

Anxiety and diabetes: Innovative approaches to management in primary care

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Abstract

Type 2 diabetes mellitus is a chief concern for patients, healthcare providers, and health care systems in America, and around the globe. Individuals with type 2 diabetes mellitus exhibit clinical and subclinical symptoms of anxiety more frequently than people without diabetes. Anxiety is traditionally associated with poor metabolic outcomes and increased medical complications among those with type 2 diabetes mellitus. Collaborative care models have been utilized in the multidisciplinary treatment of mental health problems and chronic disease, and have demonstrated success in managing the pathology of depression which often accompanies diabetes. However, no specific treatment model has been published that links the treatment of anxiety to the treatment of type 2 diabetes mellitus. Given the success of collaborative care models in treating depression associated with diabetes, and anxiety unrelated to chronic disease, it is possible that the collaborative care treatment of primary care patients who suffer from both anxiety and diabetes could be met with the same success. The key issue is determining how to implement and sustain these models in practice. This review summarizes the proposed link between anxiety and diabetes, and offers an innovative and evidence-based collaborative care model for anxiety and diabetes in primary care.

Keywords: Diabetes, anxiety, primary care, comorbidity, collaborative care

Experimental Biology and Medicine 2016; 241: 1724–1731. DOI: 10.1177/1535370216657613

Introduction

Disparities

Type 2 diabetes mellitus. Diabetes mellitus affects approximately 29.18 million persons in the United States, which accounts for 9.3% of the American population.¹ Individuals with diabetes have difficulty producing insulin and/or effectively utilizing the insulin that the body generates. As a result, glucose accumulates in the blood and can lead to morbidity and mortality. Uncontrolled diabetes is associated with an increased risk of heart disease, stroke, vision loss, kidney failure, and amputations.¹ The seventh leading cause of death in the United States,² and Americans spend approximately \$245 billion dollars of in direct and indirect costs of medical care associated with diabetes.² Those living with diabetes spend twice as much on medical expenses as their counterparts without diabetes.¹

Type 2 diabetes mellitus (T2DM) is the most common form of diabetes, affecting approximately 95% of individuals with the disease.³ In T2DM, the cells do not use insulin properly, either because of insufficient insulin production, insulin resistance, or both. As insulin deficiency increases over time, the pancreas loses its ability to produce insulin.⁴ T2DM is linked to an increased prevalence of mental health

problems, primarily depression and anxiety disorders.^{5–9} Individuals with T2DM and a mental health condition are at increased risk for hyperglycemia,^{10,11} diabetic complications,¹² coronary heart disease,¹³ poor quality of life,^{12,14} and increased health care costs¹⁵ when compared to those with diabetes alone.

Anxiety and T2DM. Anxiety can be described as a feeling of worry, nervousness, or unease about an impending circumstance, or event, with an uncertain outcome. Symptoms of anxiety include avoidance of certain people, places or events, and physical sensations such as rapid heartbeat, dizziness, and sweating, and somatic complaints such as headaches and gastrointestinal distress.¹⁶ Humans frequently experience states of anxiety in response to a stressful life experience; however, the anxiety is sometimes experienced on a more chronic and debilitating basis, at which point they may be diagnosed with clinically significant anxiety.¹⁷ There are several clinically significant sub-types of anxiety disorders; the most commonly seen in primary care are generalized anxiety disorder (GAD), post-traumatic stress disorder, social anxiety disorder, and panic disorder.¹⁸ A recent survey demonstrated that anxiety disorders are the most frequently diagnosed mental health condition in the

United States, with lifetime estimates reaching 32.5%, and a 19.1% prevalence rate for any anxiety disorder in the last year.¹⁹ Previous studies have identified a robust association between anxiety and diabetes. Prevalence rates of clinically significant anxiety among individuals with diabetes range from 14% in a comprehensive review⁶ to 55.10% in a Mexican population.²⁰ One study found that clinically significant anxiety was 20% higher among Americans with diabetes, compared to Americans without diabetes, after controlling for age, smoking, education, employment, physical activity, body mass index (BMI), and marital status.²¹ Additionally, rates of GAD and phobias are considerably higher among diabetic populations when compared to community samples.^{22,23}

While the aforementioned studies address clinically significant anxiety, individuals with diabetes are also likely to experience subclinical anxiety.⁷ Presentations of subclinical anxiety are linked to decreased quality of life^{24,25} and poor functioning.^{24,26–28} Importantly, those who experience subclinical anxiety consume a large proportion of health care resources in the primary care setting, compared to those without anxiety.^{29–31}

Research has produced two primary hypotheses regarding the association between anxiety and diabetes. The first hypothesis focuses on the physiological association between the two diagnoses. Chronic clinical and subclinical anxiety may cause T2DM or exacerbate existing T2DM by initiating the activation of the hypothalamic-pituitary-adrenal axis (HPA axis), which in turn triggers release of counter-regulatory hormones such as glucagon, epinephrine (adrenaline), norepinephrine (noradrenaline), cortisol, and growth hormone.^{2,32} These counter-regulatory hormones increase glucose levels in the blood via catabolic processes like ketosis.³² In small doses, these processes are benign, and even protective, but chronically elevated anxiety can lead to an excess of the counter-regulatory hormones, which can lead to insulin sensitivity, visceral adiposity, dyslipidemia, and hypertension, all of which increase the risk for developing T2DM.^{7,32} Further, cortisol stimulates the sympathetic nervous system, which can elicit, or exacerbate the experience of anxiety.³³ Indeed, research has found that, among individuals predisposed to develop diabetes, stressful life experiences may be catalytic to the development of the disease.^{34–37}

Another hypothesis regarding the association between diabetes and anxiety, which is derived from the Lazarus and Folkman transactional model of stress and coping (1984), suggests that diabetes leads to anxiety in two ways.^{38,39} First, there is robust evidence that individuals experience symptoms of anxiety when they are diagnosed with diabetes.^{38,40–46} A diagnosis of diabetes may induce anxiety because individuals perceive that the disease will necessitate undesirable lifestyle changes, cause them to lose control over their health, and lead to diabetes-related complications, such as diabetic retinopathy, neuropathy, sexual dysfunction, and macrovascular complications.⁴⁷

Second, the daily management of diabetes may result in the experience of anxiety.³⁸ Diabetes self-care can involve dietary modifications, complicated medication regimens, exercise routines, smoking cessation, and blood glucose

monitoring. Approximately 60% of individuals with diabetes report anxiety related to managing their T2DM, and this distress was associated with lower levels of adherence to diabetes care regimens, higher incidence of uncontrolled diabetes, and increased rates of diabetes-related complications.^{48–50} One study demonstrated that individuals with anxious coping styles (i.e. avoidance, escape, and denial) showed reduced adherence to diabetes self-care regimens and poorer glycemic control.⁵¹ Another study highlights the complex and reciprocal nature of this relationship, demonstrating that elevated anxiety was associated with subsequent poor self-care, and poor self-care was associated with subsequent elevated anxiety, after controlling for depressive symptoms as a covariate.⁵²

In summary, several theories attempt to describe the relationship between anxiety and diabetes; some suggest that the emotional impact of a diabetes diagnosis, compounded with the burden of daily diabetes management, can lead to anxiety, while others propose that anxiety leads to, or exacerbates, T2DM through physiological mechanisms. Regardless of the direction or source of the relationship, the literature supports the importance of addressing both conditions simultaneously, as one condition cannot be treated in isolation from the other.

Collaborative care interventions to treat comorbid diabetes and mental health. Type 2 diabetes is increasingly managed in primary care due to the increasing prevalence of type 2 diabetes, and the strain on limited specialist resources. Treating T2DM in the primary care setting has demonstrated effectiveness comparable to diabetes treatment in a specialist setting, such as endocrinology.⁵² Indeed, in a recent study of greater than 17,000 subjects, no difference in glycemic control after insulin initiation was seen between primary versus specialist care.⁵³

However, the management of patients with diabetes and concomitant mental health conditions in primary care is fragmented, when diabetes is managed by the primary care doctor and mental health interventions are delivered by behavioral health providers (BHPs) outside the primary care office.^{54,55} Historically, communication between physicians and behavioral health providers about shared patients has been infrequent and often non-existent,⁵⁶ thus facilitating the provision of health care in “silos.” This practice is inefficient for a variety of reasons. First, primary care patients who are referred to off-site mental health providers often fail to initiate treatment secondary to financial difficulties, transportation issues, and the inconvenience of taking time off work or procuring child care.⁵⁷ Research has shown that patients are 62% more likely to follow through with a mental health referral if those services are offered within the primary care practice.⁵⁸ Second, because health care providers are less likely to communicate about shared patients when they practice in different locations, the treatment plans of BHPs and physicians may be duplicative, or in direct conflict with each other.^{57,59–64} This health care “disconnect” can effectively compromise patient care. Third, many primary care providers report having difficulty identifying quality mental health services

Table 1 Collaborative care interventions, based on HbA1c levels and anxiety and depression screening assessments.

	Anxiety/ depression screen	Health coaching session	Deep breathing exercise	Psychotropic medication management	Contact info for follow-up health coaching/ therapy	Depression interventions
HbA1c > 5.8 GAD-7 < 5 PHQ-9 < 5	X	X			X	
HbA1c > 5.8 GAD-7 score 5–9 PHQ-9 score 5–14	X	X	X	Clinician judgment	X	Clinician judgment
HbA1c > 5.8 GAD-7 > 10 PHQ-9 < 5	X	X	X	X	X	
HbA1c > 5.8 GAD-7 < 5 PHQ-9 > 10	X	X		X	X	X

GAD: generalized anxiety disorder; PHQ: patient health questionnaire.

to which they can refer patients, and if those services exist, they are frequently unable to accommodate the high patient volume seeking their services.⁶⁵ Research has shown that mental health care is twice as difficult to access than any other medical specialty.⁶⁶ Finally, privacy of health information is governed by Federal and State laws, including 42 C.F.R. Part 2, which requires patient consent for information to be disclosed regarding their substance abuse treatment. Behavioral health information has historically been associated with additional protection and privacy safeguards that are generally not required for standard medical health information, due to the sensitive nature of behavioral health conditions and the stigma that sometimes surrounds them. Typically, health care systems have restricted access to behavioral health records, even from physicians within the same healthcare system. When explicit protection is not in place, BHPs may choose to restrict access to their patient's behavioral health information if it is not directly relevant to their medical care. Sharing patient information between providers often takes time, administrative effort, and patient consent. The stress of navigating these additional barriers can potentially impede effective collaboration between providers about shared patients.

For the reasons mentioned above, recent healthcare policy changes have promoted significant system reorganization, with a goal of increasing the cohesiveness of services, and providing comprehensive care for our patients.⁶⁷ The collaborative care model (CCM) is one approach to managing concomitant diabetes and mental health issues in the primary care setting. First described by Coleman and Patrick,⁶⁸ collaborative care provides interventions for physical and behavioral health needs in the primary care setting, through systematic coordination and collaboration among health care providers from various disciplines. It is a healthcare philosophy that has many names, models, and definitions. Common derivatives of collaborative care include "Integrated Collaborative Care (ICC)", "Colocation", "Primary Care Behavioral Health (PCBH)" and "Care Management Model (CMM)".^{69–72} ICC is synonymous with

the broad definition of "collaborative care" and is defined as a range of models in which BHPs and primary care physicians systematically communicate to co-manage the mental health and biomedical needs of patients through collaboration and coordination of care.^{70–73}

The "colocation" model offers traditional hour-long psychotherapy sessions in the primary care setting. Though the patient may benefit from the convenience of having their primary care and mental health care in the same setting, the services are offered separately without standardized communication and collaboration about treatment plans.^{70,73} There may or may not be shared medical records between BHPs and physicians. In this model, the mental health services are not viewed as part of the patient's "medical care"; rather as an adjunct service to which a patient is formally referred.⁶⁹

In the primary care behavioral health model (PCBH), mental health providers are embedded within the primary care setting. Ideally, the primary care provider introduces the mental health provider to the patient as part of the medical team during routine primary care visits.⁷¹ As part of their interaction with the patient, mental health providers may facilitate self-management goal setting (SMG) related to chronic disease management and/or provide individual psychotherapy to process emotions or treat mental health diagnoses. The primary care provider and the mental health provider systematically share information via shared medical records.⁶⁹

The care management model (CMM) was developed for use in patients with a specific clinical problem, such as depression. CMM uses a care manager, usually a member of the nursing staff who is employed by the primary care clinic, to follow a standard protocol of treatment to address the specific disease state.^{69,71} The care manager may provide patient education regarding the specific disease state, engage the patient in SMG, or discuss coordination of care with the patient's multiple providers. They may engage in such interventions in-person, in the primary care setting, or via telephone between the patient's clinic visits.

Models of collaborative care have consistently demonstrated cost-effectiveness^{59,61,62,74–77} and have been associated with increased satisfaction among both patients and health care providers.⁷⁸ Patients involved in collaborative care report improved satisfaction because they have the opportunity to address all their physical and mental health concerns in one setting.⁷⁹ Provider satisfaction improves because the integration of mental and physical health reduces confusion and communication barriers about diagnostic paradigms and treatment strategies.⁵⁷ While multiple iterations of collaborative care exist, the shared goals are better health outcomes for patients, better care experience for patients, and reduced costs for the patient and the health care system.^{27,70–72,80} Here, collaborative care will be broadly defined as the integration of mental health providers and services into primary care.⁸¹

Several standardized CCMs of diabetes and mental health have been developed for use in primary care settings, all focused specifically on *depression* and diabetes.^{82–87} These models involve routine depression screening among individuals with uncontrolled diabetes, on-site care managers providing between-visit phone calls to assess diabetes self-care adherence, and on-site behavioral health providing brief interventions and SMG during the clinic visit. CCMs of diabetes and depression yield improvements in depression-related outcomes,^{87–91} increased adherence to diabetes and depression self-management,^{92,93} and decreased rates of mortality, compared to usual care.⁹⁴ Limited quantitative data are available supporting the association of collaborative care with improvement in HbA1c; however, one study showed that the incorporation of health coaching into diabetes management was associated with accelerated HbA1c reduction and improved mood as measured by Hospital Anxiety and Depression Scale (HADS).⁹⁵

Another case study involving care coordination with an interdisciplinary treatment team with patients diagnosed with depression, dementia, anxiety, and PTSD showed, over a six-month period, improvements in strength, social functioning, decreased caregiver burden, and compliance with treatment plan.⁹⁶

Collaborative care interventions for diabetes and depression may also be helpful for those suffering from anxiety. Indeed, the extant literature suggests that nearly half of patients with depression also experience anxiety.⁹⁷ SMG may help individuals with anxiety gain a sense of control over their health, thus alleviating their symptoms of anxiety.⁹⁸ Between-visit phone calls to assess adherence and self-care can mitigate some of the anxiety that patients with diabetes feel about their diabetes care,⁹⁸ and many brief behavioral health interventions used in collaborative care involve elements of cognitive behavioral therapy (CBT), which is effective in treating anxiety, as well as depression.⁹⁸ Yet, there are evidence-based interventions for anxiety that are not incorporated into CCMs of depression and diabetes. Despite the high prevalence of anxiety among individuals with diabetes, to date no standardized CCMs have been developed specifically for the management of concomitant anxiety and diabetes.

Three studies have measured the impact of a CCM on outcomes for anxiety in a primary care setting, though not specifically among people with diabetes.^{93–95} One study found that adults with anxiety who received collaborative care treatment for their anxiety symptoms experienced clinically and statistically significant improvements in anxiety outcomes, compared to individuals with anxiety who received care as usual.⁹⁹ These effects were present immediately after the collaborative care intervention was delivered, and up to 24 months post intervention.⁹⁹ Additionally, those in the study who received collaborative care for anxiety demonstrated increased medication adherence, improved mental health quality of life, and better patient satisfaction scores than those who received treatment as usual.⁹⁹

In another study, assessing collaborative care for anxiety,¹⁰¹ patients with anxiety received a telephone-based care management intervention that included psychoeducation and follow-up visits between their regularly scheduled in-office appointments versus usual care. The collaborative care intervention was associated with improved symptoms of anxiety, health-related quality of life, and work-related outcomes compared to standard care. The effects remained statistically significant one year post-intervention.¹⁰⁰

Finally, a randomized controlled trial evaluated the effectiveness of a collaborative care intervention, called Coordinated Anxiety Learning and Management (CALM), compared to standard care among patients with anxiety.¹⁰¹ Patients receiving the CALM intervention were given the choice of participating in CBT, medication management, or both, and they also had access to computerized CBT resources.¹⁰¹ Results indicated that patients with anxiety disorders (with and without major depression), who received the CALM collaborative care intervention in the primary care clinic, demonstrated greater improvement in anxiety and depression symptoms, increased functional ability, and improved quality of care, compared to care as usual.¹⁰¹

Proposed collaborative care intervention for comorbid diabetes and anxiety. In response to the limited availability of CCMs for anxiety and diabetes, we suggest the following CCM, consisting of four evidence-based interventions for anxiety and diabetes, based on a multidisciplinary team approach to care where BHPs are integrated into a primary care setting.¹⁰²

The first intervention in the CCM of anxiety and diabetes involves a screening assessment for anxiety and depression. This screening assessment will be administered by the BHPs to all patients with HbA1c levels > 5.8 who present for an appointment in the clinic. Screening for anxiety and depression among individuals with diabetes is widely recommended,^{18,103} as accurate recognition of anxiety disorders in primary care is the first step in providing effective treatment. Anxiety symptoms will be assessed using the GAD – 7 self-report questionnaire.¹⁰⁴ The patient health questionnaire (PHQ) – 9¹⁰⁵ will be used to screen patients for symptoms of depression. Some patients who score > 5 on the GAD-7 will also report symptoms of

depression on the PHQ-9. Patients with anxiety who score between 5 and 14 on the PHQ-9 (scores 5–9 represent mild depressive symptoms; 10–14 represent moderate depression) will receive the collaborative care intervention for anxiety and diabetes, as well as pertinent additional interventions for depression (to be determined by the provider and BHP). Patients with PHQ-9 scores > 10, and GAD-7 scores < 5, will receive collaborative care interventions for depression and diabetes (See Table 1).

Following an assessment for anxiety and depression, BHPs will engage all patients in the second intervention in the CCM; a brief health coaching session, consisting of diabetes education and SMG. In 2008, the National Institute for Health and Care Excellence (NICE) disseminated the guideline that all patients with diabetes should be offered health coaching; specifically, a structured diabetes education and self-management program.¹⁰⁶ Diabetes health coaching is a patient-centered, evidence-based intervention, that draws from principles of motivational interviewing to encourage those with diabetes to make informed decisions about their diabetes care, problem solve to maximize behavior change, and to play an active role in the health care team with an overarching goal of improving their own diabetes-related outcomes and quality of life.¹⁰⁷ All patients will receive at least one health coaching session, which will include a review of diabetes education handouts, the development of a short-term health goal using motivational interviewing techniques, and an invitation to schedule follow-up health coaching sessions with BHPs to address symptoms of mental health issues and/or diabetes-related concerns.

The final intervention of the CCM for anxiety and diabetes will involve the BHP, leading the patient through a brief deep breathing exercise – the 4–7–8 (or relaxing breath) exercise.¹⁰⁸ Deep breathing exercises have been shown to improve glycemic control and blood pressure among individuals with T2DM.¹⁰⁹ A systematic review found that mindfulness-based interventions, including deep breathing exercises, improve depression, anxiety, and diabetes-related distress.¹¹⁰ The patient will be given information on how to download the free My Calm Beat[®] smart phone app to help them practice their deep breathing exercise in their daily life, and the deep breathing exercise will be practiced in the room with the BHP. The patient will be encouraged to utilize the deep breathing exercise at least three times per day.

Patients who score > 10 on the GAD-7 will be eligible to participate in the fourth intervention of the CCM, which is psychotropic medication management. Previous research suggests that appropriate management of anxiolytic medication can improve glycemic control in adults with poorly controlled diabetes.¹¹¹ Primary care providers will utilize evidence-based guidelines and shared decision making techniques to approach medication management with patient.

At the end of the collaborative care intervention, all patients will be provided with contact information for the BHPs, and encouraged to schedule follow-up appointments for health coaching or psychotherapy sessions, if desired.

Summary and conclusions

Mental health and primary care are intricately linked, making it necessary and appropriate to address them in chorus. Recent healthcare policies and federal research agencies call for the evaluation of treatments that address concomitant diabetes and mental health issues.^{112–118} While the extant literature has identified a high prevalence of anxiety among individuals with T2DM, there are no evidence-based protocols of treatment for individuals with these comorbid issues. Research on CCMs of mental health and diabetes has been encouraging, but more research is needed to identify effective, sustainable, and cost-effective models of implementation in primary care settings across disease states. Given the success of CCMs for treatment for depression and diabetes, and the effect of collaborative care on anxiety alone, primary care patients may benefit from a standardized collaborative care protocol for addressing anxiety and diabetes, focusing on how best to implement and sustain these models in practice.

Authors' contributions: This work was conceived by AB and HT. Literature search was conducted by AB and HT who both contributed to the writing of the manuscript.

ACKNOWLEDGMENTS

We would like to gratefully acknowledge Amy Peterman, PhD, from the University of North Carolina at Charlotte. This work was supported by Carolinas Healthcare System.

DECLARATION OF CONFLICTING INTERESTS

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

- Centers for Disease Control and Prevention. *National diabetes fact sheet: national estimates and general information on diabetes and pre-diabetes in the United States, 2011*. Atlanta, GA: U.S. Department of Health and Human Services, 2011
- American Diabetes Association (ADA). Standards of medical care in diabetes. *Diabetes Care* 2011;**34**:S11–61
- Centers for Disease Control and Prevention. *Diabetes report card 2012*. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services, 2012
- Centers for Disease Control and Prevention. *Collaborative practice agreements and pharmacists' patient care services: a resource for doctors, nurses, physician assistants, and other providers*. Atlanta, GA: US Department of Health and Human Services, 2013
- Collins MM, Corcoran P, Perry IJ. Anxiety and depression symptoms in patients with diabetes. *Diabet Med* 2009;**26**:153–61
- Grigsby AB, Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. Prevalence of anxiety in adults with diabetes: a systematic review. *J Psychosom Res* 2002;**53**:1053–60
- Khuwaja AK, Lalani S, Dhanani R, Azam IS, Rafique G, White F. Anxiety and depression among outpatients with type 2 diabetes: a multi-centre study of prevalence and associated factors. *Diabetol Metabol Syndr* 2010;**2**:72
- Smith KJ, Beland M, Clyde M, Garipey G, Page V, Badawi G, Rabasa-Lhoret R, Schmitz N. Association of diabetes with anxiety: a systematic review and meta-analysis. *J Psychosom Res* 2013;**74**:89–99

9. Thomas J, Jones G, Scarinci I, Brantley P. A descriptive and comparative study of the prevalence of depressive and anxiety disorders in low-income adults with type 2 diabetes and other chronic illnesses. *Diabetes Care* 2003;**26**:2311–7
10. Brieler JA, Lustman PJ, Scherrer JF, Salas J, Schneider FD. Antidepressant medication use and glycaemic control in co-morbid type 2 diabetes and depression. *Fam Pract* 2016;**33**:30–6
11. Katon WJ, Young BA, Russo J, Lin EH, Ciechanowski P, Ludman EJ, Von Korff MR. Association of depression with increased risk of severe hypoglycemic episodes in patients with diabetes. *Ann Fam Med* 2013;**11**:245–50
12. de Groot M, Anderson R, Freedland KE, Clouse RE, Lustman PJ. Association of depression and diabetes complications: a meta-analysis. *Psychosom Med* 2001;**63**:619–30
13. Kinder LS, Kamarck TW, Baum A, Orchard TJ. Depressive symptomatology and coronary heart disease in Type I diabetes mellitus: a study of possible mechanisms. *Health Psychol* 2002;**21**:542–52
14. de Groot M, Pinkerman B, Wagner J, Hockman E. Depression treatment and satisfaction in a multicultural sample of type 1 and type 2 diabetic patients. *Diabetes Care* 2006;**29**:549–53
15. Egede LE, Zheng D, Simpson K. Comorbid depression is associated with increased health care use and expenditures in individuals with diabetes. *Diabetes Care* 2002;**25**:464–70
16. Lang PJ. Fear reduction and fear behavior: Problems in treating a construct. In: Schlien JM (ed) *Research in Psychotherapy*, Vol. 3. Washington, DC: American Psychological Association, 1968, pp. 90–103
17. Stanley R. *Anxiety and its disorders – the nature and treatment of anxiety and panic*. New York: The Guilford Press, 2002
18. Kroenke K, Spitzer RL, Williams JB, et al. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Ann Intern Med* 2007;**146**:317–25
19. Kessler R. *National Comorbidity Survey: Reinterview (NCS-2), 2001-2002*. ICPSR35067-v2. Ann Arbor, MI: Inter-university Consortium for Political and Social Research [distributor], <http://doi.org/10.3886/ICPSR35067.v2> (accessed 13 January 2015)
20. Tovilla-Zárate C, Juárez-Rojop I, Peralta Jimenez Y, Jiménez MA, Vázquez S, Bermúdez-Ocaña D, Ramón-Frías T, Genis Mendoza AD, García SP, Narváez LL. Prevalence of anxiety and depression among outpatients with type 2 diabetes in the Mexican population. *PLoS One* 2012;**7**:e36887
21. Li C, Barker L, Ford ES, Zhang X, Strine TW, Mokdad AH. Diabetes and anxiety in US adults: findings from the 2006 behavioral risk factor surveillance system. *Diabet Med* 2008;**25**:878–81
22. Anderson RJ, Grigsby AB, Freedland KE, de Groot M, McGill JB, Clouse RE, Lustman PJ. Anxiety and poor glycemic control: a meta-analytic review of the literature. *Int J Psychiatry Med* 2002;**32**:235–47
23. Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry* 2005;**62**:617–27
24. Spitzer RL, Kroenke K, Linzer M, Hahn SR, Williams JB, deGruy FV, Brody D, Davies M. Health-related quality of life in primary care patients with mental disorders. Results from the PRIME-MD 1000 Study. *JAMA* 1995;**274**:1511–7
25. Mendlowicz MV, Stein MB. Quality of life in individuals with anxiety disorders. *Am J Psychiatry* 2000;**157**:669–82
26. Fifer SK, Mathias SD, Patrick DL, Mazonson PD, Lubeck DP, Buesching DP. Untreated anxiety among adult primary care patients in a health maintenance organization. *Arch Gen Psychiatry* 1994;**51**:740–50
27. Ormel J, van den Brink W, van der Meer K, Jenner J, Giel R. [Prevalence, indication and course of depression in family practice]. *Ned Tijdschr Geneesk* 1994;**138**:123–6
28. Schonfeld WH, Verboncoeur CJ, Fifer SK, Lipschutz RC, Lubeck DP, Buesching DP. The functioning and well-being of patients with unrecognized anxiety disorders and major depressive disorder. *J Affect Disord* 1997;**43**:105–19
29. de Beurs E, Beekman AT, van Balkom AJ, Deeg DJ, van Dyck R, van Tilburg W. Consequences of anxiety in older persons: its effect on disability, well-being and use of health services. *Psychol Med* 1999;**29**:583–93
30. Katon W, Von Korff M, Lin E, Lipscomb P, Russo J, Wagner E, Polk E. Distressed high utilizers of medical care. DSM-III-R diagnoses and treatment needs. *Gen Hosp Psychiatry* 1990;**12**:355–62
31. Kennedy BL, Schwab JJ. Utilization of medical specialists by anxiety disorder patients. *Psychosomatics* 1997;**38**:109–12
32. Stein BC, Levin RI. Natriuretic peptides: physiology, therapeutic potential, and risk stratification in ischemic heart disease. *Am Heart J* 1998;**135**(5 Pt 1): 914–23
33. Champaneri S, Wand GS, Malhotra SS, Casagrande SS, Golden SH. Biological basis of depression in adults with diabetes. *Curr Diab Rep* 2010;**10**:396–405
34. Kisch ES. Stressful events and the onset of diabetes mellitus. *Israel J Med Sci* 1985;**21**:356–8
35. Kawakami N, Araki S, Takatsuka N, Shimizu H, Ishibashi H. Overtime, psychosocial working conditions, and occurrence of non-insulin dependent diabetes mellitus in Japanese men. *J Epidemiol Commun Health* 1999;**53**:359–63
36. Kawakami N, Takatsuka N, Shimizu H, Ishibashi H. Depressive symptoms and occurrence of type 2 diabetes among Japanese men. *Diabetes Care* 1999;**22**:1071–6
37. Vialettes B, Ozanon JP, Kaplansky S, Farnarier C, Sauvaget E, Lassmann-Vague V, Bernard D, Vague P. Stress antecedents and immune status in recently diagnosed type I (insulindependent) diabetes mellitus. *Diabete Metab* 1989;**15**:45–50
38. Maes S, Leventhal H, Ridder DTD. Coping with chronic diseases. In: Zeidner M, Endler N (eds). *Handbook of coping: theory, research and applications*. New York: Wiley, 1996
39. Lazarus RS, Folkman S. *Stress, appraisal, and coping*. New York: Springer, 1984
40. Alberti G. The dawn (diabetes attitudes, wishes and needs) study. *Pract Diab Int* 2002;**19**:22–4
41. Cherrington A, Ayala GX, Sleath B, Corbie-Smith G. Examining knowledge, attitudes, and beliefs about depression among Latino adults with type 2 diabetes. *Diabetes Educ* 2006;**32**:603–13
42. Delahanty LMI, Grant RW, Wittenberg E, Bosch JL, Wexler DJ, Cagliero E, Meigs JB. Association of diabetes-related emotional distress with diabetes treatment in primary care patients with Type 2 diabetes. *Diabet Med* 2007;**24**:48–54
43. Drum D, Zierenberg T. *Type II diabetes source book*, 3rd ed. USA: McGraw-Hill Companies, 2005
44. Manderson L, Kokanovic R. “Worried all the time”: distress and the circumstances of everyday life among immigrant Australians with type 2 diabetes. *Chronic Illn* 2009;**5**:21–32
45. Penckofer S, Ferrans CE, Velsor-Friedrich B, Savoy S. The psychological impact of living with diabetes: women’s day-to-day experiences. *Diabetes Educ* 2007;**33**:680–90
46. Goldstein BJ, Muller-Wieland D. Text book of type 2 diabetes, <http://books.google.com.pk/books?id=pn3doJE0dF8C&pg=PA67&lpg=PA66&ots=LvhdecSHZW&dq=psychosocial+problems+of+type+2+diabetics#v=onepage&q=&f=false> (2003 accessed 15 March 2010)
47. Pouwer F. Should we screen for emotional distress in type 2 diabetes mellitus? *Nat Rev Endocrinol* 2009;**5**:665–71
48. Polonsky WHI, Anderson BJ, Lohrer PA, Welch G, Jacobson AM, Aponte JE, Schwartz CE. Assessment of diabetes-related distress. *Diabetes Care* 1995;**18**:754–60
49. Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. *Arch Intern Med* 2000;**160**:3278–85
50. Surwit RS, Schneider MS, Feinglos MN. Stress and diabetes mellitus. *Diabetes Care* 1992;**15**:1413–22
51. Peyrot M, McMurry JF Jr, Kruger DF. A biopsychosocial model of glycemic control in diabetes: stress, coping and regimen adherence. *J Health Soc Behav* 1999;**40**:141–58
52. Brennan C, Harkins V, Perry JJ. Management of diabetes in primary care: a structured-care approach. *Eur J Gen Pract* 2008;**14**:117–22

53. Orozco-Beltran D, Pan C, Svendsen A, Faerch L, Caputo S. Basal insulin initiation in primary vs. specialist care: similar glycaemic control in two different patient populations. *Int J Clin Pract* 2016;**70**:236–43
54. Archer J, Bower P, Gilbody S, Lovell K, Richards D, Gask L, Dickens C, Coventry P. Collaborative care for depression and anxiety problems. *Cochrane Database Syst Rev* 2012;**10**:CD006525.
55. Prins MA, Verhaak PF, Hilbink-Smolanders M, Spreeuwenberg P, Laurant MG, van der Meer K, van Marwijk H, Penninx B, Bensing JM. Outcomes for depression and anxiety in primary care and details of treatment: a naturalistic longitudinal study. *BMC Psychiatry* 2011;**11**:180
56. Doherty WJ, McDaniel SH, Baird MA. Five levels of primary care/behavioral healthcare collaboration. *Behav Healthcare Tom* 1996;**5**:25–7
57. Pincus HA, Hough L, Houtsinger JK, Rollman BL, Frank RG. Emerging models of depression care: multi-level ('6 P') strategies. *Int J Meth Psychiat Res* 2003;**12**:54–63
58. Tice JA, Ollendorf DA, Reed SJ, Shore KK, Weissburg J, Pearson SD. Integrating behavioral health into primary care. BHI Final Report 2015, http://icer-review.org/sites/default/files/u148/BHI_Final_Report_060215.pdf (accessed 16 June 2016)
59. Blount A. Integrated primary care: organizing the evidence. *Fam Syst Health* 2003;**21**:121–33
60. VandenBos G, DeLeon P. The use of psychotherapy to improve physical health. *PsychotherTheory Res Pract Train* 1998;**25**:335–43
61. Cummings NA. Behavioral health in primary care: dollars and sense. In: Cummings NA, Johnston JN, Cummings J (eds). *Behavioral health in primary care: a guide for clinical integration*. Madison, CT: Psychosocial Press, 1997, pp. 3–21
62. O'Donohue WT, Cummings NA, Ferguson KE. Clinical integration: the promise and the path. In: Cummings NA, O'Donohue WT, Ferguson KE (eds). *Behavioral health as primary care: beyond efficacy to effectiveness*. Reno, NV: Context, 2003, pp. 15–30
63. Hornik-Lurie T, Lerner Y, Zilber N, Feinson MC, Cwikel JG. Physicians' influence on primary care patients' reluctance to use mental health treatment. *Psychiatr Serv* 2014;**65**:541–5
64. Cwikel J, Zilber N, Feinson M, Lerner Y. Prevalence and risk factors of threshold and sub-threshold psychiatric disorders in primary care. *Soc Psychiatry Psychiatr Epidemiol* 2008;**43**:184–91
65. Cunningham PJ. Beyond parity: a primary care physicians' perspectives on access to mental health care. *Health Affairs* 2009;**26**:153–61
66. Kessler R, Stafford D, Messier R. The problem of integrating behavioral health in the medical home and the questions it leads to. *J Clin Psychol Med Settings* 2009;**16**:4–12
67. Harkness E, Macdonald W, Valderas J, Coventry P, Gask L, Bower P. Identifying psychosocial interventions that improve both physical and mental health in patients with diabetes: a systematic review and meta-analysis. *Diabetes Care* 2010;**33**:926–30
68. Coleman JV, Patrick DL. Integrating mental health services into primary medical care. *Med Care* 1976;**14**:654–61
69. Landis SE, Barrett M, Galvin SL. Effects of different models of integrated collaborative care in a family medicine residency program. *Fam Syst Health* 2013;**31**:264–73
70. Curtis R, Christian E. (eds). *Integrated care: applying theory to practice*. New York: Routledge, 2012
71. Hunter C, Goodie J, Oordt M. *Integrated behavioral health in primary care: Step-by-step guidance for assessment and intervention*. Washington, DC: American Psychological Association, 2009
72. Robinson PJ, Reiter JT. *Behavioural consultation and primary care: a guide to integrating services*. New York: Springer, 2007
73. Collins C, Hewson DL, Munger R, Wade T. *Evolving models of behavioral health integration in primary care*. New York: Milbank Memorial Fund, 2010
74. Olfson M, Sing M, Slesinger HJ. Mental health/medical cost care offsets: opportunities for managed care. *Health Affairs* 1999;**18**:79–93
75. Simon GE, Katon WJ, Lin EH, Rutter C, Manning WG, Von Korff M, Ciechanowski P, Ludman EJ, Young BA. Cost-effectiveness of systematic depression treatment among people with diabetes mellitus. *Arch Gen Psychiatry* 2007;**64**:65–72
76. Simon GE, Katon WJ, VonKorff M, Unützer J, Lin EH, Walker EA, Bush T, Rutter C, Ludman E. Cost-effectiveness of a collaborative care program for primary care patients with persistent depression. *Am J Psychiatry* 2001;**158**:1638–44
77. Simon G, Wagner E, Vonkorff M. Cost-effectiveness comparisons using "real world" randomized trials: the case of new antidepressant drugs. *J Clin Epidemiol* 1995;**48**:363–73
78. Begley CE, Hickey JS, Ostermeyer B, Teske LA, Vu T, Wolf J, Kunik ME, Rowan PJ. Integrating behavioral health and primary care: the Harris County Community Behavioral Health Program. *Psychiatr Serv* 2008;**59**:356–8
79. Balestrieri M, Williams P, Wilkinson G. Specialist mental health treatment in general practice: a meta-analysis. *Psychol Med* 1988;**18**:711–7
80. Berwick DM, Nolan TW, Whittington J. The triple aim: care, health, and cost. *Health Affairs* 2008;**27**:759–69
81. Miller BF, Mendenhall TJ, Malik AD. Integrated primary care: an inclusive three-world view through process metrics and empirical discrimination. *J Clin Psychol Med Settings* 2009;**16**:21–30
82. Bogner HR, Morales KH, de Vries HF, Cappola AR. Integrated management of type 2 diabetes mellitus and depression treatment to improve medication adherence: a randomized controlled trial. *Ann Fam Med* 2012;**10**:15–22
83. Ciechanowski PS1, Russo JE, Katon WJ, Von Korff M, Simon GE, Lin EH, Ludman EJ, Young BA. The association of patient relationship style and outcomes in collaborative care treatment for depression in patients with diabetes. *Med Care* 2006;**44**:283–91
84. Katon WJ, Lin EH, Von Korff M, Ciechanowski P, Ludman E, Young B, Rutter C, Oliver M, McGregor M. Integrating depression and chronic disease care among patients with diabetes and/or coronary heart disease: the design of the TEAMcare study. *Contemp Clin Trials* 2010;**31**:312–22
85. Katon WJ, Von Korff M, Lin E, Simon G, Ludman E, Bush T, Walker E, Ciechanowski P, Rutter C. Improving primary care treatment of depression among patients with diabetes mellitus: the design of the pathways study. *Gen Hosp Psychiatry* 2003;**25**:158–68
86. Kinder LS, Katon WJ, Ludman E, Russo J, Simon G, Lin EH, Ciechanowski P, Von Korff M, Young B. Improving depression care in patients with diabetes and multiple complications. *J Gen Intern Med* 2006;**21**:1036–41
87. Williams JW, Katon W, Lin EH, Noël PH, Worchel J, Cornell J, Harpole L, Fultz BA, Hunkeler E, Mika VS, Unützer J IMPACT Investigators. The effectiveness of depression care management on diabetes-related outcomes in older patients. *Ann Intern Med* 2004;**140**:1015–24
88. Katon WJ, Von Korff M, Lin EH, Simon G, Ludman E, Russo J, Ciechanowski P, Walker E, Bush T. The pathways study: a randomized trial of collaborative care in patients with diabetes and depression. *Arch Gen Psychiatry* 2004;**61**:1042–9
89. Agius M, Murphy CL, Zaman R. Does shared care help in the treatment of depression? *Psychiatr Danub* 2010;(22 Suppl 1):S18–22
90. Ell K, Katon W, Xie B, Lee PJ, Kapetanovic S, Guterman J, Chou CP. Collaborative care management of major depression among low-income, predominantly Hispanic subjects with diabetes: a randomized controlled trial. *Diabetes Care* 2010;**33**:706–13
91. Gask L, Ludman E, Schaefer J. Qualitative study of an intervention for depression among patients with diabetes: how can we optimize patient-professional interaction? *Chronic Illn* 2006;**2**:231–42
92. Huang Y, Wei X, Wu T, Chen R, Guo A. Collaborative care for patients with depression and diabetes mellitus: a systematic review and meta-analysis. *BMC Psychiatry* 2013;**13**:260
93. Whittemore R, Liberti LS, Jeon S, Chao A, Minges KE, Murphy K, Grey M. Efficacy and implementation of an Internet psychoeducational program for teens with type 1 diabetes. *Pediatr Diabetes* 2015;**22**:22
94. Bogner HR, Morales KH, Post EP, Bruce ML. Diabetes, depression, and death: a randomized controlled trial of a depression treatment program for older adults based in primary care (PROSPECT). *Diabetes Care* 2007;**30**:3005–10
95. Wayne N, Perez DF, Kaplan DM, Ritvo P. Health coaching reduces HbA1c in type 2 diabetic patients from a lower-socioeconomic status community: a randomized controlled trial. *J Med Intt Res* 2015;**17**:e224

96. Sorocco KH, Bratkovich KL, Wingo R, Qureshi SM, Mason PJ. (Integrating care coordination home telehealth and home based primary care in rural Oklahoma: a pilot study. *Psychol Serv* 2013;**10**:350–3
97. Hirschfeld RMA. The comorbidity of major depression and anxiety disorders: recognition and management in primary care. *Prim Care Comp J Clin Psychiatry* 2001;**3**:244–54
98. NICE Guidelines. Manchester, UK: National Institute for Health and Care Excellence. Generalized anxiety disorder and panic disorder (with or without agoraphobia) in adults: Management in primary, secondary and community care 2011, www.nice.org.uk/guidance/cg113/chapter/guidance. (accessed 16 June 2016)
99. Archer J, Bower P, Gilbody S, Lovell K, Richards D, Gask L, Dickens C, Coventry P. Collaborative care for depression and anxiety problems. *Cochrane Database Syst Rev* 2012;**10**:CD006525
100. Rollman BL1, Belnap BH, Mazumdar S, Houck PR, Zhu F, Gardner W, Reynolds CF 3rd, Schulberg HC, Shear MK. A randomized trial to improve the quality of treatment for panic and generalized anxiety disorders in primary care. *Arch Gen Psychiatry* 2005;**62**:1332–41
101. Roy-Byrne P, Craske MG, Stein MB, Sullivan G, Bystritsky A, Katon W, Golinelli D, Sherbourne CD. A randomized effectiveness trial of cognitive-behavioral therapy and medication for primary care panic disorder. *Arch Gen Psychiatry* 2005;**62**:290–8
102. Tapp H, Phillips SE, Waxman D, Alexander M, Brown R, Hall M. Multidisciplinary team approach to improved chronic care management for diabetic patients in an urban safety net ambulatory care clinic. *J Am Board Fam Med* 2012;**25**:245–6
103. Roy-Byrne P, Craske MG, Stein MB. A randomized effectiveness trial of cognitive-behavioral therapy and medication for primary care panic disorder. *Arch Gen Psychiatry* 2005;**62**:290–8
104. Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 2006;**166**:1092–7
105. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;**16**:606–13
106. Home P, Mant J, Diaz J, Turner C. Management of type 2 diabetes: updated NICE guidance. *Br Med J* 2008;**336**:306–8
107. Home P, Mant J, Diaz J, Turner C. Management of type 2 diabetes: summary of updated NICE guidance. *BMJ* 2008;**336**:1306–8
108. Weill A. Three breathing exercises 2006, www.drweil.com/drw/u/ART00521/three-breathing-exercises.html. (accessed 6 June 2016)
109. Esposito P, Mereu R, De Barbieri G, Rampino T, Di Toro A, Groop PH, Dal Canton A, Bernardi L. Trained breathing-induced oxygenation acutely reverses cardiovascular autonomic dysfunction in patients with type 2 diabetes and renal disease. *Acta Diabetol* 2016;**53**:217–26
110. Noordali F, Cumming J, Thompson J. Effectiveness of mindfulness-based interventions on physiological and psychological complications in adults with diabetes: a systematic review. *J Health Psychol*. Epub ahead of print 30 December 2015. DOI: 10.1177/1359105315620293
111. Lustman PJ, Griffith LS, Clouse RE, Freedland KE, Eisen SA, Rubin EH, Carney RM, McGill JB. Effects of alprazolam on glucose regulation in adult diabetic patients: results of a double-blind, placebo-controlled trial. *Diabetes Care* 1995;**18**:1133–9
112. Kinman CR, Gilchrist EC, Payne-Murphy JC, Miller MF. National Institute of Mental Health. Anxiety disorders, www.nimh.nih.gov/health/publications/anxiety-disorders/complete-index.shtml (2009, accessed 12 February 2016)
113. Agency for Healthcare Research and Quality (AHRQ). Provider- and practice-level competencies for integrated behavioral health in primary care: a literature review, https://integrationacademy.ahrq.gov/sites/default/files/AHRQ_AcadLitReview.pdf (2015, accessed 2 January 2016)
114. National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). National Diabetes Education Plan (2014). www.niddk.nih.gov/health-information/health-communication-programs/ndep/about-ndep/Pages/index.aspx (accessed 12 February 2016)
115. Lustman PJ, Griffith LS, Clouse RE, Freedland KE, Eisen SA, Rubin EH, Carney RM, McGill JB. Effects of nortriptyline on depression and glycemic control in diabetes: results of a double-blind, placebo-controlled trial. *Psychosom Med* 1997;**59**:241–50
116. Esposito P, Mereu R, De Barbieri G, Rampino T, Di Toro A, Groop PH, Dal Canton A, Bernardi L. Trained breathing-induced oxygenation acutely reverses cardiovascular autonomic dysfunction in patients with type 2 diabetes and renal disease. *Acta Diabetol* 2015;**53**:217–26
117. Chaiopant S. Hypoglycemic effect of sitting breathing meditation exercise on type 2 diabetes at Wat Khae Nok Primary Health Center in Nonthaburi province. *J Med Assoc Thai* 2008;**91**:93–8