MANAGEMENT PERSPECTIVE

Comorbid diabetes and depression: do E-health treatments achieve better diabetes control?



Christina van der Feltz-Cornelis*

Practice Points

- Treatment of comorbid depression in diabetes mellitus is effective in achieving improvement of depression outcomes, with the largest effects seen for psychotherapy and pharmacotherapy.
- However, treatment effects are inconclusive or small in terms of diabetes control; the effects of face-to-face psychotherapeutic treatment and pharmacotherapy are largest.
- Treatment with E-health and M-health so far shows disappointing results. Effects on diabetes control are small to nil, and mortality rates may be higher, demonstrating that newer treatments are not always better.
- Claims of cost-effectiveness of E-health so far have not been substantiated for this kind of treatment either and there is no basis for grand-scale implementation of E-health or M-health at the moment.
- Future research should be aimed at interventions combining depression treatment with treatment specifically aimed at diabetes control, taking into account not only glycemic control, but also complications and mortality, in patients with depression and diabetes.
- Future research should evaluate blended models combining E-health with clinical care, which may have the best potential.

SUMMARY Research in the field of comorbid depression in diabetes shows that the optimum treatment to attain better diabetes disease control is still undecided. Although several treatment models are effective and available, interventions aimed at improving disease control, such as glycemic control, are less effective, with moderate evidence for pharmacological treatment and a lot of evidence for psychotherapy in combination with self-management techniques. New developments such as M-health and E-health are much less effective and show much less effect in terms of glycemic control than earlier developed, face-to-face psychotherapeutic treatments, and demonstrate higher mortality rates in patients with diabetes mellitus or with multimorbidity, which gives reason for caution in the evaluation, testing and implementation of E-health and M-health models in patients with diabetes and depression. Further research into blended E-health models, in which the clinical diagnostic and treatment evaluation is strongly embedded, and with a focus not only on depression treatment, but also on diabetes control and taking mortality into account as outcome, is needed.

^{*}Tilburg University, Tranzo department, TIAS building T620, Postbox 90153, 5000 LE, Tilburg, The Netherlands; GGz Breburg, Tilburg, The Netherlands; and Trimbos Instituut, Utrecht, The Netherlands; Tel.: +31 134662969; Fax: +31 134663637; c.m.vdrfeltz@tilburguniversity.edu



The frequent co-occurrence of diabetes mellitus and depression has widely been established in the literature [1-4] and is associated with a lower quality of life [5], lower adherence to diabetes treatment, impaired general functioning, and higher healthcare and loss of productivity costs [6]. Patients with comorbid depression in diabetes mellitus experience a higher symptom burden, independent of severity of the diabetes [7]. Depression is associated with the onset of diabetes mellitus [8] and with the occurrence of complications in patients with diabetes mellitus [9]. The association also works the other way round, as depression was found to occur approximately twice as often in diabetes mellitus patients, with two or more complications in the general hospital setting [10]. The association, therefore, is considered to be bidirectional [11]. The co-occurrence of depression in diabetes mellitus is associated with a negative impact on glycemic control [12-15], and this may be a consequence of less self-management or an expression of depression as a diabetes-related complication (i.e., in diabetes with hard to control hypoglycemias). Co-occurrence of depression is also associated with higher mortality rates in diabetic patients with and without macrovascular complications [16-21]. Quality of life is important in this comorbidity and glycemic control may play an important role in this. This warrants research in which treatment of comorbid depression in diabetes not only evaluates outcome in terms of depression and quality of life, but also in terms of diabetes control, such as glycemic control, complications and mortality.

Several treatments for comorbid depression in diabetes mellitus have been evaluated, such as counseling [22-24], cognitive-behavioral therapy (CBT) [25,26], antidepressant treatment [27-32] and collaborative care [33,34]. A systematic review and meta-analysis evaluating these randomized controlled trials (RCTs) was published in 2010 [35]. Since then, several new RCTs were published that evaluate a new form of therapy for comorbid depression in diabetes, namely E-health (i.e., a web-based CBT intervention) [36] or M-health (mobile health; i.e., a CBT intervention by telephone) [37]. In a large systematic review of 108 systematic reviews, Black et al. identified three main areas of E-health technologies: storing, managing and transmission of data; clinical decision support, which is mostly meant to support the healthcare provider; and facilitating care from a distance (web-based treatments and

M-health) [38]. Such new interventions might be an alternative for chronic medically ill individuals as it can be followed from home and the patient does not have to visit hospital and spend time travelling or in waiting rooms. In addition, such new interventions might be cost effective. Insurance companies and governmental agencies have high expectations from E-health and there is a tendency to implement them rapidly on a grand scale. In light of this, a review is needed that compares the benefits of several treatment modes, including E-health and M-health.

This review aims to address the question: what treatments of comorbid depression in diabetes mellitus can positively impact diabetes disease control, and what evidence for this view has emerged since 2010, with a focus on psychotherapeutic and pharmacotherapeutic versus E-health or M-health interventions? Moreover, this review will address not only depression as an outcome, but also glycemic control and complications, or other outcomes for disease control, such as mortality rates. The review will discuss relevant systematic reviews and RCTs that have been published, starting with the 2010 review [35].

2010 review

A meta-analysis was performed in a total of 1724 patients with diabetes and depression. It showed that treatment is effective in terms of clinical impact - that is, the combination of depression-related outcomes and diabetes control outcomes. The effect sizes differ from small to moderate or large, the latter having an effect size of Cohen's d = 0.5 or higher. The combined effect of all interventions on clinical impact is moderate (-0.370; 95% CI: -0.470 to -0.271); it is large for psychotherapeutic interventions that are often combined with diabetes self-management (-0.581; 95% CI: -0.770 to -0.391; n = 310) and moderate for pharmacological treatment (-0.467; 95% CI: -0.665 to -0.270; n = 281). Pharmacotherapy aimed to reduce depressive symptoms and succeeded but, apart from sertraline, had no effect on glycemic control. The conclusion was that psychotherapy with attention to diabetes mellitus self-management had the best results, closely followed by antidepressive treatment [35]. However, from this review it also became clear that simply treating the depression may improve the depressive symptoms, but is insufficient to improve glycemic control. For improvement of glycemic control, a specific effort seems to

be needed. In addition, this review shows that RCTs evaluating treatment of comorbid depression in diabetes in terms of other diabetes-related outcomes, such as complications and mortality, are lacking. Therefore, there is only limited evidence regarding what treatments are effective for this comorbidity in terms of disease control, such as glycemic control [35].

Cochrane review 2012

Since 2010, one systematic review was published in the Cochrane library that focused on psychotherapeutic and psychopharmacological treatment in diabetes and depression; it included E-health and M-health interventions, labeled as psychotherapeutic interventions [39].

Pharmacological interventions: depression outcomes & diabetes control

The Cochrane review found that antidepressants had a moderate effect on depression severity, which was a similar finding to the 2010 review. Selective serotonin re-uptake inhibitors (SSRIs) had a much lower effect size than other antidepressants. Diabetes complications and mortality have not been examined in the pharmacological intervention trials. Medical adverse events were only reported in the pharmacological RCTs and were rare [39]. Glycemic control improved with a mean difference for glycosylated HbA1c of -0.4% (95% CI: -0.6 to -0.1; p = 0.002) [36].

Interpretation of pharmacotherapeutic outcomes: antidepressants

In terms of depression outcomes as well as glycemic outcomes for pharmacotherapeutic interventions, the findings were in the same vein as those in the 2010 review. The finding that the effect of SSRIs is much lower than that of other antidepressants differs from the finding in the 2010 review. This may be because of the inclusion of some studies that focus on other chronic medical illnesses as well as diabetes, in the Cochrane review. As we focus on diabetes here, we will describe the findings in the 2010 study regarding SSRIs versus other antidepressants. In the 2010 review, most SSRI studies did almost as well as the only non-SSRI study, with nortriptyline, which had a slightly higher effect size; all effect sizes were large except in one small study [31]. Fluoxetine [27,28], sertraline [38], nortryptiline [29] and paroxetine [30-32] yielded significant improvements in depressive symptoms. Fluoxetine was also associated with weight loss, lower

glucose and lipids [27,28]. Sertraline was effective in relapse prevention [40], and both sertraline and paroxetine improved comorbid anxiety, quality of life and general functioning [30-32,40]. There was no influence on glycemic control except in cases of fluoxetine [27,28] and sertraline [40]. Although the improvement of glycemic control seems hopeful, the reported level of improvement (-0.4% of HbA1c) is too low to be clinically relevant in view of regular strategies to improve blood glucose levels such as those described by the Institute for Healthcare Improvement. For example, the range of desirable glucose levels in terms of conventional control is described as 81-180 mg/dl or 4.5-10.0 mmol/l and a difference of -0.4% can be considered to make no clinical difference within that range [101]. The finding in the Cochrane review that the number of medical adverse events was low is similar to findings described earlier, indicating that antidepressants in general can be prescribed safely to patients with diabetes [41,42].

Psychotherapeutic interventions: depression outcomes & diabetes control

Eight RCTs with psychological interventions, including E-health and M-health studies, were included; three more than the 2010 review. They showed similar beneficial effects on depression severity. However, evidence regarding glycemic control in psychological intervention trials and E-health or M-health trials taken together was heterogeneous and inconclusive. This differs from the 2010 review, which found high effects in terms of glycemic control for psychotherapeutic interventions [35]. Diabetes complications and mortality had not been examined in the psychotherapy trials [39].

Interpretation of psychotherapeutic interventions

In order to interpret the inconclusive findings for glycemic control in psychotherapeutic interventions in the Cochrane review compared with the positive findings for psychotherapeutic interventions in the 2010 review, a closer look was taken at the psychotherapeutic intervention studies that have been published since 2010. There were two new psychotherapeutic intervention RCTs specifically aimed at the treatment of comorbid depression in diabetes since 2010. The RCTs with psychotherapeutic interventions and their effect sizes, calculated with a meta-analysis program [101], are shown in Table 1.

Table 1. Psychotherapeutic interventions (n = 856).								
Study (year)	Patients; n (completers)	Diabetes type	Mean age (years) ± SD	Depression at baseline	Intervention conditions	Follow-up		
Lustman <i>et al.</i> (1998)	41 (100%)	Type 2 DM	53.1–56.4 ± 10.5–9.7	MDD according to DIS and BDI ≥14	CBT plus diabetes education vs diabetes education alone	11 weeks, 6 months		
Huang <i>et al.</i> (2002)	59 (100%)	Type 2 DM	-	SDS >50	Antidiabetics plus diabetic education plus psychological treatment plus relaxation and music treatment vs antidiabetics only	3 months		
Li <i>et al</i> . (2003)	120 (not stated)	Type 1 and 2 DM	50.5-52.3 ± 10.4-11.2	SDS ≥50	Antidiabetics plus diabetic education plus psychological treatment vs antidiabetics only	4 weeks		
Lu <i>et al.</i> (2005)	60 (100%)	Type 2 DM	65.6-64.9 ± 9.8-9.5	Mental maladjustment caused by CVA according to the CCMD-2-R and HAMD-17 ≥8	Diabetes and CVA education plus electromyographic treatment plus psychological treatment vs usual care	4 weeks		
Simson <i>et al.</i> (2008)	30 (80%)	Type 1 and 2 DM	60.5 ± 10.9	HADS depression score ≥8 Diabetic foot as DM complication	Individual supportive psychotherapy vs usual care	Discharge (3–20 weeks)		
Piette <i>et al.</i> (2011)	291 (not stated)	Type 1 DM	56 ± 1	BDI ≥14	Telephone CBT counseling for 12 weeks plus monthly boost plus walking vs CAU (M-health)	12 months		
van Bastelaar et al. (2011)	255 (not stated)	Type 1 and 2 DM	50 ± 12	CESD ≥16	8 sessions of web-based CBT vs WL (E-health)			

Δ: Cohen's d (effect size); BDI: Beck Depression Inventory; CAU: Care as usual; CBT: Cognitive—behavioral therapy; CCMD-2-R: Chinese Classification of Mental Disorders, Second Edition, Revised; CESD: Center for Epidemiologic Studies Depression Scale; CVA: Cerebrovascular accident; DIS: Diagnostic Interview Schedule; DM: Diabetes mellitus; HADS: Hospital Anxiety and Depression Scale; HAMD-17: Hamilton Depression Rating Scale; MDD: Major depressive disorder; PAID: Problem areas in diabetes questionnaire; SD: Standard deviation; SDS: Zung Self-Rating Depression Scale; WL: Waiting list.

The third trial in the Cochrane review evaluated a minimal intervention provided by nurses to patients with chronic obstructive pulmonary disease or diabetes [43]; however, the results were disappointing, showing a very small effect on depression outcome and no significant improvement in quality of life or reporting of glycemic control outcomes. Therefore, this RCT is not shown in Table 1.

New psychotherapeutic interventions for depression in diabetes: E-health & M-health

Two RCTs were published that both evaluated a form of E-health (i.e., a web-based CBT intervention) [36] or M-health (i.e., a CBT intervention by telephone) [37]. Compared with the older psychotherapeutic interventions that were delivered in face-to-face contact in clinical settings by therapists, the two new interventions were less successful both in terms of depression outcome and in terms of glycemic control

outcome, with the Cohen's d ranging from 0.00 [36] to -0.045 [37] for glycemic control, which is extremely low. In addition, the E-health CBT study yielded an effect size of only -0.29 for depression outcome [36] and the M-health study yielded an effect size of 0.366 [37]. These small effects are, again, much lower than the effect sizes for the psychotherapy including diabetes self-management improvement RCTs. In other words, the new M-health and E-health psychotherapeutic intervention trials provided worse results in terms of depression outcomes, and much worse effects or no effect at all in terms of glycemic control, compared with older, faceto-face psychotherapeutic treatments. E-health and M-health interventions aim to easily deliver therapy by telephone or by the internet; this is supposed to be practical for patients with a high illness burden, as it spares them the journey to a therapist, and spending time on public transportation and in waiting rooms. However,

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Outcome assessment	Effect size	Comments	Ref.
Depression: response (reduction BDI \geq 50%; p < 0.001) present in CBT group Diabetes: HbA1c lower in CBT group (p < 0.03)	Depression: Δ -1.112 Diabetes: Δ -0.704	Improvement in depression as well as glycemic control in CBT vs control	[25]
Depression: SDS total score difference in means = 0.07 (p < 0.05) Diabetes: HbA1C difference in means = 1.7 (p < 0.05)	Depression: Δ -0.521 Diabetes: Δ -0.521	Improvement in depression as well as glycemic control in CBT vs control	[22]
Depression: SDS total score difference in means = 13.4 (p < 0.01) Diabetes: fasting blood glucose difference in means = 2.09 (p < 0.05)	Depression: Δ -0.478 Diabetes: Δ -0.362	Anxiety (SAS ≥50) taken into account as well. Improvement in depression as well as glycemic control in CBT vs control	[23]
Depression: HAMD-17 total score difference in means = 7.3 (p < 0.01) Diabetes: difference in mean fasting plasma glucose = 1.54 (p < 0.05)	Depression: Δ -0.688 Diabetes: Δ -0.517	Hemiplegia after CVA as DM complication. Improvement in depression as well as glycemic control in CBT vs control	[26]
Depression: HADS depression scale total score mean difference = 1.9 (p = 0.018) Diabetes: PAID mean difference = 7.6 (p = 0.008)	Depression: Δ -0.918 Diabetes: Δ -1.043	Improvement in depression as well as glycemic control in supportive psychotherapy vs control	[24]
Depression: 58 remitted vs 39% remitted in CAU group (p = 0.002) Diabetes: no difference in HbA1c, RR blood pressure = 4.26 mmHg drop vs CAU (p = 0.05)	Depression: Δ -0.366 Diabetes: Δ -0.045	-	[37]
Depression: symptom reduction vs CAU (p < 0.001) Diabetes: no effect on glycemic control (p > 0.05)	Depression: Δ 0.29 Diabetes: Δ 0.00	-	[36]

the impact of this treatment in patients with diabetes and depression in RCTs, so far, is much lower than that of other treatments, or is even zero, as can be seen in Table 1. Clinically delivered psychotherapy, such as CBT plus self-management of diabetes care, still has the best results in diabetes patients with comorbid depression.

■ E-health & M-health in diabetes without depression: how much improvement can be attained in glycemic control by E-health?

In order to enable us to better appraise the possible impact of E-health in attaining glycemic control in diabetes patients if depression does not interfere with treatment, another systematic review that evaluates 40 RCTs in patients with diabetes without comorbid depression may be relevant. The review identified three kinds of interventions: computerized prompting of diabetes care; utilization of home glucose records

in computer-assisted insulin dose adjustment; and computer-assisted diabetes patient education. The results of the systematic review were somewhat disappointing [44]. Although glycated hemoglobin and blood glucose levels were significantly improved, and a meta-analysis of the studies using home glucose records in insulin dose adjustment documented a mean decrease in glycated hemoglobin of 0.14 mmol/l (95% CI: 0.11-0.16) and a decrease in blood glucose of 0.33 mmol/l (95% CI: 0.28-0.39), this was only the case in six or seven trials of the 40 in the review, a very limited number [44]. This level of improvement can be considered as too low to be clinically relevant, in view of regular strategies to improve blood glucose levels, such as those described by the Institute for Healthcare Improvement. For example, the range of glucose levels that is considered desirable (conventional control) is 4.5-10.0 mmol/l or 81-180 mg/l, and a difference of 0.14-0.33 mmol/l can

be considered to make no clinically relevant difference within that range [102].

These results are similar to the finding in the Cochrane review evaluating interventions for comorbid depression in diabetes [39], suggesting that there may not be much difference in the ability to attain glycemic control in diabetes patients with and without comorbid depression. The RCTs evaluating E-health and M-health in diabetes patients with depression [36,37] did not combine the intervention with one of the E-health interventions mentioned in the systematic review above [45], which was specifically aimed at improving glucose control. It would have been interesting to see if such a combination would have produced better results in terms of glycemic control in depressed diabetes patients.

■ E-health & M-health in diabetes without depression: cost-effectiveness is unclear

There are indications that the expectations regarding cost—effectiveness may be overstretched. In a large systematic review of 108 systematic reviews, Black *et al.* found that "There is a large gap between the postulated and empirically demonstrated benefits of E-health technologies. In addition, there is a lack of robust research on the risks of implementing these technologies and their cost—effectiveness has yet to be demonstrated, despite being frequently promoted by policy makers and 'techno-enthusiasts' as if this was a given" [38]. This lack of research regarding cost—effectiveness as an outcome is also lacking in RCTs evaluating treatment of comorbid depression in diabetes, and it is a major concern.

■ E-health & M-health in diabetes without depression: higher mortality

Other studies indicated a lack of safety for E-health interventions. For example, Takahashi et al. performed a RCT with telemonitoring (M-health) aimed at reducing emergency room visits or hospital admissions in elderly patients with three comorbid conditions: chronic obstructive pulmonary disease, heart failure and diabetes. They found that the number of admissions did not decrease in the intervention group, which was an intended aim of the intervention. Furthermore, they found that the mortality rate was increased 14.7% in the M-health group versus 3.9% in the usual care group, a highly disconcerting finding. The M-health intervention, therefore, did not achieve the expected aim and turned out to be less safe than regular care [45].

Regarding the safety of telehealth, another study at first promised good results of a telehealth approach for patients with comorbid diabetes, heart failure or chronic obstructive pulmonary disease; the Whole System Demonstrator cluster randomized trial reported fewer hospital admissions (odds ratio: 0.82; 95% CI: 0.70-0.97; p = 0.017) and lower mortality (odds ratio: 0.54; 95% CI: 0.39-0.75; p < 0.001) in patients receiving the telehealth intervention [46]. However, it was unclear if this was due to the telehealth intervention, as the difference was due to an initial deterioration in the usual care group; and in a comment it was suggested that this might have been an artifact of the trial itself on the delivery of care [47]. Nevertheless, this telehealth intervention is currently being implemented on a grand scale in the UK. These findings bring Chavannes et al. to the conclusion that E-health and M-health should be considered with caution in patients with chronic medical illnesses or multimorbidity [48].

This is highly relevant, as diabetes is very common in patients with multimorbidity [9], and depression is more often a comorbid condition in diabetes with two or more complications [10]. To date, the improvement of glycemic control by E-health interventions in diabetes is, although hopeful, very limited in patients with and without comorbid depression, and the improvement on depressive outcomes of the E-health or M-health interventions in depressed diabetes patients was much smaller than the results of face-to-face CBT. The low effect sizes and higher risk may have been due to healthcare provider withdrawal and patient disengagement that may have not been in accordance with the actual needs of the patient. To date, E-health interventions have been mostly developed from a provider and insurance company perspective; the patient perspective has not been taken into account and this may also play a role in patient disengagement.

Collaborative care, screening & treatment according to the needs of the patient

A recent review exploring delivery of care for patients with comorbid depression in diabetes concluded that, although a lot of basic research exists, as well as some clinical research with relevant outcomes, so far this has insufficiently led to improved treatment and outcomes in diabetes mellitus with comorbid depression [49]. Collaborative care may provide an organizational model of

care suitable for that purpose. Collaborative care implies delivery of care by a team of professionals, ideally a nurse care manager, a general practitioner and a consultant psychiatrist, who aim to address the medical problem of the patient. In two recent systematic reviews it was shown that collaborative care presents good results for treatment of depression and anxiety [50] in patients with and without chronic medical illness, including diabetes [51]. In the 2010 systematic review, collaborative care was found to be effective in the treatment of depression in diabetes, especially in terms of improvement of depression outcomes. Delivery of collaborative care, which provided a stepped care intervention with a choice of starting with psychotherapy or pharmacotherapy, to a primary care population, yielded an effect size of -0.292 (95% CI: -0.429 to -0.155; n = 1133); indicating the effect size that might be attained on a population scale. So far, the effect sizes for collaborative care have been smaller than in the psychotherapeutic or pharmacotherapeutic RCTs, possibly because this treatment is usually delivered in a primary care setting, not a specialist setting [35]. However, this approach certainly has potential, due to the possibility of combining E-health interventions aimed at improved diabetes control with face-to-face depression treatment and treatment aimed at improving self-management. Currently, several new trials are underway [52-55]. Furthermore, it provides the opportunity to include screening in the clinical setting in order to identify depressed patients with diabetes.

A recent review looking into state-of-the-art screening for depression in diabetes mellitus, based on the UK National Screening Committee criteria for appraising screening programs [56], found that there may be a rationale for introducing screening for depression in patients with diabetes mellitus; however, research is needed to evaluate the most clinically effective and costeffective way of doing so in structured screening programs [56]. In another review, screening in the clinical setting is suggested, not only for depression, but also for problems in diabetes management in diabetic patients, and to address both issues depending on their occurrence, whether in combined or separate treatment approaches, in order to attain not only improvement of depression but also better diabetes control [57]. Trained nurses could follow such an approach [58]; however, RCTs evaluating such an approach are still lacking. In view of this, collaborative care may

be useful for future research, as it may provide a proper routing or organization of care so that interventions can be provided in a timely manner. This can be done by introducing screening and the use of risk profiles for addressing the proper mix of interventions depending on the needs of the patient, aimed at depressive symptoms as well as diabetes control.

Conclusion & future perspective

This review shows that there is only a limited number of studies evaluating treatment of depression in diabetes mellitus. In terms of interventions, face-to-face treatment appears to remain the treatment mode of choice, be it psychotherapy or pharmacotherapy. CBT, as well as pharmacotherapy, is effective in terms of depression outcomes, and, to a certain extent, in terms of diabetes control; however, there is certainly a need for interventions that are aimed more directly at controlling diabetes.

Results of E-health and M-health are disappointing so far. Improvement of glycemic control was small, both in diabetes patients with and without depression. Possible health hazards may exist due to withdrawal of the professional when using E-health or M-health, and disengagement of the patient, which is not in accordance with the actual patient needs, especially in diabetic patients with multimorbidity. As depression occurs more frequently in diabetes, especially in patients with diabetes complications, this is a relevant risk factor that should be well explored and weighed against the originally expected benefits of E-health.

As interventions specifically aimed at improving glycemic control by E-health or M-health only show limited results, and in light of the possible risks, RCTs are needed to evaluate other interventions aimed at improved selfmanagement and also address other diabetesrelated outcomes, such as complications and mortality. This is even more important in view of the finding that mortality rates and complications have not been evaluated as outcomes in RCTs for depression in diabetes so far, and indications are that RCTs evaluating E-health and M-health interventions without face-toface treatment contacts have results that are too insignificant from a clinical perspective and may lead to higher mortality rates. In addition, cost-effectiveness of such interventions in comorbid depression in diabetes has been insufficiently substantiated.

Furthermore, studies that evaluate screening plus follow-up as an intervention in diabetes are lacking, despite the fact that patients ask for screening programs. It may well be a question of how cost effective screening programs would be; so cost–effectiveness studies in that field would be needed as well.

■ Future preferred models of management of comorbid depression in diabetes

The future perspective may be that we will have to make an extra effort to actively engage our patients better into treatment, in order to avoid patient disengagement; to develop collaborative care models tailoring treatment to patients needs and risk profiles; and to develop interventions that not only address depression but also diabetes control, as treatment of depression only does not improve glucose levels enough. Collaborative care including psychotherapy with a diabetes self-management approach and combined with blended E-healthcare interventions (which combine E-health with close scrutiny and face-to-face contact by healthcare professionals) may be an option that allows for tailoring interventions to the risk profile and needs of the patient. This approach should aim to reduce complications and mortality risks. It can be expected that such developments will have a considerable impact on diabetes care in the following 5–10 years.

Disclosure

Table 1 was presented by the author in an invited lecture: Evidence based treatment of co-morbid depression in diabetes mellitus patients: treatment effect and diabetes mellitus disease control at the treatment session at the International Conference of Diabetes and Depression, organised by the NIDDK, WA, USA, 9–10 October 2012.

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6 Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive symptoms on adherence, function,

3278–3285 (2000). Ludman EJ, Katon W, Russo J *et al.* Depression and diabetes symptom burden.

Gen. Hosp. Psychiatry 26, 430-436 (2004).

and costs. Arch. Intern. Med. 160,

- 8 Knol MJ, Twisk JW, Beekman AT et al. Depression as a risk factor for the onset of Type 2 diabetes mellitus. A meta-analysis. Diabetologia 49, 837–845 (2006).
- 9 de Groot M, Anderson R, Freedland KE et al. Association of depression and diabetes complications: a meta-analysis. Psychosom. Med. 63, 619–630 (2001).
- Steenbergen-Weijenburg KM, van Puffelen A, Horn EK et al. More co-morbid depression in patients with Type 2 diabetes with multiple complications. An observational study at a specialized outpatient clinic. Diabet. Med. 28(1), 86–89 (2011).
- 11 Golden SH, Lazo M, Carnethon M et al. Examining a bidirectional association between depressive symptoms and diabetes. JAMA 299(23), 2751–2759 (2008).

- 12 Lustman PJ, Clouse RE. Depression in diabetic patients: the relationship between mood and glycemic control. *J. Diabet.* Complications 19(2), 113–122 (2005).
- 13 Lustman PJ, Anderson RJ, Freedland KE et al. Depression and poor glycemic control: a meta-analytic review of the literature. Diabetes Care 23(7), 934–942 (2000).
- 4 Groot M, Jacobson AM, Samson JA et al. Glycemic control and major depression in patients with Type 1 and Type 2 diabetes mellitus. J. Psychosom. Res. 46, 425–435 (1999).
- 15 Ciechanowski PS, Katon WJ, Russo JE et al. The relationship of depressive symptoms to symptom reporting, self-care and glucose control in diabetes. Gen. Hosp. Psychiatry 25, 246–252 (2003).
- 16 Katon WJ, Rutter C, Simon G et al. The association of comorbid depression with mortality in patients with Type 2 diabetes. *Diabetes Care* 28(11), 2668–2672 (2005).
- 17 Katon W, Fan MY, Unutzer J et al. Depression and diabetes: a potentially lethal combination. J. Gen. Int. Med. 23(10), 1571–1575 (2008).

References

Papers of special note have been highlighted as:

- of interest
- of considerable interest
- Anderson RJ, Freedland KE, Clouse RE et al.
 The prevalence of comorbid depression in adults with diabetes: a meta-analysis. *Diabetes Care* 24(6), 1069–1078 (2001).
- 2 Lloyd CE, Dyer PH, Barnett AH. Prevalence of symptoms of depression and anxiety in a diabetes clinic population. *Diabet. Med.* 17(3), 198–202 (2000).
- 3 Ali S, Stone MA, Peters JL et al. The prevalence of co-morbid depression in adults with Type 2 diabetes: a systematic review and meta-analysis. *Diabet. Med.* 23, 1165–1173 (2006).
- 4 Barnard KD, Skinner TC, Peveler R. The prevalence of co-morbid depression in adults with Type 1 diabetes: systematic literature review. *Diabet. Med.* 4, 445–448 (2006).
- Goldney RD, Phillips PJ, Fisher LJ et al. Diabetes, depression, and quality of life: a population study. *Diabetes Care* 27, 1066–1070 (2004).

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- 18 Zhang X, Norris XL, Gregg EW et al. Depressive symptoms and mortality among persons with and without diabetes. Am. J. Epidemiol. 161(7), 652–660 (2005).
- 19 Gallo JJ, Bogner HJ, Morales KH et al. Depression, cardiovascular disease, diabetes, and two-year mortality among older, primary-care patients. Am. J. Ger. Psychiatry 13(9), 748–755 (2005).
- 20 Egede LE, Nietert PJ, Zheng D. Depression and all-cause and coronary heart disease mortality among adults with and without diabetes. *Diabetes Care* 28(6), 1339–1345 (2005).
- 21 Lin EH, Heckbert SR, Rutter CM et al. Depression and increased mortality in diabetes: unexpected causes of death. Ann. Fam. Med. 7(5), 414–421 (2009).
- 22 Huang X, Song L, Li T et al. Effect of health education and psychosocial intervention on depression in patients with Type II diabetes. Chin. Mental Health J. 16, 149–151 (2002).
- 23 Li SC, Li M, Song SJ et al. The effect of psychological intervention in treating the diabetic patients with negative emotion. Shandong J. Psychol. Med. 16, 148 (2003).
- 24 Simson U, Nawarotzky U, Friese G et al. Psychotherapy intervention to reduce depressive symptoms in patients with diabetic foot syndrome. *Diabet. Med.* 25, 206–212 (2008)
- 25 Lustman PJ, Griffith LS, Freedland KE et al. Cognitive behavior therapy for depression in Type 2 diabetes mellitus. A randomized, controlled trial. Ann. Intern. Med. 129, 613–621 (1998).
- 26 Lu XS, Lu BX, Gu X. Cognitive therapy in combination with electromyographic feedback in treatment of diabetes patients with depression after cerebral infarction. *Chin. J. Clin. Psychol.* 13, 215–216 (2005).
- 27 Gulseren L, Gulseren S, Hekimsoy Z et al. Comparison of fluoxetine and paroxetine in Type II diabetes mellitus patients. Arch. Med. Res. 36, 159–165 (2005).
- 28 Lustman PJ, Freedland KE, Griffith LS et al. Fluoxetine for depression in diabetes: a randomized double-blind placebo-controlled trial. *Diabetes Care* 23, 618–623 (2000).
- 29 Lustman PJ, Griffith LS, Clouse RE et al. Effects of nortriptyline on depression and glycemic control in diabetes: results of a double-blind, placebo-controlled trial. Psychosom. Med. 59, 241–250 (1997).
- 30 Paile-Hyvarinen M, Wahlbeck K, Eriksson JG. Quality of life and metabolic status in mildly depressed women with Type 2 diabetes treated with paroxetine: a single-blind randomised

- placebo controlled trial. *BMC Fam. Pract.* 4, 7 (2003)
- 31 Paile-Hyvarinen M, Wahlbeck K, Eriksson JG. Quality of life and metabolic status in mildly depressed patients with Type 2 diabetes treated with paroxetine: a double-blind randomised placebo controlled 6-month trial. BMC Fam. Pract. 8, 34 (2007).
- 32 Xue H. Paroxetine for depression in diabetes: a randomized controlled trial. *Chin. Mental Health J.* 18, 735–737 (2004).
- 33 Katon WJ, Von Korff M, Lin EH et al. The Pathways Study: a randomized trial of collaborative care in patients with diabetes and depression. Arch. Gen. Psychiatry 61, 1042–1049 (2004).
- Williams JW Jr, Katon W, Lin EH et al. The effectiveness of depression care management on diabetes-related outcomes in older patients. Ann. Intern. Med. 140, 1015–1024 (2004).
- 35 van der Feltz-Cornelis CM, Nuyen J, Stoop C et al. Effect of interventions for major depressive disorder and significant depressive symptoms in patients with diabetes mellitus: a systematic review and meta-analysis. Gen. Hosp. Psychiatry 32(4), 380–395 (2010).
- First systematic review and meta-analysis evaluating the effect of interventions for major depression or significant depressive symptoms in patients with diabetes. It is innovative and introduces a new method of synthesizing effects to accomplish a pooled estimate of disease burden. It is among the most cited articles in general hospital psychiatry.
- 36 van Bastelaar K, Pouwer F, Cuijpers P et al. Web-based depression treatment for Type 1 and Type 2 diabetic patients. *Diabetes Care* 34(2), 320–325 (2011).
- 37 Piette JD, Richardson C, Himle J et al. A randomized trial of telephonic counselling plus walking for depressed diabetes patients. Med. Care 49(7), 641–648 (2011).
- 38 Black AD, Car J, Pagliari C et al. The impact of eHealth on the quality and safety of healthcare: a systematic overview. PLoS Med. 8(1), e1000387 (2011).
- Excellent systematic review, synthesizing data from a large body of studies concerning the safety and quality of E-health across settings.
- 39 Baumeister H, Hutter N, Bengel J. Psychological and pharmacological interventions for depression in patients with diabetes mellitus and depression. *Cochrane Database Syst. Rev.* 12, CD008381 (2012).
- Excellent systematic review and meta-analysis evaluating the effect of

- interventions for depression in patients with diabetes and, in some randomized controlled trials, other chronic medical illnesses.
- 40 Echeverry D, Duran P, Bonds C et al. Effect of pharmacological treatment of depression on A1C and quality of life in low-income Hispanics and African Americans with diabetes: a randomized, double-blind, placebo-controlled trial. *Diabetes Care* 32(12), 2156–2160 (2009).
- 41 Goodnick PJ. Use of antidepressants in treatment of comorbid diabetes mellitus and depression as well as in diabetic neuropathy. Ann. Clin. Psychiatry 13, 31–41 (2001).
- 42 Musselman DL, Betan E, Larsen H et al. Relationship of depression to diabetes Types 1 and 2: epidemiology, biology, and treatment. Biol. Psychiatry 54, 317–329 (2003).
- 43 Lamers F, Jonkers C, Bosma H et al. Treating depression in diabetes patients: does a nurse administered minimal psychological intervention affect diabetes-specific quality of life and glycaemic control? A randomized controlled trial. J. Adv. Nursing 67(4), 788–799 (2011).
- 44 Balas EA, Krishna S, Kretschmer RA et al. Computerized knowledge management in diabetes care. Med. Care 42, 610–621 (2004)
- Thorough systematic review of all E-health intervention randomized controlled trials in diabetes patients.
- 45 Takahashi PY, Pecina JL, Upatising Bet al. A randomized controlled trial of telemonitoring in older adults with multiple-health issues to prevent hospitalizations and emergency department visits. Arch. Intern. Med. 172(10), 773–779 (2012).
- ••• Well-performed, groundbreaking randomized, controlled trial, providing evidence for higher mortality of telemonitoring compared with usual care in the multimorbid elderly.
- 46 Steventon A, Bardsley M, Billings J et al. Effect of telehealth on use of secondary care and mortality: findings from the Whole System Demonstrator cluster randomised trial. BMJ 344, e3874 (2012).
- 47 Car J, Huckvale K, Hermens H. Telehealth for long term conditions. *BMJ* 344, e4201 (2012).
- Important comment on the interpretation of the results of Steventon et al. [46] that should not be missed by the reader.
- 48 Chavannes NH, Sont JK, van der Boog PJ Assendelft WJ. [E-Health in chronic diseases:

- not yet feasible for everyone in every setting]. *Ned. Tijdschr. Geneeskd.* 156, A5345 (2012).
- Timely review raising the issue of safety of E-health in the chronic medically ill.
- 49 Roberts RG, Gask L, Arndt B et al. Depression and diabetes: the role and impact of models of healthcare systems. J. Affect. Disord. 142(Suppl.) S80–S88 (2012).
- 50 Archer J, Bower P, Gilbody S et al. Collaborative care for depression and anxiety problems. Cochrane Database Syst. Rev. 10, CD006525 (2012).
- Comprehensive systematic review synthesizing data from a large body of studies concerning the effects of collaborative care for depressive and anxiety disorders.
- 51 Woltmann E, Grogan-Kaylor A, Perron B et al. Comparative effectiveness of collaborative chronic care models for mental health conditions across primary, specialty, and behavioral healthcare settings: systematic review and meta-analysis. Am. J. Psychiatry 169, 790–804 (2012).

- Comprehensive systematic review synthesizing data from studies concerning the effects of collaborative care across treatment settings.
- 52 Katon W, Lin EHB, Von Korff M et al. Collaborative care for patients with depression and chronic illnesses. N. Engl. J. Med. 363, 2611–2620 (2011).
- 53 Harkness E, Coventry P, Macdonald W et al. Identifying psychosocial interventions that improve both physical and mental health in patients with diabetes: a systematic review and meta-analysis. Diabetes Care 33, 926–930 (2010).
- 54 Hermanns N, Caputo S, Dzida G et al. Screening, evaluation and management of depression in people with diabetes in primary care. Prim. Care Diabetes 7(1), 1–10 (2012).
- 55 Coupe N, Garrett C, Gask L. Depression and diabetes – a significant challenge for people with diabetes and healthcare providers. *Diabetes Voice* 57(4), 38–41 (2012).
- 56 Holt RI, van der Feltz-Cornelis CM. Key concepts in screening for depression in people

- with diabetes. *J. Affect. Disord.* 142(Suppl.), S72–S79 (2012).
- 57 van der Feltz-Cornelis CM. Depression in diabetes mellitus: to screen or not to screen? A patient-centred approach. *Br. J. Diabetes* Vasc. Dis. 11(6), 276–281 (2011).
- Meeuwissen JAC, Holleman GJM, De Jong FJ et al. Screening and guided self-help intervention for anxiety and depression in patients with Type 2 diabetes. Eur. Diabetes Nurs. 8(2), 47–52 (2011).

Websites

- 101 Comprehensive Meta-Analysis Version 2. Biostat, NJ, USA (2005). www.meta-analysis.com/index.html (Accessed 22 July 2013)
- 102 Glycemic control goal. Institute for Healthcare Improvement, MA, USA. www.ihi.org/knowledge/Pages/Measures/ GlycemicControlGoal.aspx (Accessed 10 July 2013)

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