

^a Heart disease, stroke, peripheral arterial disease.

^b Retinopathy, neuropathy, kidney problems.

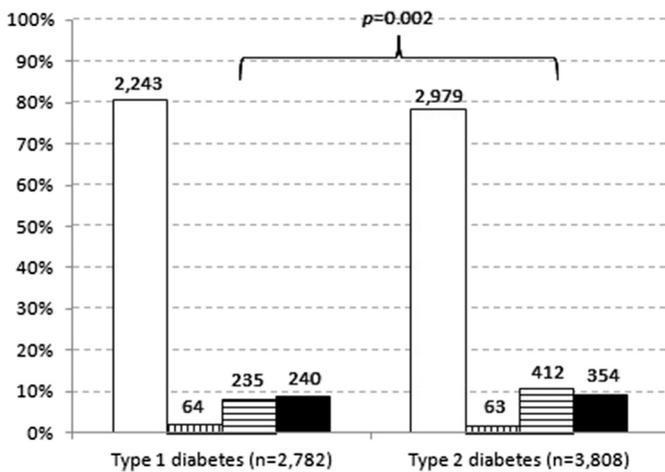


Fig. 1. Percentage of participants with (i) no/minimal anxiety/depressive symptoms, (ii) elevated symptoms of anxiety only, (iii) elevated symptoms of depression only, or (iv) comorbid elevated symptoms of anxiety/depression; stratified by diabetes type. White bars = No/minimal symptoms; Vertically-stripped bars = Elevated symptoms of anxiety only; Horizontally-stripped bars = Elevated symptoms of depression only; Black bars = Co-morbid elevated symptoms of anxiety/depression.

symptoms) by 8% of those with type 1 diabetes and 11% of those with type 2 diabetes. Comorbidity status differed significantly between diabetes types (Fig. 1).

With respect to symptom severity in participants with type 1 diabetes, those with comorbid elevated anxiety/depressive symptoms had higher PHQ-9 total scores than those with elevated symptoms of depression alone (16.1 ± 4.3 versus 12.7 ± 2.9 , $p < 0.001$; Cohen's $d = 0.86$) and higher GAD-7 total scores than those with elevated symptoms of anxiety alone (14.0 ± 3.1 versus 12.5 ± 2.7 , $p < 0.001$; Cohen's $d = 0.48$). Similar patterns were found for participants with type 2 diabetes, with PHQ-9 total scores 16.9 ± 4.5 and 12.6 ± 2.6 ($p < 0.001$; Cohen's $d = 1.01$) and GAD-7 total scores 14.2 ± 3.4 and 12.1 ± 2.3 ($p < 0.001$; Cohen's $d = 0.62$).

Table 2 displays the results for the multinomial logistic regression analyses, stratified by diabetes type. Compared with participants reporting no/minimal anxiety and depression symptoms (reference group), participants in all three other groups (elevated symptoms of anxiety alone, elevated symptoms of depression alone, elevated symptoms of comorbid anxiety/depression) were more likely to be of younger

age. They were also more likely to have comorbid vascular conditions, with the exception of elevated symptoms of anxiety alone in the type 2 diabetes group. The odds of having comorbid vascular conditions were highest in the group with comorbid elevated symptoms of anxiety/depression. Elevated symptoms of depression alone were associated with increased odds of being female in both diabetes groups and with increased odds of low educational level in type 1 diabetes. In type 2 diabetes, elevated symptoms of anxiety alone and elevated symptoms of depression alone were associated with diabetes duration and insulin use. Participants with elevated symptoms of anxiety alone had a longer diabetes duration and were less likely to use insulin and participants with elevated symptoms of depression alone had a shorter duration and were more likely to use insulin, compared with the reference group. In type 1 diabetes, participants with comorbid elevated symptoms of anxiety/depression had shorter diabetes duration. The full model of demographic and clinical correlates explained 6% of variance in anxiety/depression symptom status for type 1 diabetes and 7% for type 2 diabetes.

Table 3 displays the results of the logistic regression analyses with anxiety/depression symptom status as independent variable (reference group: no/minimal symptoms) and various self-care behaviors as dependent factors, adjusted for demographics and clinical factors. In a first overall visual inspection of the odds ratios for elevated symptoms of anxiety alone, elevated symptoms of depression alone, and comorbid elevated symptoms of anxiety/depression as compared to the reference group, the odds of suboptimal self-care behaviors were almost always highest for adults with comorbid elevated symptoms of anxiety/depression.

More specifically for the comorbid group, the odds of not taking blood pressure lowering tablets as recommended were higher compared to the reference group for type 1 and type 2 diabetes. For type 2 diabetes, they also had higher odds of not taking their glucose and cholesterol lowering medications as recommended; while, for type 1 diabetes, they were less likely to adjust insulin for special occasions and monitor their glucose levels as recommended. Inspecting feet less than once a week was the only self-care behavior specifically associated with elevated symptoms of depression alone and not with comorbid symptoms and only in type 1 diabetes. People with type 1 diabetes and elevated symptoms of anxiety alone were more likely not to take the number of injections as required compared to the reference group. This relationship was also found for elevated symptoms of depression alone and comorbid elevated symptoms of anxiety/depression.

Regarding general health behaviors, those with comorbid elevated symptoms of anxiety/depression were less likely to meet the recommended guidelines for healthy eating, exercise and were more likely

Table 2
Multinomial logistic regression analyses examining the demographic and clinical correlates of (a) elevated symptoms of anxiety alone, (b) elevated symptoms of depression alone, (c) comorbid elevated symptoms of anxiety/depression, with no/minimal anxiety/depression symptoms as the reference group.

	Type 1 diabetes			Type 2 diabetes		
	n = 2702			n = 3612		
	Elevated anxiety symptoms alone	Elevated depression symptoms alone	Comorbid elevated anxiety/depression symptoms	Elevated anxiety symptoms alone	Elevated depression symptoms alone	Comorbid elevated anxiety/depression symptoms
	n = 61	n = 222	n = 232	n = 57	n = 385	n = 322
Female gender	0.89 (0.52–1.51)	1.44 (1.06–1.95) [†]	1.26 (0.94–1.70)	1.25 (0.72–2.14)	1.57 (1.26–1.97) [§]	1.19 (0.93–1.51)
Age	0.98 (0.96–0.99) [†]	0.98 (0.97–0.99) [‡]	0.98 (0.97–0.99) [§]	0.95 (0.92–0.97) [§]	0.96 (0.95–0.98) [§]	0.95 (0.94–0.96) [§]
Low education	0.74 (0.26–2.10)	1.58 (1.04–2.41) [†]	1.17 (0.73–1.86)	1.09 (0.55–2.15)	0.97 (0.74–1.28)	1.30 (0.98–1.72)
Diabetes duration	0.99 (0.96–1.01)	1.00 (0.98–1.01)	0.98 (0.97–0.99) [‡]	1.05 (1.01–1.09) [†]	0.98 (0.96–0.99) [†]	1.01 (0.99–1.03)
Insulin treatment (type 2 only)	NA	NA	NA	0.30 (0.16–0.60) [‡]	1.40 (1.10–1.77) [‡]	1.16 (0.90–1.51)
Comorbid vascular conditions ^a	2.12 (1.14–3.94) [†]	2.48 (1.78–3.45) [§]	3.34 (2.41–4.61) [§]	1.06 (0.58–1.92)	2.00 (1.59–2.51) [§]	2.29 (1.79–2.93) [§]

Values are OR (95% CI).

No/minimal symptoms is GAD-7 < 10 and PHQ-9 < 10; elevated symptoms of anxiety alone is GAD-7 ≥ 10 and PHQ-9 < 10; elevated symptoms of depression alone is GAD-7 < 10 and PHQ-9 ≥ 10; and comorbid elevated symptoms of anxiety/depression is GAD-7 ≥ 10 and PHQ-9 ≥ 10. NA: not applicable.

^a Heart disease, stroke, peripheral arterial disease, retinopathy, neuropathy, kidney problems.

[†] $p < 0.05$.

[‡] $p < 0.01$.

[§] $p < 0.001$.

Table 3

Logistic regression analyses examining the relation of (a) elevated symptoms of anxiety alone, (b) elevated symptoms of depression alone, (c) comorbid elevated symptoms of anxiety/depression (with no anxiety/depression symptoms as the reference group), with suboptimal self-care behaviors, stratified by diabetes type.

Health behavior	Type 1 diabetes (<i>n</i> differs per behavior)				Type 2 diabetes (<i>n</i> differs per behavior)			
	Suboptimal behavior	Elevated anxiety symptoms alone	Elevated depression symptoms alone	Comorbid elevated anxiety/depression symptoms	Suboptimal behavior	Elevated anxiety symptoms alone	Elevated depression symptoms alone	Comorbid elevated anxiety/depression symptoms
Insulin injections	13% (235)	2.82 (1.42–5.62)*	2.99 (1.94–4.61)*	3.16 (2.13–4.69)*	13% (197)	1.46 (0.31–6.96)	1.29 (0.81–2.06)	1.52 (0.93–2.46)
Insulin adjustments (injections or pump)	63% (1692)	1.05 (0.61–1.79)	1.18 (0.87–1.58)	1.40 (1.03–1.89)*	NA	NA	NA	NA
Self-monitoring of blood glucose	39% (1034)	1.29 (0.75–2.21)	1.14 (0.85–1.52)	1.56 (1.17–2.07)*	NA	NA	NA	NA
Blood glucose lowering tablets	NA	NA	NA	NA	14% (404)	1.31 (0.57–3.01)	1.39 (0.99–1.95)	2.49 (1.81–3.42)*
Cholesterol lowering tablets	20% (187)	0.66 (0.14–3.00)	1.32 (0.76–2.28)	1.58 (0.94–2.66)	21% (556)	1.23 (0.57–2.63)	1.12 (0.81–1.54)	1.71 (1.25–2.33)*
Blood pressure lowering tablets	13% (101)	1.12 (0.24–5.19)	1.78 (0.89–3.56)	2.42 (1.16–5.04)*	17% (411)	1.21 (0.49–2.97)	1.31 (0.92–1.87)	2.22 (1.59–3.11)*
Healthy diet	12% (302)	1.59 (0.76–3.31)	2.41 (1.65–3.53)*	3.47 (2.44–4.93)*	13% (475)	1.40 (0.62–3.16)	3.75 (2.86–4.93)*	4.63 (3.50–6.14)*
Healthy exercise	36% (987)	0.96 (0.56–1.66)	2.28 (1.72–3.03)*	2.54 (1.92–3.37)*	43% (1640)	1.64 (0.96–2.79)	2.75 (2.20–3.45)*	2.75 (2.15–3.52)*
Inspecting feet	27% (740)	1.42 (0.81–2.49)	1.76 (1.30–2.38)*	0.81 (0.58–1.14)	17% (608)	1.18 (0.61–2.29)	1.03 (0.77–1.38)	0.98 (0.70–1.36)
Not smoking daily	12% (322)	1.40 (0.65–3.01)	2.16 (1.48–3.15)*	2.30 (1.60–3.31)*	9% (336)	0.89 (0.32–2.50)	1.56 (1.11–2.19)*	2.20 (1.58–3.06)*

Values are % (*n*) or OR (95% CI). Odds ratios are adjusted for gender, age, education, diabetes duration, comorbid vascular conditions, and insulin use (type 2 diabetes only). Suboptimal behavior was defined as any response lower than (“almost”) always for all medication taking items and adjusting insulin dosage (type 1 diabetes only); any response lower than “regularly” for diet and exercise; <28 measurements per week for self-monitoring of blood glucose (type 1 diabetes only); less than one inspection of feet per week; and daily smoking. NA: not applicable.

* $p < 0.05$.

to be smokers compared to the reference group. This was also the case for both types of diabetes and elevated symptoms of depression alone.

4. Discussion

In this large combined study of Australian and Dutch adults with type 1 and type 2 diabetes, comorbid elevated symptoms of anxiety/depression based on questionnaires were present in 9% of participants, elevated symptoms of anxiety alone in 2% and elevated symptoms of depression alone in 8 and 11% of adults with type 1 and type 2 diabetes respectively. In type 1 diabetes, only a shorter diabetes duration distinguished people with comorbid symptoms from those with elevated symptoms of anxiety alone or elevated symptoms of depression alone. In type 2 diabetes, none of the examined demographic and clinical correlates uniquely distinguished those with comorbid elevated symptoms of anxiety/depression from those with elevated symptoms of anxiety or depression alone.

The rates of comorbid elevated symptoms and elevated symptoms of anxiety alone observed here are comparable to previous studies in type 2 diabetes using the PHQ-9 and GAD-7 with total score cut-off ≥ 10 , while the rate of elevated symptoms of depression alone was slightly higher compared to the 6% reported earlier.¹⁸ This difference appeared driven by a somewhat higher rate of elevated symptoms of depression alone in the Australian compared to the Dutch Diabetes MILES subsample. Using the same measures but a lower cut-off score validated for the primary care setting, previous research has shown similar prevalence rates.²⁵ Studies using other self-report measures have found considerably higher rates for comorbid elevated symptoms of anxiety/depression (38%) and elevated symptoms of anxiety alone (8% and 18% respectively), but lower rates of elevated symptoms of depression alone (5%).^{13,26} Apart from differences in sample characteristics, these diverging prevalence estimates could be associated with the item content of the measures. It is important to note that both the PHQ-9 and GAD-7 appear to follow the DSM criteria more closely than

other anxiety and depression symptom scales, hence our decision to use them in the Diabetes MILES studies. Bruce et al. used the PHQ-9 and GAD-7 but reported a prevalence rate of 3% for depression alone, 2% for anxiety alone and 3% for comorbid anxiety/depression in adults with type 2 diabetes.¹² These lower rates of depression are likely explained by the fact that Bruce et al. used a diagnostic algorithm rather than the total score method, which does not impose the diagnostic restriction that at least one of the two core symptoms of depression (dysphoria or anhedonia) needs to be present.

Irrespective of diabetes type, participants with comorbid elevated symptoms of anxiety/depression had more severe symptoms than those with elevated anxiety or elevated depressive symptoms alone (moderate and large effect sizes, respectively). Similar results were found by Smith et al. in their sample of adults with type 2 diabetes.¹⁸ These relationships also appear to exist in the general population, where comorbid anxiety and depression have been associated not only with more severe symptomatology but also with increased disability and a higher frequency of therapist contact.²⁷ However, the relationship is especially relevant in people with diabetes, as comorbid anxiety/depression is more prevalent in this group than in those without this condition, and as diabetes is associated with greater intensity of care and suboptimal outcomes of psychological therapy.^{17,28}

The only factor uniquely distinguishing those with comorbid elevated symptoms of anxiety/depression was a shorter diabetes duration, and only in those with type 1 diabetes. An explanation for this finding remains speculative, as most participants have lived with the diagnosis of type 1 diabetes for several years. With regard to the association between emotional comorbidity and self-care behaviors, the results of our study are mixed. The odds for most suboptimal diabetes self-care behaviors were significantly higher in those with comorbid elevated symptoms of anxiety and depression but not in those with elevated symptoms of anxiety or depression alone, compared to those with no/minimal anxiety/depression symptoms. As for more general health behaviors, those with comorbid elevated symptoms of anxiety/depression

as well as those with elevated symptoms of depression alone were less likely to meet recommended targets for diet and exercise, and were more likely to smoke. Smith et al. also found that people with elevated symptoms of depression alone and those with comorbid elevated symptoms of anxiety/depression did not differ in terms of smoking, physical activity or eating habits.¹⁸

Limitations of this study include the lack of a diagnostic interview for anxiety and depression, self-report of clinical data and health behaviors and the relatively low number of people with elevated symptoms of anxiety only (thus limiting the type of analyses and number of predictors that could be examined). Due to the number of missing values, the potential for self-report error and bias, and a problem with the HbA_{1c} data in the Australian study, both HbA_{1c} and Body Mass Index were excluded from the analyses. It could be that the mediating factors in the relation between comorbid elevated symptoms of anxiety/depression and suboptimal health outcomes are pathophysiological rather than behavioral. For example, it has been suggested that the coexistence of depressive and anxiety symptoms aggravates the dysregulation of the hypothalamic-pituitary-adrenal axis.²⁶ Future research should also examine the role of diabetes-specific distress in these relations. Strengths include the large samples of adults with type 1 and type 2 diabetes enabling analyses by diabetes type and anxiety/depression symptoms subgroup, and the diversity in measured demographic, clinical and psychological data derived from validated measures.

Given the low prevalence of elevated symptoms of anxiety alone in this study, the relationship between symptoms of anxiety and behavior needs to be interpreted with caution. However, if anxiety has a dampening rather than an exaggerating effect on the negative health effects of depression as suggested by some, we would have expected clearer differences between those with comorbid symptoms and those with depression symptoms alone. However, it could be that we did not study the most relevant health behaviors. For example, Huang et al. reported that health visits were higher among people with diabetes and comorbid anxiety disorders than among those without anxiety disorders.²⁹ Future research needs to examine the motivational aspects of anxiety, e.g. through additional quantitative analyses focusing on health care consumption or through interviews with people from all four anxiety/depression groups about their health perceptions and decisions.

Apart from potentially negative effects on physical health, comorbid anxiety/depression could have other relevance for clinical practice. Most notably, this group reported a higher severity of anxiety/depressive symptoms. Additional attention to people presenting with this comorbidity is therefore warranted when planning treatment and allocating resources. Unfortunately, but unsurprisingly, neither the present study or any previous work has been able to identify a clear demographic/clinical profile that distinguishes those with comorbid anxiety/depression from those with anxiety or depression alone. Meanwhile, it is important that health professionals screen for psychological comorbidity, by putting it on the agenda in regular care and using questionnaires, as effective treatments for anxiety and depression are available.^{30,31} Apart from medication, cognitive behavioral therapy and mindfulness-based interventions have both proved their merit in this respect.^{32,33} Treatment could be introduced according to the stepped care model and might be especially successful when simultaneously taking into account the distress specific to living with diabetes.^{34,35} The implications of comorbid (elevated symptoms of) anxiety/depression for treatment design and implementation could be further explored in planned interventions or be the focus of secondary data analyses of existing trials.

In summary, in a large Australian and Dutch sample of adults with type 1 or type 2 diabetes, those with comorbid elevated symptoms of anxiety/depression were more likely to have sub-optimal diabetes self-care behaviors compared with the reference group (no/minimal anxiety/depression symptoms). They were also less likely to meet recommendations for healthy lifestyle. However, this was also the case for those

with elevated symptoms of depression alone, confirming (irrespective of comorbid anxiety) the importance of depression as a driver of sub-optimal self-care.

Acknowledgements

The Diabetes MILES–Australia 2011 Survey was funded by a National Diabetes Services Scheme (NDSS) Strategic Development Grant. The NDSS is an initiative of the Australia Government administered with the assistance of Diabetes Australia. NDSS funding supported data collection (including distribution, return and scanning of postal surveys; the development of the online survey). In addition, Diabetes MILES–Australia received an unrestricted educational grant from sanofi-aventis to support the development of the study website. JLB, CH and JS were supported by the core funding provided to The Australian Centre for Behavioural Research in Diabetes (ACBRD) by Diabetes Victoria and Deakin University.

The Diabetes MILES – The Netherlands Study was supported by the Prof. dr. J. Terpstra Young Investigator Award 2010 from the Dutch Association for Diabetes Research (Nederlandse Vereniging voor Diabetes Onderzoek)/Lilly Diabetes to GN. We thank the Dutch Diabetes Association and the Dutch Diabetes Research Foundation for their kind and very valuable assistance in the recruitment of participants.

The funding bodies had no role in the design, data collection, analysis or interpretation of the study, or in the decision to submit the manuscript for publication. In particular, we thank all people with diabetes who participated in the Diabetes MILES studies in Australia and The Netherlands.

Author contributions

JS and FP lead the Diabetes MILES Study International Collaborative. GN and CH researched data and wrote the manuscript. PR, JLB, MB, JD, MK, JS, and FP reviewed/edited the manuscript. All authors take responsibility for the contents of the article and approve the final version.

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