



Published in final edited form as:

J Psychosom Res. 2012 December ; 73(6): 418–423. doi:10.1016/j.jpsychores.2012.09.018.

Anxiety and risk of type 2 diabetes: Evidence from the Baltimore Epidemiologic Catchment Area Study

Lauren E. Edwards, MPH¹ and Briana Mezuk, PhD¹

¹ Department of Epidemiology and Community Health Virginia Commonwealth University School of Medicine

Abstract

Objective—Depression is increasingly recognized as a risk factor for type 2 diabetes, and is also commonly comorbid with anxiety. However, few studies have examined whether anxiety is predictive of diabetes risk. The objectives of this study are to examine the prospective relationship between anxiety disorders (generalized anxiety disorder, panic disorder, social phobia, and agoraphobia) and risk of type 2 diabetes over an 11-year period, and to investigate the association between anxiety and risk of diabetes-related complications among those with prevalent type 2 diabetes.

Methods—Data come from the 1993/6 and 2004/5 waves of the Baltimore Epidemiologic Catchment Area Study (N=1920), a population-based prospective cohort. Anxiety disorders were assessed using the Diagnostic Interview Schedule. The prospective association between anxiety and incident type 2 diabetes was evaluated using a series of nested multivariable logistic regression models.

Results—At baseline, 315 participants (21.8%) had an anxiety disorder. The relationship between anxiety and risk of developing type 2 diabetes was not statistically significant after controlling for demographic characteristics (Odds Ratio (OR): 1.28, 95% Confidence Interval (CI): 0.75, 2.18). There was no relationship between anxiety and diabetes risk after controlling for health behaviors and depression status (OR: 1.00, 95% CI: 0.53, 1.89). There was no significant relationship between anxiety and development of diabetes-related complications among those with prevalent type 2 diabetes (OR: 2.02, 95% CI: 0.61, 6.74).

Conclusion—Anxiety disorders are not associated with increased risk of type 2 diabetes or risk of diabetes complications among those who have diabetes in the present study.

Keywords

Anxiety; Anxiety Disorders; Cohort; Diabetes; Epidemiology; Public Health

© 2012 Elsevier Inc. All rights reserved.

Corresponding Author: Briana Mezuk Department of Epidemiology and Community Health Virginia Commonwealth University School of Medicine PO Box 980232 Richmond, VA 23298-0212 Phone: (804) 828-9785 Fax: (804) 828-9773 bmezuk@vcu.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

AUTHORSHIP

L. Edwards developed the study design, conducted the data analysis, and wrote the first draft of the manuscript. B. Mezuk supervised the development of the data analysis plan and edited the manuscript.

INTRODUCTION

Anxiety disorders affect approximately 40 million American adults, or about 18% of the US population.¹ Anxiety-based mental illness encompasses many different conditions including generalized anxiety disorder, panic disorder, agoraphobia, social phobia, and specific phobias.¹ Anxiety symptoms typically include excessive worry, irritability, muscle tension, and fatigue.¹⁻² This excessive worry is associated with significant impairment in social and occupational functioning. Recently, research has suggested that anxiety is also associated with poor medical health outcomes, such as chronic disease complications and premature mortality.³

Diabetes affects about 25.6 million adults (approximately 11.3%) in the US, with 1.9 million new cases of diabetes diagnosed every year.⁴ Type 2 diabetes is characterized by underproduction of insulin by the pancreas, or a failure of the body to appropriately recognize insulin production.⁵ This insulin resistance results in hyperglycemia; normal fasting glucose levels are less than 100 mg/dl, pre-diabetes is indicated by fasting glucose between 100 and 125 mg/dl or Hemoglobin A1c (HbA1c) between 5.7 and 6.4%, and diabetes is indicated by glucose levels ≥ 126 mg/dl or HbA1c $\geq 6.5\%$.⁶ Poor glycemic control (indicated by HbA1c $>7.0\%$) among persons who have type 2 diabetes is associated with increased risk of cardiovascular disease, diabetes-related microvascular complications such as neuropathy and retinopathy, and overall mortality.⁷ In addition, poor disease management contributes to higher healthcare costs and more days of missed work.⁸

Although other common psychiatric conditions, such as major depression, have been extensively investigated as predictors and consequences of medical conditions, there has been less attention in the literature to the potential relationship between anxiety and risk of chronic conditions such as type 2 diabetes.⁹⁻¹¹ This lack of data is surprising given the fact that major depression and anxiety often co-occur.¹² Anxiety may contribute to risk of type 2 diabetes via both biological and behavioral pathways. Anxiety is associated with dysregulation of the hypothalamic-pituitary-adrenal axis (HPA) which can initiate insulin resistance.¹⁴⁻¹⁶ Life-style factors may also be relevant.¹⁷⁻¹⁸ For example, Strine et al. (2006) reported that smoking, physical inactivity, obesity, and heavy drinking are significantly associated with lifetime diagnosis of anxiety; these behaviors are known to increase diabetes risk.¹⁸⁻¹⁹

The relationship between non-specific anxiety symptoms, pathological forms of anxiety such as generalized anxiety disorder and social phobia, and type 2 diabetes is complex. Modest amounts of anxiety symptoms may promote approach-oriented coping behaviors,⁷ but more severe forms may impair efforts to change health behaviors to reduce diabetes risk. It is also possible that diabetes care self-management behaviors may themselves be a source of stress and anxiety.²⁰⁻²¹ Recent studies have shown that diabetes is associated with greater overall burden of anxiety symptoms relative to healthy controls.¹⁷ A recent study by Hall and colleagues (2009) indicated that an anxious temperament may potentially facilitate earlier detection of, but not subsequent adjustment to, type 2 diabetes.⁷ Engum et al. (2007) reported that anxiety symptoms were a significant risk for onset of type 2 diabetes; however, this study assessed anxious and depressive symptoms jointly using the Hospital Anxiety and Depression Scale and did not examine whether anxiety symptoms were independently predictive of diabetes.²² Other studies have found that anxiety is not significantly associated with development of type 2 diabetes.²³⁻²⁴ In a cross-sectional study, Hildrum et al. (2009) reported that anxiety was not linked to increased prevalence of type 2 diabetes (odds ratio: 0.98, 95% CI (0.84-1.15)).²³ In contrast, Hermanns et al. reported that clinical anxiety disorders were less prevalent among persons with diabetes relative to controls.²⁵ Hildrum et al. confirmed this finding, reporting that high anxiety symptoms were more common among

persons without metabolic syndrome (10.8%) than with metabolic syndrome (8.3%). Notably, the opposite was observed for elevated depressive symptoms (6.9% vs. 4.1% for those with vs. without metabolic syndrome).²³ Together these findings beg the question of whether depression and anxiety, although typically comorbid, contribute to diabetes risk through different pathways altogether.

The relationship between anxiety and diabetes complications is also unclear. While it is possible that anxiety may facilitate approach-related self-management behaviors, such as regular visits to the physician post-diagnosis, Khan Khuwaja (2009) reported that anxious individuals were less likely to comply with diabetes self-care recommendations and more likely to remain physically inactive and smoke, behaviors which contribute to lack of diabetes control and increased risk of complications.^{3, 7} It is unresolved whether anxiety disorders are associated with increased risk of type 2 diabetes, and there is inconclusive evidence to support the hypothesis that anxiety may actually promote healthy management of type 2 diabetes.^{18, 26}

In summary, most epidemiological studies have only examined the cross-sectional relationship between anxiety disorders and type 2 diabetes, and findings from the few longitudinal studies are inconclusive. Therefore, this study aims to address three hypotheses in a community-based prospective cohort design: (1) Anxiety is associated with increased risk of developing type 2 diabetes; (2) The relationship between anxiety and type 2 diabetes is partially, but not entirely, attributable to poor health behaviors; and (3) Among those with type 2 diabetes, anxiety is associated with lower risk of developing diabetes complications.

METHODS

Sample

Data come from the Baltimore Epidemiologic Catchment Area (ECA) Study, a population-based cohort originally interviewed in 1981 (N = 3,481) and followed up in 1982 (N = 2,768), 1993/6 (N = 1,920), and 2004/5 (N = 1,071). The goal of the ECA Study was to assess the prevalence and incidence of psychiatric disorders in the community.²⁷ The baseline sample was approximately 63% white and 33% black, and all respondents were at least 18 years or older. Complete details of the Baltimore ECA have been described elsewhere.²⁷ At each wave, approximately 75% of the surviving cohort was successfully re-interviewed. The youngest possible age of participants in 1993/6 was 30 years old. This study utilizes data from the 1993/6 and 2004/5 waves only because information on some of the anxiety disorders (e.g., generalized anxiety disorder) was not collected in prior waves.

The Baltimore ECA Study is approved by the Johns Hopkins School of Public Health Institutional Review Board (IRB), and this analysis received an exemption from the IRB at Virginia Commonwealth University.

Anxiety disorders

Anxiety disorders were assessed using the Diagnostic Interview Schedule (DIS).²⁷⁻²⁸ The DIS is a fully-structured interview based on the Diagnostic and Statistical Manual of Mental Disorders (DSM) and is administered by lay interviews. Each disorder was assessed using symptom-level data, including the causal attribution of each symptom (e.g., due to medications, drugs, or alcohol, or due to a physical illness or injury) assessed via probe questions. Only symptoms determined to be “plausibly” psychiatric in nature contribute to the determination of whether a disorder is present or not. The DIS has moderate concordance with clinical psychiatric interviews.²⁷⁻²⁹ Four common anxiety disorders were assessed: generalized anxiety disorder, social phobia, panic disorder, and agoraphobia. These disorders were examined individually and as a combined variable (any anxiety

disorder vs. none). Major depression (MD) was also assessed using the DIS. All disorders were assessed in 1993/6 and 2004/5 and reflect the DSM diagnostic criteria in use at the time.

Type 2 diabetes

Type 2 diabetes was measured by self-report in 1993/6 and 2004/5. Participants were asked, "Have you ever had high sugar or diabetes?" Those who responded yes were also asked, "Do you have high blood sugar or diabetes now?" and "At what age did the diabetes begin?" Only participants who reported that diabetes onset at age 30 later were included in the case definition of type 2 diabetes order to reduce misclassification of type 1 and type 2 diabetes.

Diabetes complications

Diabetes complications were assessed by self-report for prevalent diabetes cases in 1993/6 and 2004/5. Complications included retinopathy, neuropathy, infections, kidney or cardiovascular disease, and impotence. These complications were analyzed individually and as a dichotomous (any vs. none) summary measure.

Health behaviors

Five behaviors associated with both anxiety disorders and type 2 diabetes were assessed by self-report as potential mediators: tobacco use, body mass index (BMI) (a proxy for eating behavior), physical activity, alcohol use, and sleeping habits. Tobacco use was categorized into three groups: current, former (last smoked more than 6 months ago) and never smokers (reference). BMI was assessed by self-reported weight and height and dichotomized as overweight or obese (BMI of ≥ 25.0 kg/m²) versus normal weight (BMI of <25.0 kg/m²) (reference). Physical activity was assessed by reported frequency of engaging in moderate exercise and dichotomized as physically active (exercise 3 or more days/week) versus inactive (exercise <3 days/week, reference). Alcohol use was indicated by number of days alcohol was drunk in the past month multiplied by the average number of drinks consumed on days when alcohol was consumed; this combined variable was used to estimate monthly alcohol consumption as a continuous variable. Sleep was dichotomized as adequate sleep (7-9 hours a night, reference) versus too little sleep (<7 hours a night) or too much sleep (>9 hours a night). This categorization was chosen because both short-term and long-term sleep have been associated with type 2 diabetes risk.³⁰⁻³²

Other covariates

Age in years, gender (reference: male), race/ethnicity (reference: White), education, income, and marital status were assessed by self-report. Education was dichotomized as having at least a high school diploma (reference) versus less than a high school education. Household income was dichotomized at the sample median in 1993/6 as \geq \$25,000 (reference) versus $<$ \$25,000. Marital status was dichotomized as currently married (reference) versus formally/never married (divorced, separated, widowed).

Analysis

The main independent variable was any anxiety disorder (generalized anxiety disorder, social phobia, panic disorder or agoraphobia) in 1993/6. The main dependent variable was incident type 2 diabetes in 2004/5. Initially, the demographic characteristics and health behaviors of participants with and without an anxiety disorder in 1993/6 were compared using Fisher's exact tests for categorical variables and *t*-tests for continuous variables.

Next, logistic regression was used to determine the prospective relationship between anxiety disorders in 1993/6 and risk of new type 2 diabetes 11 years later in 2004/5. Prevalent cases

of type 2 diabetes in 1993/6 (N = 88) were removed for this analysis. In order to assess whether the prospective relationship between anxiety disorders and type 2 diabetes was mediated by health behaviors, a series of logistic regression models were fit: unadjusted, adjusted for demographic characteristics, and additional adjustment for health behaviors. A fourth model that additionally adjusted for MD was also fit to assess the degree to which any association between anxiety disorders and type 2 diabetes risk was attributable to comorbidity between MD and anxiety.

Next, the sample was restricted to participants who had prevalent type 2 diabetes in 1993/4 or 2004/5 (N = 119) in order to assess whether anxiety disorders were associated with risk of diabetes complications among those with type 2 diabetes. The relationship between anxiety conditions in 1993/4 and onset of diabetes-related complications in 2004/5 was assessed using logistic regression. Participants re-interviewed in 2004/5 who had prevalent diabetes complications at 1993/6 were excluded from this analysis (N = 23). Models were adjusted for demographic characteristics and health behaviors, as described above.

Analyses were conducted using SAS (v. 9.2) software and all p-values refer to two-sided tests.

RESULTS

Table 1 describes the demographic characteristics, health behaviors, and mental and physical health of the sample in 1993/6 stratified by anxiety status. Of those with an anxiety disorder, 261 (82.9%) had social phobia, 27 (8.6%) had generalized anxiety disorder, 52 (16.5%) had agoraphobia, and 31 (9.8%) had panic (disorders were not mutually exclusive).

Approximately 8.6% of respondents with any type of anxiety disorder had prevalent type 2 diabetes. Respondents with an anxiety disorder at baseline were younger ($P < 0.01$) and more likely to be women ($P < 0.01$) relative to those without an anxiety disorder; respondents with an anxiety disorder were also less likely to be currently married ($P < 0.05$) and more likely to have major depression ($P < 0.01$) than those without. There was no difference in health behaviors between respondents with and without an anxiety disorder, although those with an anxiety disorder were marginally more likely to be physically active ($P < 0.049$). Overall, there was no significant difference between respondents with and without an anxiety disorder in prevalent type 2 diabetes status.

Table 2 shows the results of four nested logistic regression models of anxiety in 1993/6 predicting incident type 2 diabetes 11 years later in 2004/5. There were 85 cases of new type 2 diabetes during the follow-up period, 21 among persons with an anxiety disorder and 64 among persons without. In unadjusted models, respondents with an anxiety disorder had a higher risk for new type 2 diabetes (Odds ratio (OR): 1.21, 95% Confidence Interval (CI): 0.72, 2.03) but this association was not statistically significant. After adjustment for demographic characteristics, health behaviors, and depression status, presence of an anxiety disorder in 1993/6 was unrelated to development of type 2 diabetes at follow-up (OR: 1.00, 95% CI: 0.53, 1.89).

Initially, the association between having an anxiety disorder and diabetes-related complications was assessed at each interview wave (1993/6 and 2004/5). Of the 88 respondents with type 2 diabetes in 1993/6, 62 also had at least one type of diabetes complication. The prevalence of retinopathy or vision problems for respondents with versus without an anxiety disorder was 21.6% vs. 78.4% ($X^2 = 0.038$, $P = 0.846$), respectively; for neuropathy, 22.2% vs. 77.8% ($X^2 = 0.091$, $P = 0.763$); for infections or gangrene, 25.0% vs. 75.0% ($X^2 = 0.162$, $P = 0.687$); for kidney disease, 40.0% vs. 60.0% ($X^2 = 1.21$, $P = 0.271$); for cardiovascular disease, 33.3% vs. 66.6% ($X^2 = 0.981$, $P = 0.322$); and 11.1 vs. 88.9% (X^2

= 0.542, $P = 0.462$) for impotence. Of the 144 respondents with type 2 diabetes in 2004/5 (which included incident as well as prevalent cases from 1993/6), 102 had at least one diabetes-related complication. The prevalence of retinopathy for respondents with versus without an anxiety disorder was 21.1% vs. 78.9% ($X^2 = 0.886$, $P = 0.347$); for neuropathy, 20.7% vs. 79.3% ($X^2 = 1.46$, $P = 0.230$); for infections or gangrene, 0.0% vs. 100% ($X^2 = 0.906$, $P = 0.341$); for kidney disease, 50.0% vs. 50.0% ($X^2 = 4.31$, $P = 0.041$); for cardiovascular disease, 36.4% vs. 63.6% ($X^2 = 4.98$, $P = 0.026$); and 35.7% vs. 64.3% ($X^2 = 6.25$, $P = 0.012$) for impotence. Overall, there was modest evidence of an association between anxiety and some prevalent diabetes complications, but only at the 2004/5 interview.

Table 3 shows the relationship between anxiety disorder in 1993/6 and development of any type of diabetes complication (i.e., retinopathy, neuropathy, infection/gangrene, kidney disease, cardiovascular disease, or impotence) at follow-up. There were 17 incident complications among 119 persons at risk (who either had type 2 diabetes in 1993 or developed diabetes prior to 2004/5, but had no prior report of diabetes-related complications). The association between anxiety and risk of complications was not significant in either the crude or fully-adjusted models. Depression was strongly associated with development of diabetes complications, but this relationship was not statistically significant as indicated by the wide confidence intervals.

Sensitivity analyses stratifying models by gender and examining specific type of anxiety disorders (i.e. social phobia, agoraphobia) were conducted to determine if these factors influenced the relationship between anxiety and development of type 2 diabetes. The association between anxiety and type 2 diabetes was similar for men and women (OR_{Men} : 1.21, 95% CI: 0.45, 3.20; OR_{Women} : 0.95, 95% CI: 0.38, 2.39). There was also no evidence of moderation by race/ethnicity or socioeconomic status. The results for the specific types of anxiety disorders were consistent with those presented here that examined anxiety disorders as a group (data not shown); there was no evidence that the relationship between anxiety disorders and diabetes varied by specific disorder.

DISCUSSION

The primary finding of this study is that a history of an anxiety disorder is not associated with increased risk of type 2 diabetes. There was no evidence that the relationship between anxiety and diabetes was mediated by poor health behaviors, such as smoking, alcohol use, physical activity, or obesity. Sensitivity analyses examining specific types of anxiety disorders were consistent with these null findings. Cross-sectional data showed that anxiety was modestly associated with prevalent cardiovascular disease, kidney disease, and impotence diabetes-related complications in 2004/5 only; however, anxiety was not associated with increased risk of diabetes complications longitudinally.

Extant research regarding the relationship between anxiety disorders and risk of type 2 diabetes is mixed.^{18, 21, 22, 33} Several prior reports are consistent with the null findings reported here. In a recent cross-sectional study, Bouwman et al. (2010) also reported that anxiety was not associated with type 2 diabetes (OR : 1.58, 95% CI: 0.82-3.06); however, the study did note that depression was associated with type 2 diabetes (OR : 2.55, 95% CI: 1.34-4.86).³³ This null finding is surprising in light of the fact that major depression and anxiety disorders commonly co-occur, as they did in this study, and depression is a known risk factor for type 2 diabetes.^{11, 17, 22} In one of the few studies to examine the differential relationship between depression and anxiety symptoms with metabolic risk, Skilton et al. (2007) found that depression was positively associated with metabolic syndrome (OR_{men} : 1.52, 95% CI: 1.06-3.42, $P < 0.0001$, OR_{women} : 2.29, 95% CI: 1.53-3.42, $P < 0.0001$) but

anxiety was not (OR: 1.12, 95% CI: 0.89-1.41, P=0.33).¹⁹ Together these findings suggest that there are potentially different biological mechanisms through which depression affects risk of type 2 diabetes but anxiety does not. Anxiety symptoms have been linked to an up-regulation of adrenocortical activity within the hypothalamus-pituitary-adrenal (HPA) axis, which is also seen in depression.³⁴ Cortisol, when elevated, can exacerbate glucose metabolism.²² However, recent research suggests that anxiety and depression have different biological mechanisms that may explain the difference in the relationship between these disorders and the subsequent development of diabetes. For example, while elevated concentrations of corticotropin releasing factor (CRF) are found in both anxiety and depression, release of this hormone by the HPA axis is regulated differently in the anxiety and depressive disorders. Anxiety is generally characterized by hypocortisolemia and up-regulation of glucocorticoid receptors; whereas, depression is generally characterized by hypercortisolemia and decreased numbers of glucocorticoid receptors.³⁵⁻³⁶

These findings should be interpreted in light of the strengths and limitations of the study. Extant research on the anxiety-diabetes relationship has relied on anxiety symptom scales, which produce a much more heterogeneous group of “cases.” Engum (2007) is the only study to current knowledge that looked at the relationship between anxiety disorders (as opposed to anxiety symptoms) and risk of type 2 diabetes using a longitudinal and population-based cohort; therefore, this study builds upon the little current research on the anxiety-diabetes relationship.²² In this study both anxiety disorders and major depression were measured using the DIS, a validated diagnostic interview.²⁷⁻²⁹ Limitations include the self-report measures of diabetes status and health behaviors; however, self-report diabetes status has substantial concordance with medical records.³⁷ Although BMI is treated as a proxy for eating behavior in this study, body size is influenced by factors other than diet including genetics and physical activity; also, measures of centralized adiposity such as waist circumference may be more relevant to the anxiety-diabetes relationship but were not available in this study. Also, due without clinical information it cannot be definitively determined that all of the diabetes cases examined here were type 2; however, over 95% of diabetes cases in the general population are type 2, and the vast majority of type 1 cases onset before age 30,⁴ cases which were excluded in this study. Due to the reliance on self-report diabetes status, there may be some individuals in the study with type 2 diabetes that have not yet been clinically-identified. Due to the smaller sample size, the analyses of anxiety and risk of diabetes complications had limited statistical power to detect and effect. The null results reported here need to be replicated in larger studies with longer follow-up periods.

These findings point to additional areas for future research. Specifically, future studies should examine potential mechanisms (biological, psychological, and behavioral) that may explain the apparent lack of association between anxiety and development of type 2 diabetes. Additional attention is also needed to understand the apparently discrepant relationships between depression and anxiety with type 2 diabetes risk, which is unexpected given the comorbidity between depression and anxiety disorders. Finally, although depression has been consistently linked to increased risk of diabetes complications, there is relatively little research on the role of anxiety and development of complications.^{33, 38} As discussed earlier, it is possible that anxiety may facilitate patient self-care regimens, but larger studies are needed to more fully investigate this hypothesis.⁸

The public health significance of this study is three-fold. Anxiety is a common disorder, affecting over 18% of the US population at some point over the life course, and thus it is important to understand how anxiety disorders may be related to overall health.¹ The findings of this study also indicate that anxiety and depressive disorders should also be looked at individually, despite the strong comorbidity between these conditions, because as

they may have different implications for onset and management of chronic diseases such as diabetes. The relationship between mental and physical health is a holistic one, and recognition and early treatment for anxiety disorders may influence better self-care management behaviors in those who currently live with a chronic disease, such as type 2 diabetes.³⁹ Early identification of anxiety and depression may alleviate the financial cost and health care burden of patients and encourage healthy coping behaviors which can assist in the delayed development or overall prevention of chronic disease.⁴⁰ Studies such as this one may inform patient care by encouraging clinicians to focus on the psychosocial aspects of individuals. Finally, a more comprehensive understanding how anxiety is related to diabetes management and risk of complications will also inform the development of patient care guidelines that reflect the bi-directional relationship between mental and physical health.

Acknowledgments

The Baltimore ECA Study (PI: William W. Eaton) is supported by the National Institute on Drug Abuse (R01-DA026652). B. Mezuk is supported by K01-MH093642. The sponsors had no role in the design, analysis, interpretation, or presentation of the results.

REFERENCES

1. Anxiety Disorders Association of America. [January 3, 2012] Facts & statistics. <http://www.adaa.org/about-adaa/press-room/facts-statistics>. Published 2010.
2. Allgulander C. Generalized anxiety disorder: What are we missing? *Eur Neuropsychopharm*. 2006; 16:S101–S108.
3. Khan Khuwaja A, 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 Metab Syndr*. 2010; 2(72)
4. National diabetes statistics. National Diabetes Information Clearinghouse: National Institute of Diabetes and Digestive and Kidney Diseases. National Institutes of Health; 2011. <http://diabetes.niddk.nih.gov/DM/PUBS/statistics>. Published 2011.
5. Mahler R, Adler M. Type 2 diabetes mellitus: Update on diagnosis, pathophysiology, and treatment. *J Clin Endocrinol Metab*. 1999; 84(4):1165–1171. [PubMed: 10199747]
6. American Diabetes Association. Standards of medical care in diabetes-2011. *Diabetes Care*. 2011; 34(1):S11–S61. [PubMed: 21193625]
7. Hall P, Rodin G, Vallis T, Perkins BA. The consequences of anxious temperament for disease detection, self-management behavior, and quality of life in type 2 diabetes mellitus. *J Psychosom Res*. 2009; 67:297–305. [PubMed: 19773022]
8. Fisher L, Skaff M, Mullan J, Arean P, Glasgow R, Masharani U. A longitudinal study of affective and anxiety disorders, depressive affect and diabetes distress in adults with type 2 diabetes. *Diabet Med*. 2008; 25:1096–1101. [PubMed: 19183314]
9. Golden SH, Williams JE, Ford DE, Paton Sanford C, Nieto FJ, Brancati FL. Depressive symptoms and the risk of type 2 diabetes: The Atherosclerosis Risk in Communities Study. *Diabetes Care*. 2004; 27:429–435. [PubMed: 14747224]
10. Grigsby AB, Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. Prevalence of anxiety in adults with diabetes: A systematic review. *J Psychosom Res*. 2002; 53:1053–1060. [PubMed: 12479986]
11. Mezuk B, Eaton W, Albrecht S, Golden SH. Depression and type 2 diabetes over the lifespan: A meta-analysis. *Diabetes Care*. 2008; 31(12):2383–2390. [PubMed: 19033418]
12. Stanley M. Anxiety disorders. *Clinical Psychology Review*. 2000; 20(6):731–754. [PubMed: 10983266]
13. Aguilar-Zavala H, Garay-Sevilla ME, Malacara JM, Perez-Luque EL. Stress, inflammatory markers and factors associated in patients with type 2 diabetes mellitus. *Stress Health*. 2008; 24:49–54.

14. Cohen B, Panguluri P, Na B, Whooley MA. Psychological risk factors and the metabolic syndrome in patients with coronary heart disease: Findings from the Heart and Soul Study. *Psychiatry Res.* 2010; 175:133–137. [PubMed: 19969373]
15. Chiodini I, Adda G, Scillitani A, et al. Cortisol secretion in patients with type 2 diabetes: Relationship with chronic complications. *Diabetes Care.* 2007; 30(1):83–88. [PubMed: 17192338]
16. Merswolken M, Deter HC, Siebenhuener S, Orth-Gomer K, Weber CS. Anxiety as predictor of the cortisol awakening response in patients with coronary heart disease. *Int J Behav Med.* 2012 [epub ahead of print].
17. Lin E, Von Korff M. Mental disorders among persons with diabetes: Results from the World Mental Health Surveys. *J Psychosom Res.* 2008; 65:571–580. [PubMed: 19027447]
18. Strine T, Mokdad A, Balluz L, et al. Depression and anxiety in the United States: Findings from the 2006 Behavioral Risk Factor Surveillance System. *Psychiatr Serv.* 2008; 59(12):1383–1390. [PubMed: 19033164]
19. Skilton MR, Moulin P, Terra JL, Bonnet F. Associations between anxiety, depression, and the metabolic syndrome. *Biol Psychiatry.* 2007; 62:1251–1257. [PubMed: 17553465]
20. Peyrot M, Rubin R. Levels and risks of depression and anxiety symptomatology among diabetic adults. *Diabetes Care.* 1997; 20(4):585–590. [PubMed: 9096984]
21. Mosaku K, Kolawole B, Mume C, Ikem R. Depression, anxiety and quality of life among diabetic patients: A comparative study. *J Natl Med Assoc.* 2008; 100(1):73–78. [PubMed: 18277812]
22. Engum A. The role of depression and anxiety in onset of diabetes in a large population-based study. *J Psychosom Res.* 2007; 62:31–38. [PubMed: 17188118]
23. Hildrum B, Mykletun A, Midthjell K, Ismail K, Dahl AA. No association of depression and anxiety with the metabolic syndrome: The Norwegian HUNT study. *Acta Psychiatr Scand.* 2009; 120:14–22. [PubMed: 19120047]
24. Zihl J, Schaaf L, Zillmer E. The relationship between adult neuropsychological profiles and diabetic patients' glycemic control. *Appl Neuropsychol.* 2010; 17:44–51. [PubMed: 20146121]
25. Hermanns N, Kulzer B, Krichbaum M, Kubiak T, Haak T. Affective and anxiety disorders in a German sample of diabetic patients: Prevalence, comorbidity and risk factors. *Diabet Med.* 2005; 22:293–300. [PubMed: 15717877]
26. Huang C, Chiu H, Lee M, Wang SY. Prevalence and incidence of anxiety disorders in diabetic patients: A national population-based cohort study. *Gen Hosp Psychiatry.* 2011; 33:8–15. [PubMed: 21353122]
27. Eaton WW, Anthony JC, Gallo J, et al. Natural history of Diagnostic Interview Schedule/DSM-IV Major Depression: The Baltimore Epidemiologic Catchment Area Follow-up. *Arch Gen Psychiatry.* 1997; 54:993–999. [PubMed: 9366655]
28. Robins LN, Helzer JE, Croughan J, Ratcliff KS. National Institute of Mental Health Diagnostic Interview Schedule: Its history, characteristics, and validity. *Arch Gen Psychiatry.* 1981; 38:381–389. [PubMed: 6260053]
29. Eaton WW, Neufeld K, Chen LS, Cai G. A comparison of self-report and clinical diagnostic interview for depression: Diagnostic Interview Schedule and schedules for clinical assessment in neuropsychiatry in the Baltimore Epidemiologic Catchment Area Follow-up. *Arch Gen Psychiatry.* 2000; 57(3):217–222. [PubMed: 10711906]
30. Yaggi HK, Araujo AB, McKinlay JB. Sleep duration as a risk factor for the development of type 2 diabetes. *Diabetes Care.* 2006; 29(3):657–661. [PubMed: 16505522]
31. Cappuccio FP, D'Elia L, Strazzullo P, Miller MA. Quantity and quality of sleep and incidence of type 2 diabetes: A systematic review and meta-analysis. *Diabetes Care.* 2010; 33(2):414–420. [PubMed: 19910503]
32. Buxton OM, Marcelli E. Short and long sleep are positively associated with obesity, diabetes, hypertension, and cardiovascular disease among adults in the United States. *Soc Sci Med.* 2010; 71:1027–1036. [PubMed: 20621406]
33. Bouwman V, Adriaanse MC, van't Riet E, Snoek FJ, Dekker JM, Nijpels G. Depression, anxiety and glucose metabolism in the general Dutch population: The New Hoorn Study. *PLoS ONE.* 2010; 5(4):e9971. [PubMed: 20376307]

34. Steudte S, Stalder T, Dettenborn L, et al. Decreased hair cortisol concentrations in generalised anxiety disorder. *Psychiatry Research*. 2011; 186:310–314. [PubMed: 20889215]
35. Krystal JH, D'Souza DC, Sanacora G, Goddard AW, Charney DS. Current perspectives on the pathophysiology of schizophrenia, depression, and anxiety disorders. *Med Clin North Am*. 2001; 85(3):559–577. [PubMed: 11349473]
36. Arborelius L, Owens MJ, Plotsky PM, Nemeroff CB. The role of corticotropin-releasing factor in depression and anxiety disorders. *J Endocrinol*. 1999; 160(1):1–12. [PubMed: 9854171]
37. Okura Y, Urban LH, Mahoney DW, Jacobsen SJ, Rodeheffer RJ. Agreement between self-report questionnaires and medical record data was substantial for diabetes, hypertension, myocardial infarction and stroke but not for heart failure. *J Clin Epidemiol*. 2004; 57(10):1096–1103. [PubMed: 15528061]
38. De Groot M, Anderson R, Freedland KE, Clouse RE, Lustman PJ. Association of depression and diabetes complications: A meta-analysis. *Psychosom Med*. 2001; 63:619–630. [PubMed: 11485116]
39. Buselli EF, Stuart EM. Influence of psychosocial factors and biopsychosocial interventions on outcomes after myocardial infarction. *J Cardiovasc Nurs*. 1999; 13(3):60–72. [PubMed: 10098006]
40. Hoffman DL, Dukes EM, Wittchen HU. Human and economic burden of generalized anxiety disorder. *Depress Anxiety*. 2008; 25:72–90. [PubMed: 17146763]

Table 1

Baseline Characteristics of Baltimore ECA Study, 1993/6

	Any anxiety disorder N (%)	No anxiety disorder N (%)	X ² or T, df, p-value
Total N	315	1131	
Type 2 diabetes	27 (8.6)	97 (8.6)	0.001, 1, 0.998
Age, y (<i>M, SD</i>)	51.5 (14.85)	55.2 (16.43)	3.57, 0.0004
Female	226 (71.7)	685 (60.6)	13.21, 1, 0.001
Race/Ethnicity			
<i>Black/Other</i>	129 (41.0)	412 (36.4)	2.15, 1, 0.142
<i>White</i>	186 (59.0)	719 (63.6)	
Household income			
<i>\$25,000 (median)</i>	141 (44.8)	472 (41.7)	0.93, 1, 0.336
<i>>\$25,000</i>	174 (55.2)	659 (58.3)	
Education			
<i>Less than high school</i>	127 (40.3)	451 (39.9)	0.02, 1, 0.888
<i>High school or greater</i>	188 (59.7)	680 (60.1)	
Marital Status			
<i>Former/Never married</i>	182 (57.8)	562 (49.7)	6.45, 1, 0.011
<i>Currently married</i>	133 (42.2)	569 (50.3)	
Tobacco Use			
<i>Current smoker</i>	117 (37.1)	408 (36.1)	0.96, 2, 0.618
<i>Former smoker</i>	107 (34.0)	364 (32.2)	
<i>Never smoker</i>	91 (28.9)	359 (22.9)	
BMI			
<i>Overweight/Obese (> 25.0 kg/m²)</i>	178 (56.5)	605 (53.5)	0.90, 1, 0.342
<i>Normal weight (<24.9 kg/m²)</i>	137 (43.5)	526 (46.5)	
Physical Activity			
<i>Not physically active</i>	229 (72.7)	882 (78.0)	
<i>Physically active</i>	86 (27.3)	249 (22.0)	3.87, 1, 0.049
Alcohol use in past month <i>M (SD)</i>	3.54 (7.35)	4.25 (8.15)	1.40, 0.161
Sleep			
<i><7 or >9 hrs/night</i>	142 (45.1)	465 (41.1)	1.59, 1, 0.207
<i>7-9 hrs/night</i>	173 (54.9)	666 (58.9)	
Depression Status			
<i>Yes</i>	48 (15.2)	38 (3.4)	62.15, 1, <0.001
<i>No</i>	267 (84.8)	1093 (96.6)	

Table 2

Risk of type 2 diabetes associated with anxiety disorder, Baltimore ECA follow-up, 1993/6 – 2004/5

Risk factors in 1993	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 4 OR (95% CI)
	N=931	N=931	N=767	N=767
History of anxiety disorder in 1993				
<i>Never</i>	1.0	1.0	1.0	1.0
<i>Any anxiety disorder</i>	1.21 (0.72, 2.03)	1.28 (0.75, 2.18)	1.06 (0.57, 1.96)	1.00 (0.53, 1.89)
Age, y		1.00 (0.99, 1.02)	0.99 (0.97, 1.01)	1.00 (0.98, 1.01)
Gender				
<i>Male</i>		1.0	1.0	1.0
<i>Female</i>		0.54 (0.34, 0.86)	0.49 (0.28, 0.85)	0.47 (0.27, 0.84)
Race/Ethnicity				
<i>White</i>		1.0	1.0	1.0
<i>Black/Other</i>		1.10 (0.67, 1.80)	1.02 (0.57, 1.83)	1.05 (0.59, 1.88)
Household income				
<i>\$25,000</i>		1.0	1.0	1.0
<i><\$25,000</i>		1.75 (1.02, 2.99)	1.75 (0.94, 3.28)	1.80 (0.96, 3.39)
Education				
<i>High school or greater</i>		1.0	1.0	1.0
<i>Less than high school</i>		1.31 (0.81, 2.14)	1.15 (0.66, 1.99)	1.16 (0.67, 2.01)
Marital Status				
<i>Current</i>		1.0	1.0	1.0
<i>Former/Never</i>		1.08 (0.66, 1.77)	1.21 (0.69, 2.15)	1.12 (0.63, 1.99)
Tobacco Use				
<i>Never</i>			1.0	1.0
<i>Former</i>			1.22 (0.61, 2.42)	1.22 (0.61, 2.44)
<i>Current</i>			1.36 (0.70, 2.66)	1.36 (0.69, 2.68)
BMI				
<i>Normal weight (<24.9 kg/m²)</i>			1.0	1.0
<i>Overweight/obese (≥ 25.0 kg/m²)</i>			2.85 (1.57, 5.17)	2.96 (1.60, 5.47)
Physical Activity				
<i>Physically active</i>			1.0	1.0
<i>Not physically active</i>			1.14 (0.60, 2.16)	1.13 (0.59, 2.14)
Alcohol use in past month				
			0.99 (0.95, 1.03)	0.99 (0.95, 1.02)
Sleep				
<i>7-9 hrs/night</i>			1.0	1.0
<i><7 or >9 hrs/night</i>			0.98 (0.59, 1.64)	0.99 (0.59, 1.65)
Depression Status				
<i>Never</i>				1.0
<i>Lifetime MD</i>				2.11 (0.91, 4.87)

OR: Odds ratio. CI: Confidence interval.

Table 3

Risk of diabetes complications associated with anxiety disorder, Baltimore ECA follow-up, 1993/6 – 2004/5

Risk factors in 1993	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 4 OR (95% CI)
	N=119	N=119	N=100	N=100
History of anxiety disorder in 1993				
<i>Never</i>	1.0	1.0	1.0	1.0
<i>Any anxiety disorder</i>	1.12 (0.47, 2.69)	1.37 (0.53, 3.52)	2.18 (0.66, 7.23)	2.02 (0.61, 6.74)
Age, y		1.01 (0.97, 1.05)	1.03 (0.99, 1.09)	1.04 (0.99, 1.09)
Gender				
<i>Male</i>		1.0	1.0	1.0
<i>Female</i>		0.58 (0.25, 1.38)	0.69 (0.22, 2.13)	0.66 (0.21, 2.07)
Race/Ethnicity				
<i>White</i>		1.0	1.0	1.0
<i>Black/Other</i>		1.04 (0.45, 2.43)	1.04 (0.39, 2.79)	1.18 (0.42, 3.33)
Household income				
<i>\$25,000</i>		1.0	1.0	1.0
<i><\$25,000</i>		1.46 (0.60, 3.56)	1.64 (0.56, 4.81)	1.52 (0.48, 4.80)
Education				
<i>High school or greater</i>		1.0	1.0	1.0
<i>Less than high school</i>		2.15 (0.87, 5.32)	3.32 (1.01, 10.87)	3.59 (1.04, 12.43)
Marital Status				
<i>Current</i>		1.0	1.0	1.0
<i>Former/Never</i>		0.86 (0.36, 2.03)	0.80 (0.26, 2.48)	0.74 (0.22, 2.43)
Tobacco Use				
<i>Never</i>			1.0	1.0
<i>Current</i>			1.51 (0.37, 6.19)	1.30 (0.32, 5.37)
BMI				
<i>Normal weight (<24.9 kg/m²)</i>			1.0	1.0
<i>Overweight/obese (≥ 25.0 kg/m²)</i>			1.40 (0.44, 4.45)	1.43 (0.45, 4.56)
Physical Activity				
<i>Physically active</i>			1.0	1.0
<i>Not physically active</i>			0.64 (0.21, 1.97)	0.70 (0.23, 2.15)
Alcohol use in past month			1.10 (1.00, 1.21)	1.10 (0.99, 1.21)
Sleep				
<i>7-9 hrs/night</i>			1.0	1.0
<i><7 or >9 hrs/night</i>			1.09 (0.40, 3.02)	0.95 (0.33, 2.67)
Depression Status				
<i>Never</i>				1.0
<i>Lifetime MD</i>				3.97 (0.52, 30.24)

OR: Odds ratio. CI: Confidence interval.