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Depression in diabetes mellitus

van der Feltz-Cornelis, C.M.

Published in:
The British Journal of Diabetes and Vascular Disease

DOI:
[10.1177/1474651411423539](https://doi.org/10.1177/1474651411423539)

Publication date:
2011

Document Version
Publisher's PDF, also known as Version of record

[Link to publication in Tilburg University Research Portal](#)

Citation for published version (APA):
van der Feltz-Cornelis, C. M. (2011). Depression in diabetes mellitus: To screen or not to screen? A patient-centred approach. *The British Journal of Diabetes and Vascular Disease*, 11(6), 276-281.
<https://doi.org/10.1177/1474651411423539>

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Christina M van der Feltz-Cornelis

British Journal of Diabetes & Vascular Disease 2011 11: 276

DOI: 10.1177/1474651411423539

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Depression in diabetes mellitus: to screen or not to screen? A patient-centred approach

CHRISTINA M VAN DER FELTZ-CORNELIS

Abstract

Background

Comorbid major depressive disorder (MDD) occurs frequently in diabetes mellitus and is associated with high symptom burden, disability and costs. Effective treatments are available but persons with diabetes with comorbid MDD are generally under-detected. A survey showed that comorbid MDD should be identified in a systematic way, such as by screening.

Aim

To identify and describe possible strategies to screen for MDD in persons with diabetes.

Method

After a survey exploring patients' needs, a description of best practice is provided based on a review of the literature and clinical experience.

Results

Valid instruments for screening are the Center for Epidemiological Studies-Depression Scale (CES-D), the Beck Depression Inventory (BDI), and the Patient Health Questionnaire (PHQ-9). Research shows that screening and informing patients and physicians about comorbid MDD in diabetes is inadequate and more intensive treatment as follow-up is needed to change treatment and outcomes. Screening should identify patients willing and able to follow treatment if comorbid MDD is detected and should be followed by a stepwise approach to tailor treatment to patient need and ability.

Conclusion

Screening is best performed in a clinical setting, not by mail, and may be achieved by healthcare professionals using a collaborative care model.

Br J Diabetes Vasc Dis 2011;**11**:276-281.

Keywords: best practice, depression, diabetes mellitus, patient-centred, review, screening, stepped care, treatment

Department of Clinical Psychology, Tilburg University, Tilburg, the Netherlands; Trimbos Institute, Utrecht; GGZ Breburg, Tilburg, the Netherlands.

Corresponding author: Prof Dr Christina M van der Feltz-Cornelis
Tilburg University, Faculty of Social Sciences, Department of Clinical Psychology, PO Box 90531, 5000 LE Tilburg, the Netherlands.
Tel: +31 134662167; Fax: +31 134662067
E-mail: c.m.vdrfeltz@uvt.nl

Christina M van der Feltz-Cornelis

Abbreviations and acronyms

BDI	Beck Depression Inventory
CES-D	Center for Epidemiological Studies-Depression Scale
CIDI	Composite International Diagnostic Interview
DDD	Diabetes and Depression Dialogue
DMI	Depression in the Medically Ill Questionnaire
DSM-IV	<i>Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition</i>
GAMIAN	Global Alliance of Mental Illness Advocacy Networks
HbA _{1c}	glycated haemoglobin A _{1c}
HADS	Hospital Anxiety and Depression Scale
MDD	major depressive disorder
MINI	Mini-International Neuropsychiatric Interview
PHQ-9	Patient Health Questionnaire
QALY	quality-adjusted life year
SCAD	Silverstone Concise Assessment for Depression

Introduction

Depressive symptoms occur as often in patients with diabetes mellitus as in those with cerebrovascular accident and acute cardiac symptoms, with a range from 31 to 33%.¹ Several reviews indicate that the prevalence of comorbid MDD in persons with diabetes ranges from 11 to 33% and that this comorbidity is associated with high symptom burden and disability.^{2,3} A mail survey of 4,168 persons with diabetes found that 'those with major depression (n=487) reported significantly more diabetic

symptoms (mean = 4.40) than participants without depression (mean = 2.46). The nine factors considered symptomatic of diabetes were cold/numb hands and feet, polyuria, excessive hunger, abnormal thirst, shakiness, blurred vision, feeling faint and feeling sleepy. The overall number of diabetic symptoms was significantly related to the number of depressive symptoms.⁴ Comorbid depressive symptoms are associated with poor glycaemic control⁵ and an increased number and severity of complications of diabetes in terms of microvascular and macrovascular complications.⁶ A systematic review of 12 studies on depression and 13 on anxiety showed that, compared with non-depressed persons with diabetes, the odds were three times greater that depressed persons with diabetes would be noncompliant with medical treatment recommendations. No such association was found in the studies concerning anxiety.⁷ The clinician should therefore be aware that self-management of diabetes may be impaired in patients with comorbid MDD, with less physical activity, less compliance with dietary advice, less adherence to treatment advice and greater difficulty to stop smoking.⁸ Comorbid MDD in diabetes decreases the ability to work and leads to higher absenteeism.⁹ It is also linked to a decreased quality of life¹⁰ and with high healthcare use and costs.¹¹

In an e-mail survey conducted by the Trimbos Instituut and the DDD with the GAMIAN-EUROPE and GAMIAN-ISRAEL patient organisations, persons with diabetes were asked about their needs with regard to depressive symptoms linked to diabetes.¹² They indicated needs in terms of recognition of the comorbid condition and treatment. Concerning the recognition of the condition, they indicated that the clinician and mental healthcare professionals who treated them needed to be aware of the possibility of comorbid MDD in diabetes. They also asked for training of mental health professionals to explore this and of diabetes professionals to routinely screen for depression. Moreover, they also expressed the need for an easy tool to routinely screen patients with diabetes for MDD.

Regarding treatment, persons with diabetes described the need for professional expert care with an integrated holistic and individual approach. They wanted treatment with medicines with fewer side-effects, information and psycho-education, relapse prevention treatment and consultations with psychologists and diet specialists on a regular basis. They preferred this to be provisioned in one setting within a combined treatment programme. The survey therefore generated qualitative input about patients' needs concerning comorbid MDD in diabetes, which may be used for clinical work and research.

In a survey held during a South Asian regional meeting in Hong Kong in March 2011 on diabetes treatment with 100 diabetes specialists, 71 responded and only approximately 30% indicated that they would screen their patients for comorbid MDD.¹³ Low recognition of comorbid depression in diabetes by non-psychiatric physicians has also been described in the USA.¹⁴ In the UK, a survey performed among doctors and nurses in 464 UK diabetes centres assessed the availability of psychological services for people with diabetes in the UK, as well as compliance with national guidelines and skills of the diabetes team in psychological aspects of diabetes management.¹⁵

Of these, 267 responded and 53 were interviewed. Less than one third (84) of the responding centres had access to specialist psychological services, over two-thirds (182) of the centres had not implemented the majority of national guidelines and only 2.6% of the centres met all the guidelines. Most (81%) expert providers interviewed by telephone were under-resourced to meet the psychological needs of their patients. The authors concluded that expert psychological support was not available to the majority of diabetes centres.

Nevertheless, not many studies have been performed evaluating the effect of screening for MDD in diabetes mellitus. Some studies have screened for MDD in the primary care setting. A study by Valenstein *et al.* reported that annual and periodic screening for MDD in the primary care setting cost more than \$50,000/QALY, but that one-off screening was cost effective.¹⁶ They suggested that cost effectiveness of screening may improve if treatment becomes more effective. A Cochrane review and meta analysis performed by Gilbody *et al.* concluded that if used without further instruction or support for the clinician, case-finding or screening questionnaires for depression had little impact on the detection and management of depression by clinicians.¹⁷

As there is a clear discrepancy between the needs of the patients and the actual clinical practice concerning screening, this article describes the rationale and requirements for screening and suggests a practical approach for the clinical setting that may meet the needs of people with comorbid diabetes and depression.

Requirements for screening

Screening procedures require (1) a clear description of the condition for which screening is needed, (2) availability of effective treatment as follow-up strategy to the screening, (3) a valid instrument for detecting the condition by screening, and (4) persons with diabetes willing to collaborate with screening and follow-up treatment. This implies that screening should be followed by proposing a suitable treatment to persons with diabetes diagnosed with comorbid MDD.

Description of the condition

As screening should be followed by proper treatment advice and persons with diabetes should be eager to follow this advice, screening should aim to identify not only if depressive symptoms are present, but also the severity of the symptoms in terms of burden for the patient, given that high symptom burden is associated with motivation to be treated. Preferably, the instrument should be able to detect if depressive symptoms are present and if they can be classified as an MDD as described in DSM-IV.¹⁸ The main criteria are shown in table 1.

Availability of effective treatment

A recent systematic review and meta-analysis established that in general, treatment of comorbid MDD in persons with diabetes is more effective than usual care.¹⁹ Providing treatment for comorbid MDD in persons with diabetes improves depressive symptoms to a large extent, no matter which treatment is provided, i.e.

Table 1. Main DSM-IV criteria for major depressive disorder**At least one of the two following symptoms for two weeks, nearly every day:**

- 1) Depressed mood
- 2) Loss of interest or pleasure

Furthermore, at least four of the following extra symptoms:

- 3) Weight loss or decrease or increase in appetite
- 4) Insomnia or hypersomnia
- 5) Psychomotor agitation or retardation
- 6) Fatigue or loss of energy
- 7) Feelings of worthlessness or guilt
- 8) Diminished ability to think or concentrate
- 9) Recurrent thoughts of death, recurrent suicidal ideation without a specific plan or a suicide attempt or a specific plan for committing suicide

psychotherapy with self-management, pharmacotherapy or collaborative care.¹⁷ However, this does not automatically improve glycaemic control and specific interventions are needed for that.¹⁷

Antidepressants

Several studies have evaluated the effects of antidepressants in patients with comorbid MDD in diabetes. Fluoxetine, sertraline, nortriptyline and paroxetine have been reported to significantly improve depressive symptoms.²⁰ Fluoxetine is associated with weight loss, lower glucose and blood lipids.²¹ Sertraline is effective in relapse prevention.²² Sertraline and paroxetine improve comorbid anxiety, quality of life and general functioning.²³ However, these antidepressants show no influence on glycaemic control except for sertraline which reduced HbA_{1c} compared with baseline and placebo.²⁴ The mechanism of this effect of sertraline is unknown. In general, the studies are small and therefore, further research in this field is certainly needed.¹³

Valid instruments for screening

On top of the criteria mentioned above, DSM-IV diagnosis of MDD requires that the symptoms do not include those that are clearly due to a general medical condition. In the case of persons with diabetes a screening instrument would therefore be required to discern between symptoms of MDD and those of diabetes. Studies should be available that test the validity of instruments in identifying MDD in patients with diabetes, assessing the instrument in patients with diabetes and comparing this to the gold standard for diagnosis of MDD, i.e. a clinical interview. Several studies have attempted this and identified the BDI,²⁵ the CES-D²⁶ and the PHQ-9²⁷ as valid instruments for this purpose.

BDI

BDI identifies people with comorbid MDD at a cut-off score ≥ 16 for the entire 21-item measure.²⁵

CES-D

McHale *et al.* found the CES-D to be superior to three other questionnaires, namely the HADS, the SCAD and the DMI, in detecting MDD in persons with diabetes.²⁶

PHQ-9

Van Steenberg-Weijenburg *et al.* validated the PHQ-9 against the MINI as gold standard in 197 patients with type 2 diabetes in a general hospital diabetes outpatient clinic.²⁷ The cut-point of a summed score of ≥ 12 on the PHQ-9 resulted in a sensitivity of 76% and a specificity of 80%. The conclusion was that the PHQ-9 is a valid instrument, but that the cut-point needed is higher than that of ≥ 10 to detect MDD in patients without diabetes.²⁸ With this difference in the cut-point, the PHQ-9 can distinguish symptomatology that may seem depressive from the diabetes symptoms.

Patients willing to collaborate with screening and follow-up treatment

Pouwer *et al.* established that depression screening by CIDI with written feedback to patient and physician had a limited impact on their use of mental healthcare and did not improve depression scores compared with care as usual.²⁹ This strongly suggests that simply providing information after screening is insufficient to change mental healthcare use patterns in patients and improve clinical outcomes. It appears that more intensive depression management is required to improve depression outcomes in those with comorbid MDD in diabetes.²⁹ However, Van Steenberg-Weijenburg *et al.* found that many patients identified with MDD by screening in the hospital outpatient setting did not want to follow such a treatment as they considered it too intensive.²⁷ Therefore, after screening, a step is needed that assesses the motivation of hospital outpatient clinic patients for treatment and that tailors the subsequent treatment steps. This post-screening assessment requires a motivational interview. In view of these findings and of those of Gilbody *et al.*, that screening per se is insufficient to change the recognition and treatment behaviour of the physician,¹⁵ screening in a clinical setting might be better than screening by mail. This can be done by the diabetes physician or by a trained diabetes nurse. Collaboration between physician and nurse in a collaborative care model as elaborated in the Pathways Study³⁰ could be a means to achieve this systematically, while providing the physician and nurse with the organisational support suggested by Gilbody *et al.*¹⁷

Risk profile

Such screening in a clinical setting should be followed by treatment tailored to patient needs in a stepwise approach. For this purpose, a risk profile should be made that charts the comorbid MDD, and the existence of intricate problems associated with diabetes that will need special attention in the treatment process. This is because people with comorbid MDD in diabetes are a heterogeneous group that might contain subtypes of depressions. These subtypes may require different treatment and management.

Subtypes of depression in persons with diabetes

In people with diabetes, MDD may not be a singular biological entity. These persons can have symptoms that appear depressive; however, these are not symptoms of MDD but related to the being ill as a consequence of diabetes. Such patients should be approached with psycho-education and self-management advice. People with diabetes can also have an MDD which is rather similar to an MDD in patients without chronic illness. In such a case, treatment with the main focus on the MDD is probably enough to improve the clinical condition and depressive outcomes. However, the person's MDD may also be closely associated with complicated diabetes. For example, it has been established that occurrence of comorbid MDD in persons with diabetes correlates with the occurrence and number of complications. Persons with diabetes with two or more complications have a more than twice elevated risk of comorbid MDD.³¹ A person with such a profile will need treatment for the MDD, and special attention on self-management and case-management of diabetes. A person with diabetes may have complicated or brittle diabetes and thus be at risk of developing an MDD, but not have it yet. Screening not only for MDD but also assessing if intricate problems associated with the diabetes exist can determine the need for preventive self-management or close monitoring of such a patient. Therefore, screening should not only detect MDD but also identify persons in need of specific interventions aimed at glycaemic control or management of complications. The risk profile and subsequent indications for stepwise treatment can be charted as in table 2.

Table 2. Risk profile and treatment indication

	MDD as indicated by PHQ-9, CES-D or BDI and clinical interview	No MDD
Diabetic hypoglycaemia, brittle diabetes, hyperglycaemia, micro- and macrovascular complications	Treatment should address diabetes management as well as MDD	Preventive attention to self-management may be provided
No such diabetes-associated intricate problems	Treatment should primarily address MDD	Monitoring is sufficient

Key: BDI = Beck Depression Inventory; CES-D = Center for Epidemiological Studies-Depression Scale; MDD = major depressive disorder; PHQ-9 = Patient Health Questionnaire

Screening: a recommended approach

The following best practice for screening, with tailored treatment steps as follow-up, has been recommended for clinical settings.³² This stepwise approach is shown in figure 1 and summarised here.

Figure 1. Screening and stepwise patient-centred treatment for comorbid major depressive disorder in diabetes in the clinical setting

Key: PHQ-9 = Patient Health Questionnaire

The first step is to look for intricate problems of comorbid depression. These can include biological phenomena, such as elevated glucose level or neuropathic pain, and healthcare utilisation behaviour, such as signs of less self-management, missed appointments or high healthcare use, dissatisfaction with care, and diminished trust in healthcare providers.

The second step is to look for signs of distress. This can be emotional distress, such as feelings of helplessness, 'giving up', demoralisation or being overwhelmed with managing diabetes. The distress can be cognitive, such as the inability to discern anxiety from diabetes symptoms, such as hypoglycaemia. The distress can also be expressed as emotional behavioural reactions that interfere with the management of diabetes, for example, emotional eating as a response to grief, loneliness or anger, bulimia, purging, or eating at night. In the case of such signs, screening for MDD in the clinical setting is recommended, by the PHQ-9 questionnaire, using a score of ≥ 12 as the cut-point.

If MDD is diagnosed in such a screening, the next step is to improve diabetes self-management, as self-management is often impaired in MDD and needs specific attention to prevent worsening of diabetes. The clinician can improve this by exploring if 'loss of control' of self-management in illness occurs in the patient, or a lack of insight into the bidirectional association between stress and sub-optimal self-management. If this is the case, the clinician should explain to the patient the difference between MDD and 'stress' and the overlap with diabetes symptoms, as well as depression-related symptom amplification. They can then identify and prioritise self-management tasks together.

It may be that the patient needs support in fulfilling these self-management tasks. Support can be provided by short-term psychotherapy, preferably in the same clinical setting. Supportive diabetes education from specialist nurses can also be of great value. Also, in the case of not being able to identify and prioritise problems, problem-solving treatment can be offered and if there is a lack of adherence to treatment, motivational interviewing might be useful, which might be performed by trained nurses. A recent pilot described screening for psychological problems and common mental disorder by diabetes nurses, followed by a psycho-educational and motivational intervention by those nurses, as a feasible method with positive outcomes in an open design.³³ If the patient suffers from moderate to severe depressive disorder or significant neuropathy, antidepressant medication may be needed as well.

Conclusion

The needs expressed by persons with diabetes, the high prevalence of MDD and the availability of effective treatment interventions warrant screening for comorbid MDD in diabetes via a patient-centred approach. Screening can be done by CES-D, BDI or PHQ-9, which are valid instruments for detecting MDD in persons with diabetes. Research shows that screening and informing both the patient and the physician about comorbid MDD in diabetes is not enough to change treatment and outcomes. More intensive treatment as follow-up after screening is needed. However, screening should include a risk profile of the

Key messages

- Comorbid depression in diabetes mellitus occurs frequently and is associated with a high symptom burden, more complications, lower quality of life and higher disability and costs
- CES-D, BDI and PHQ-9 are validated instruments for screening for comorbid major depressive disorder in diabetes mellitus
- More intensive treatment as follow-up is needed
- Screening is best performed in the clinical setting, not by mail

patient in order to tailor stepwise follow-up treatment and identify the patients willing and able to follow the treatment. For these reasons, screening is best performed in the clinical setting by the diabetes physician or by a trained diabetes nurse such as in a collaborative care model.

Acknowledgements

Corine Stoop, MSc, performed the survey with assistance of Cathy Lloyd and Helen Millar from the DDD, the Dialogue on Diabetes and Depression — the international collaborative effort addressing problems related to the comorbidity of diabetes and depression — and GAMIAN Europe and GAMIAN Israel. Yoram Cohen, vice president of GAMIAN EUROPE, presented these findings first in a Symposium of DDD in Athens, 2009. Anna Muntingh, MSc Trimbos Instituut, assisted with the layout of figure 1. Prof Dr Frank Snoek, PhD, VU University Amsterdam, assisted with the layout of table 2.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflict of interest

In the last three years, Prof Dr van der Feltz-Cornelis has received royalties for books written on the topic of psychiatry. Trimbos Instituut received a grant from Eli Lilly for her writing a systematic review and presenting a lecture on diabetes and depression.

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