

PATHWAYS Annotated Bibliography - Epidemiological

Epidemiologic Research Papers: These papers describe the adverse impact of depression on symptom burden, self-management [diet, exercise, adherence to medication], functioning, blood glucose levels, medical complications, mortality and medical costs in patients with diabetes.

Lin EHB, Rutter CM, Katon W, et al. Depression and advanced complications of diabetes: a prospective cohort study. *Diabetes Care* 33:264-269, 2010. In 4,623 primary care patients with diabetes, major depression was found to be associated with significantly higher risks of adverse Microvascular complications (HR 1.36, 95% CI 1.05- 1.75) and adverse Macrovascular complications (HR 1.24, 95% CI 1.00 - 1.54) after controlling for sociodemographic differences, clinical factors, and health behaviors.

Young BA, Von Korff M, Heckbert SR, et al. Association of major depression and mortality in stage 5 diabetic chronic kidney disease. *Gen Hosp Psychiatry* 32: 119-124, 2010. Among 4,128 enrollees with diabetes, 110 were identified with state 5 chronic kidney disease (CKD). Of those, 34 (22%) met criteria for comorbid major depression. Over a 5-year period, major depression was associated with a 2.95-fold greater risk of mortality (95% CI 1.24 – 7.02) compared to those with no or few depressive symptoms.

Katon W, Lin EHB, Williams LH, et al. Comorbid depression is associated with an increased risk of dementia diagnosis in patients with diabetes: a prospective cohort study. *J Gen Intern Med* 25: 423-429, 2010. In 3,837 primary care patients with diabetes, comorbid major depression was associated with a 2.69-fold (95%CI 1.77 – 4.07) increased risk of dementia over a 5-year period compared to those with diabetes alone after controlling for socioeconomic, clinical and health-risk behaviors.

Heckbert SR, Rutter CM, Oliver M, et al. Depression in relation to long-term control of glycemia, blood pressure, and lipids in patients with diabetes. *J Gen Intern Med* 25(6): 524-529, 2010. In 3,762 patients with diabetes enrolled in the Pathways Epidemiologic Study who were followed for 5 years, among those who had an indication for drug treatment of glucose, blood pressure (SBP) or low density lipids (LDL), average long-term HbA1c, SBP and LCL did not differ in patients with diabetes and minor or major depression compared to those with diabetes alone.

Katon W, Russo J, Heckbert S, et al. The relationship between changes in depression symptoms and changes in health risk behaviors in patients with diabetes. *Int J Geriatr Psychiatry* 25:466-475, 2010. In the Pathways epidemiologic study, at 5-year follow-up, patients with diabetes with either persistent (at baseline and 5-year follow-up) or worsening depressive symptoms compared to those in the never depressed (at baseline and 5-year follow-up) group had significantly fewer days per week of following a healthy diet or participating in >30 minutes of exercise. At 5-year follow-up, patients with clinical improvement in depression symptoms (from baseline to 5-year follow-up) showed no differences compared to the no depression group on number of days per week of adherence to diet but showed deterioration in adherence to exercise on some, but not all, measures.

Ludman EJ, Russo JE, Katon WJ, et al. How does changes in depressive symptomology influence weight change in patients with diabetes? Observational results from the Pathways Longitudinal Cohort. *J Gerontol* 2010 65:93-98, 2010. In the Pathways epidemiologic study, patients who became more depressed at 5 years compared to baseline in comparison to those with persistently low depression

symptoms did not differ in their pattern of weight change ($z = 1.54, p = .12$). Both groups weighed approximately 92 kg at baseline and lost approximately 2 kg. A significantly different pattern of changes over time was observed for those with persistently high depression symptoms in comparison to those whose depression improved at 5-year follow-up ($z = 1.98, p = .04$). Although the groups had almost identical weight at baseline (approximately 100 kg), at the 5-year assessment, those with persistently high depression symptoms had about half the weight loss (mean = 1.71 kg, $SD = 9.08$) in comparison to those whose depression improved (mean = -3.62 kg, $SD = 19.93$).

Lin EHB, Heckbert S, Rutter CM, Katon W, et al. Depression and increased mortality in diabetes: unexpected causes of death. *Ann Fam Med* 7:414-421, 2009. Among 4,184 primary care patients with diabetes, after adjusting for baseline sociodemographic and clinical characteristics, major depression was associated with an increased risk of all-cause mortality (HR 1.52, 95% CI 1.19 – 1.95), and with death not due to cancer or atherosclerotic cardiovascular disease (HR 2.15, 95% CI 1.43 – 3.24), but not other causes of mortality.

Katon W, Russo J, Lin EHB, et al. Diabetes and poor disease control: Is comorbid depression associated with poor medication adherence or lack of treatment intensification? *Psychosom Med* 71: 965-972, 2009. In a cohort of 4,117 patients with diabetes, in those with poor disease control (HbA1c >8.0%, LDL >130, systolic blood pressure >140), major depression was associated with poor adherence to diabetes glucose control medications (OR = 1.98, 95% CI 1.31, 2.98), antihypertensives (OR = 2.06, 95% CI 1.47, 2.88) and LDL control medications (OR = 2.43, 95% CI 1.19, 4.97). Among those with poor disease control but adequate adherence to disease control medication, depression was not associated with lack of physician intensification of treatment.

Katon W, Russo J, Lin EHB, et al. Depression and diabetes: factors associated with major depression at 5-year follow-up. *Psychosomatics* 50:570-579, 2009. After controlling for baseline severity of depressive symptoms and history of depression, in 2,759 primary care patients with diabetes having one or more cardiac procedures during follow-up and baseline severity of diabetes symptoms were strong predictors of having major depression at 5-year follow-up. Over 80% of patients with major depression at 5-year follow-up met DSM-IV criteria for either minor depression or major depression at baseline, showing the chronicity of depression in patients with diabetes.

Gensichen J, VonKorff M, Katon W, et al. Practical support for diabetes patients and clinical outcomes in primary care. *BMC Public Health* 9: 367, 2009. Approximately 4000 patients with diabetes rated physician provision of empowerment and practical support by using the Health Care Climate Questionnaire, supplemented with questions on practical support. The empowerment and practical support subscales were used to measure providers' mean levels of support (the between-physician or practice-variation effect) and patients' deviation from their physician's mean (the within-physician effect). Glycemic control was assessed at baseline and follow-up (an average of 23 months apart) by glycosylated hemoglobin levels (HbA1c). Patients' ratings of physicians' average level of practical support (the between-physician effect) was associated with more favorable HbA1c outcome at follow-up after controlling for baseline HbA1c. Empowerment support did not predict differences in HbA1c outcome.

Young B, Lin EHB, Von Korff M, et al. Diabetes Complications Severity Index (DCSI) and risk of mortality, hospitalization and health care utilization. *Am J Managed Care* 14 (1): 15-23, 2008. An 11-point Diabetes Complication Severity Index (DCSI) was developed from automated clinical data from over 4000 patients with diabetes. Each level of the DCSI was associated with a 1.34 (95% CI

1.28-1.41) greater risk of death over 4 years as well as a greater risk of hospitalization and time to first hospitalization. This new diabetes complication measure is an important new measure of diabetes severity that can be used by health services researchers as a case mix adjuster.

Ciechanowski P, Russo J, Katon W, et al. Where is the patient? The association of psychosocial factors and missed primary care appointments in patients with diabetes. *Gen Hosp Psychiatry* 28:9-17, 2006. Among 3923 primary care patients with diabetes, those with major depression had more scheduled office visits ($p < .0001$), same-day appointments ($p < .001$) and missed scheduled visits ($p < .01$) compared to non-depressed patients. Patients with preoccupied attachment style had more scheduled office visits ($p < .05$) and same-day appointments ($p < .05$) and patients with fearful attachment had more same-day appointments ($p < .05$) but less preventative care visits (OR = 0.75 95% CI 0.61, 0.92) as compared to those with secure attachment. Among nondepressed patients, there were more missed scheduled office visits among those with dismissing versus secure attachment (OR = 1.46, 95% CI 1.18, 1.81).

Ludman E, Katon W, Russo J, et al. Panic episodes among patients with diabetes. *Gen Hosp Psychiatry* 28:475-81, 2006. Panic disorder is a frequent primary care disorder as well as a common comorbid illness in patients with major depression. Approximately 4% of patients with diabetes met criteria for panic disorder, and after controlling for depression, panic was associated with higher HbA1c ($p < .01$), greater number of diabetes complications ($p < .05$) and diabetes symptoms ($p < .001$), increased disability ($p < .001$) and poorer self-rated health ($p < .001$).

Morse SA, Ciechanowski PS, Katon WJ, et al. Isn't this just bedtime snacking? The potential adverse effects of night-eating symptoms on treatment adherence and outcomes in patients with diabetes. *Diabetes Care* 29:1800-4, 2006. Night-eating syndrome is characterized by excessive eating in the evening and nocturnal awakening with ingestion of food. Psychosocial variables and emotional triggers may be associated with these behaviors. In patients with diabetes, such behaviors may lead to glucose dysregulation and contribute to obesity and complications. In 714 tertiary care patients with type 1 and 2 diabetes, night-eating behaviors were reported in 9.7% of patients. Compared to patients without night-eating behaviors, those with these behaviors were less adherent to diet, exercise and glucose monitoring and more likely to be depressed, to report childhood maltreatment histories, to have insecure attachment styles and to report eating in response to anger, sadness, loneliness, worry and being upset. Controlling for age, sex, race and major depression, patients with night-eating behaviors compared to patients without night-eating behaviors were more likely to be obese [OR = 2.6 (95% CI 1.5-4.5)], to have HbA1c values $>7\%$ [OR = 2.2 (CI 1.1-4.1)] and to have 2 or more diabetes complications [OR = 2.6 (1.5-4.5)].

Von Korff M, Katon W, Lin EHB, et al. Potentially modifiable risk factors for disability among persons with diabetes. *Psychosom Med* 67:233-40, 2005. Among 4357 patients with diabetes, comorbid major depression was associated with a 10-fold increase in risk of elevated WHO-DAS-II scores and low SF-36 social function scores and a 4-fold increase in the risk of having 20 or more days of reduced ability to do housework in the last 30 days after controlling for medical comorbidity. The number of diabetic complications and the number of ten diabetes symptoms were also independently associated with increased disability risks, but had less impact compared to comorbid depression. An increased frequency of exercise was protective, i.e. it was associated with decreased risk of disability.

Young B, Katon W, Von Korff M, et al. Racial and ethnic differences in microalbuminuria prevalence in a diabetes population: the Pathways Study. *J Am Soc Nephrology* 16:219-28, 2005. The unadjusted prevalence of micro or macroalbuminuria was 32.3%. Among those without hypertension, microalbuminuria was 2-fold greater (OR = 2.0, 95% CI = 1.1 -3.5) and macroalbuminuria was 3-fold greater (OR = 3.2, 95% CI= 1.1 - 9.3) for Asian Americans compared to Caucasians. Among those with hypertension, the adjusted odds of microalbuminuria were greater for Hispanics (OR = 3.8, 95% CI = 1.2- 12.6) than Caucasians , while the adjusted odds of macroalbuminuria were 3-fold greater for African-Americans (OR = 3.3, 95% CI = 1.3 - 8.8) than Caucasians.

Von Korff M, Katon W, Lin EHB, et al. Work disability among persons with diabetes. *Diabetes Care* 28:1326-32, 2005. Among persons with diabetes (N=1642) enrolled in a large HMO, excluding homemakers and retirees, we assessed the relationship of diabetes severity, chronic disease comorbidity, depressive illness and behavioral risk factors with work disability. Depressive illness and diabetic symptoms were associated with significantly greater work disability, including missing 5 or more days of work in the prior month and severe difficulty performing work tasks. Depressive illness, diabetes symptoms, medical comorbidity, diabetes complications, poor glycemic control and type 1 status were all significantly associated with unemployment.

Simon G, Katon W, Lin EHB, et al. Diabetes complications and depression as a predictors of health care costs. *Gen Hosp Psychiatry* 27:344-55, 2005. Among 4398 patients with diabetes, total health care services were approximately 70% higher in those with major depression compared to those without depression (\$5361 over 6 months versus \$3120, $p < .001$) and this difference was consistent across all categories of health services costs. Diabetes complications was the strongest predictor of costs, but depression remained strongly associated with increased costs at all levels of diabetes severity.

Katon W, Rutter C, Simon G, et al. The association of comorbid depression with mortality in patients with type 2 diabetes. *Diabetes Care* 28:2668-72, 2005. Over a 3-year period, there were 277 (8.3%) deaths in the 3344 patients without depression compared to 48 (13.4%) deaths in the 350 patients with minor depression and 59 (11.2%) deaths among the 505 patients with major depression. A proportional hazards model with adjustment for age, gender and educational attainment found that, compared to the nondepressed group, minor depression was associated with a 1.66-fold and major depression with a 2.26-fold increase in mortality. A second model that controlled for potentially behavioral (obesity, smoking, sedentary lifestyle) and clinical (diabetes complications, HbA1c, other nondiabetes medical comorbidity, insulin treatment) mediators found that both major and minor depression continued to be significant predictors of mortality.

Katon W, Von Korff M, Ciechanowski P, et al: Behavioral and clinical factors associated with depression among individuals with diabetes. *Diabetes Care* 27:914-20, 2004. This population-based study was able to attain a 61.7% response rate successfully in surveying approximately 4800 patients with diabetes enrolled in 9 primary care clinics of a Seattle HMO. 11.7% of patients were found to meet DSM IV criteria for major depression (14.2% of women, 9.2% of men). Demographic, behavioral and clinical risk factors that predicted meeting criteria for major depression included younger age, female gender, less education, single marital status, BMI ≥ 30 , smoking, higher nondiabetic medical comorbidity, type 2 diabetes, higher number of diabetes complications, being treated with insulin and having higher HbA1c levels in patients less than age 65.

Ludman E, Katon W, Russo J, et al. Depression and diabetes symptom burden. *Gen Hosp Psychiatry* 26:430-6, 2004. Patients with comorbid major depression and diabetes were 1.93 to 4.96 times more likely to report each of 10 diabetes symptoms compared to patients with diabetes who were not depressed after controlling for demographics, HbA1c, diabetes complications and medical comorbidity. In contrast, patients with diabetes mellitus with two or more complications compared to those with 0 to 1 complication were more likely to report experience 9 out of 10 diabetes symptoms with odds ratios of 1.26 to 1.96. Diabetic patients with HbA1c levels ≥ 8.0 compared to diabetic patients with HbA1c < 8.0 were only more likely to report 4 out of 10 symptoms with odds ratios of 1.17 to 1.34. Comorbid depression is a more robust predictor of a standard checklist of diabetic symptoms in patients with diabetes compared to metabolic control based on HbA1c or number of diabetes complications.

Katon W, Lin EBH, Ciechanowski P, et al. Cardiac risk factors in patients with diabetes mellitus and major depression. *J Gen Intern Med* 19:1192-9, 2004. In this population-based sample of 4225 patients with diabetes, those with major depression had almost twice the rate of having 3 or more of eight cardiovascular risk factors compared to nondepressed diabetics (62.5% vs 38.4%) in those without a history of cardiovascular disease (CVD) as well as those with a history of CVD (61.3% vs. 45%). Patients with diabetes without CVD who were depressed were significantly more likely to be smokers, have a BMI >30 kg/m² and to have a more sedentary lifestyle than the nondepressed diabetics without CVD. Patients with major depression, diabetes and evidence of heart disease were significantly more likely to have BMI >30 kg/m², to have a more sedentary lifestyle and to have triglyceride levels of >400 mg/dl compared to the nondepressed group with evidence of heart disease.

Katon W, Simon G, Russo J, et al. Quality of depression care in a population-based sample of patients with diabetes and major depression. *Med Care* 42:1222-9, 2004. A total of 524 (12%) of our sample of patients met DSM IV criteria for major depression. Of those with depression, only 36.3% received a depression diagnosis in the previous 12-month period and 43% filled one or more prescriptions for antidepressant medication. However, only 31.3% receive adequate dosage and duration of antidepressant medication for 90 days or more. A much smaller percentage (13.5%) had a mental health visit in the 12-month period and only 6.7% had 4 or more psychotherapy visits. Logistic regression analysis showed that women were more likely to be accurately recognized as being depressed (OR = 1.58, 95% CI = 1.26 to 1.97) as were those with comorbid dysthymia (OR = 3.44, 95% CI = 2.08 to 5.72), current panic attacks (OR = 1.55, 95% CI = 1.19 to 2.19), and those with more than 7 primary care visits (OR = 1.42, 95% CI = 1.06 to 1.91). Those who reported having poor health also had more chance of being recognized (OR = 1.62, 95% CI = 1.04 to 2.53).

Ciechanowski P, Russo J, Katon W, et al. The influence of patient collaborative style on self-care and outcomes in diabetes. *Psychosom Med* 66:720-8, 2004. Patients with insecure attachment styles, particularly fearful and dismissing attachment, have been shown to have problems trusting and collaborating with physicians. In this population-based sample of patients with diabetes, dismissing attachment style was shown to be associated with lower levels of exercise ($p < .005$), foot care ($p < .05$), adherence to diet ($p < .001$), adherence to oral hypoglycemic medications ($p < .05$) and higher rates of smoking ($p < .05$). These relationships were mediated by the doctor patient relationship. Greater patient-physician collaboration mediated the relationship of dismissing and fearful attachment to poor adherence. No differences in HbA1c levels were found between those with insecure and secure attachment after controlling for demographic factors, diabetes severity and

medical comorbidity and depression.

Lin EHB, Katon W, Von Korff M, et al. Relationship of depression and diabetes self-care, medication adherence and preventive care. *Diabetes Care* 27:2154-2160, 2004. In this sample of 4,463 primary care patients with diabetes, major depression was associated with a higher likelihood compared to nondepressed patients of less than two days a week of healthy eating (OR = 2.1, 1.59 -2.72) and eating 5 servings of fruits and vegetables (OR =1.8, 1.43-2.17), eating high fat foods 6 or more days per week (OR = 1.3, 1.01 - 1.73), less than two days a week of physical activity (OR = 1.9, 1.53-2.27) or specific exercise session (OR = 1.7, 1.43 - 2.12) and being a smoker (OR = 1.9, 1.42-2.51). Depression was also associated with significantly more lapses in taking oral hypoglycemic, lipid lowering and antihypertensive medications.

Katon W, Von Korff M, Lin EHB, et al. Improving primary care treatment of depression among patients with diabetes mellitus: the design of the Pathways Study. *Gen Hosp Psychiatry* 25:158-68, 2003. This paper described the methodology involved in developing: 1) a mail survey that was sent to a population-based sample of approximately 9,000 primary care patients with diabetes; and 2) the methodology involved in the large treatment trial that randomized 330 patients with depression and diabetes to test a nurse collaborative care intervention versus usual care in improving quality of care and depression outcomes for patients with depression and diabetes.