EFFECTS OF DEPRESSION AND ANTIDEPRESSANT USE ON GOAL SETTING AND BARRIER IDENTIFICATION AMONG PATIENTS WITH TYPE 2 DIABETES

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Diabetes self-care plays a vital role in achieving better diabetes outcomes. To enhance diabetes self-care, the strategies of goal setting and barrier identification are widely used to assist people in making behavior change. Depression is a common co-morbidity and a barrier to self-care in people with diabetes. The purpose of this study was to examine the effects of depression and antidepressant use on goal setting and barrier identification in patients with type 2 diabetes.

In patients with type 2 diabetes enrolled in the American Association of Diabetes Educators (AADE) Outcomes System as part of their routine diabetes education, 778 patients were included into this analysis. Self-report depression, 7 self-identified behavior change goals, and 13 barriers to diabetes self-care were collected from the Diabetes Self-management Assessment Report Tool (D-SMART®); antidepressant use was determined from the Diabetes Educator Tool (D-ET®). Multiple linear regression was used for the number of goals and the number of barriers with controls for relevant covariates.

Patients with and without depression had a similar number of self-identified behavior change goals (P = 0.47), whereas patients with depression had 1.01 barriers to diabetes self-care greater than those without depression (P = 0.0001). In the depressed subgroup, there was no

significant difference between those with and without antidepressant use in the number of goals (model 3A, P = 0.18; model 3B, P = 0.35) and in the number of barriers (P = 0.99).

Since depression was related to a greater number of barriers to self-care, depression screening is important in patients with diabetes. Although antidepressant use had no association with the number of goals or the number of barriers, antidepressants are still useful in treating depression in patients with diabetes. In addition, collaborative treatment should be integrated to provide maximal benefit to improve both diabetes and depression. These conclusions are of public health significance and can be used to develop behavior change strategies to improve diabetes self-care.

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1.0 INTRODUCTION

1.1 DIABETES

Diabetes is the seventh leading cause of death reported on U.S. death certificates in 2006.[1] The Centers for Disease Control and Prevention (CDC) estimates that 7.8% of the U.S. population (nearly 23.6 million people) suffered from diabetes in 2007.[1] While an estimated 17.9 million people are diagnosed with diabetes, 5.7 million people (nearly one quarter) are unaware that they have the disease.[1]

Diabetes is marked by high levels of blood glucose resulting from a shortage of insulin or a decreased ability to use insulin. Diabetes can lead to serious complications, such as cardiovascular disease, kidney disease, nerve damage, and blindness. People with diabetes also have higher premature mortality along with reduced life expectancy by 7-7.5 years.[2] In order to prevent these complications, achieving adequate control of risk factors is important.

1.2 DIABETES SELF-CARE

Diabetes self-care behaviors play a vital role in achieving optimal glycemic control, retarding the progression of complications, and decreasing morbidity and mortality associated with diabetes.[3-6] Defined by American Association of Diabetes Educators (AADE), self-care behaviors are

healthy eating, being active, monitoring blood glucose, taking medication, problem solving, risk reduction activities, and healthy coping. There are known as AADE7 Self-Care Behaviors.[7] A previous study[8] showed that 95% of the routine daily care essential for maintaining glucose control needs to be provided by the diabetes patient, demonstrating the necessity for good diabetes self-care. According to a recent survey of US nurses and physicians[9], promotion of effective self-care behaviors is also regarded as one of five key goals that need to be accomplished to improve diabetes outcomes.

1.3 GOAL SETTING AND BARRIER IDENTIFICATION

To improve diabetes self-care behaviors, the strategies of goal setting and barrier identification are widely used to assist people in making behavior change.[10-12] Goal setting is a collaborative process in which the patient is an active participant in deciding their own diabetes regimens.[11] This method may help people to improve recall of daily demands of diabetes and motivate them to participate in diabetes self-care. People with diabetes usually identify diabetes self-care goals as linked to their life goals, such as longevity, spending time with family, and maintaining independence.[13, 14] Factors influencing diabetes self-care goals include health care providers, family, and ancillary and outside resources.[13, 14] In addition, Estabrooks et al.[15] found that diabetes patients who were involved in selecting goals for diabetes self-care often selected the goals for which they needed to make the most change. For instance, those selecting a goal to increase physical activity were significantly less active at baseline than those choosing a goal to decrease fat consumption or to increase fruit and vegetable consumption.[15] People who

participate in the goal-setting process are more likely to overcome potential barriers to self-care and to achieve favorable diabetes outcomes.[11, 14-18] (See Table 1 and Table 2)

Barrier identification also minimizes adverse effects on adherence to self-care behaviors.[19] Most diabetes patients encounter barriers to self-care and these barriers are a major challenge when they deal with daily demands of diabetes.[20-22] The most frequently reported barriers to diabetes self-care include cost, time constraints, inconvenience, low self-efficacy, limited coping skills and knowledge, reduced quality-of-life, complications and functional disabilities, inadequate resources, limited social and family support, complex regimen, poor patient–provider relationship, invasive characteristic for glucose monitoring, and depression or distress.[13, 23-28] Diabetes patients with multiple barriers are also likely to reduce adherence to diabetes self-care.[26, 29] (See Table 3 and Table 4)

1.4 DEPRESSION AND DIABETES

Depression is a common co-morbidity and a barrier to diabetes self-care in people with diabetes mellitus.[30] The risk of depression is 50–100% higher in people with diabetes compared to the general population.[31] People with diabetes not only need to continuously pay attention to their complex regimens, but also have the fear of hypoglycemia and diabetes complications. These reasons can increase perceived stress, leading to high rates of depression.[32] In addition, because of loss of energy and motivation, negative cognition, pessimistic attributional style, and passive coping strategies,[33] people with depression are less likely than those without depression to optimally manage their diabetes.

For people with diabetes, depression is associated with poor glycemic control, leading to more complications,[34] higher mortality rates,[35] and greater health care costs.[36] Depression is also related to poor adherence to diabetes self-care. Most studies show that diabetes patients with depression are more likely than those without depression to have an unhealthy diet[37-41] and low medication adherence,[37, 39-43] while those with and without depression are similar in compliance with glucose monitoring[37-41] and with foot care.[39, 41] There are inconsistent findings regarding the association between depression and exercise.[37-41] To clarify the relationships between depression, poor diabetes self-care, and adverse diabetes outcomes, McKellar et al.[44] used structural equation models to find that depression increased symptoms of poor glucose control through lowering adherence to diabetes self-care. Accordingly, if these people receive appropriate depression treatment, they may improve diabetes outcomes by increasing adherence to diabetes self-care. (See Table 5 and Table 6)

1.5 DEPRESSION TREATMENT AND DIABETES

Several randomized controlled trials evaluated the effects of depression treatment (antidepressants, behavior therapies, or both) in people with diabetes and depression.[45-50] Most studies found a significant improvement in depression for those receiving antidepressants and/or behavior therapies, while effects of depression treatment on glycemic control have been mixed.[45, 47-50] In addition to effects on depression and glycemic control, four studies[46, 48-50] investigated the association between enhanced depression treatment (antidepressants, behavior therapies, or both) and diabetes self-care. Among those with type 2 diabetes and major depression, people receiving cognitive behavior therapy plus diabetes education had reduced adherence to self-monitoring of

blood glucose compared to those receiving diabetes education alone during the 10-week treatment period.[49] In a study of older people with diabetes and depression, the intervention (including antidepressants and behavior therapies) increased people's physical activity but had no effects on other self-care behaviors (diet, diabetes medication, glucose monitoring, and foot inspection) relative to usual care during the 12-month intervention period.[50] In another 12-month trial comparing collaborative depression treatment (antidepressants and/or behavior therapies) with usual care among people with diabetes and depression, the two groups reported no difference in diabetes self-care (diet, exercise, smoking, and medication adherence to lipid-lowering and antihypertensive medicines) except a higher rate of non-adherence to oral hypoglycemic agents in intervention group.[46] A trial comparing nortriptyline with placebo in people with poorly controlled diabetes also showed no effects on compliance with glucose monitoring and with medication regimen over the 8-week treatment period.[48] From these studies, the relationship between treatment of depression and diabetes self-care seems to be inconsistent, and only one study[48] specifically investigated the effects of antidepressant on diabetes self-care. (See Table 7 and Table 8)

1.6 PURPOSE OF THE STUDY

Diabetes self-care is not a small task from a patient's perspective. Depression increases difficulties in achieving good diabetes self-care. Although a number of studies[37-43] investigated the association between depression and diabetes self-care behaviors, there is no literature addressing the effects of depression on goal setting and barrier identification in people with diabetes. There is only one study to the best of our knowledge examining the effects of

depression on goal achievement for control of glucose, lipids, and blood pressure,[51] rather than on goal setting for adherence to diabetes self-care behaviors. Moreover, whether goal setting and barrier identification are improved by alleviated depression due to antidepressant use is still unanswered. Therefore, our first study aim is to evaluate the effects of depression on the number of self-identified behavior change goals and the number of barriers to diabetes self-care among patients with type 2 diabetes. Our second aim is to study the treatment effects of antidepressants on the number of self-identified behavior change goals and the number of barriers to diabetes self-care in the depressed subgroup.

2.0 METHODS

2.1 STUDY SETTING

This analysis was conducted using data from AADE Outcomes System, which was developed to facilitate the delivery, documentation, and evaluation of patient behavior change in the provision of diabetes self-management education (DSME).[7] The AADE Outcomes System was integrated into Internet, touch-screen, and telephonic systems within 8 sites in the Pittsburgh Regional Initiative for Diabetes Education (PRIDE) network.[10] PRIDE is a regional health care collaboration established by the University of Pittsburgh Diabetes Institute to improve diabetes education and care in western Pennsylvania.[52] Patients with type 1 or type 2 diabetes were enrolled in the system as part of their routine diabetes education visits from 2005 to 2008. To be eligible for this study, complete data in the following fields were needed: self-report depression, antidepressant use, self-identified behavior change goals, and barriers to diabetes self-care. Also, only patients with type 2 diabetes were included. Therefore, final sample size was 778 (Figure 1). This study was approved by the Institutional Review Boards of the University of Pittsburgh.

2.2 MEASUREMENT

Two instruments were developed to collect data from patients (the Diabetes Self-management Assessment Report Tool, D-SMART®) and from diabetes educators (the Diabetes Educator Tool, D-ET®).[10] The D-SMART is a self-report instrument that gathers information about (1) demographics and health history and (2) behaviors and behavior change goals, organized in terms of the domains of the AADE7 Self-Care Behaviors.[10] Patients were asked to complete a baseline D-SMART prior to the start of DSME program. The D-ET was completed by the diabetes educator during the provision of DSME, and provided an opportunity for the educator to record medical information about the patient and the educator's assessment of the patient's needs and progress. In the present study, self-report depression, 7 self-identified behavior change goals, and 13 barriers to self-care were collected from the D-SMART®; antidepressant use was determined from the D-ET®. Demographic (age, gender, race, education status, smoking, alcohol drinking, family history of diabetes, diabetes duration, and diabetes education) and clinical (BMI, HbA1c, complications, and insulin use) data were obtained from either the D-SMART or the D-ET.

Depression status was identified if patients reported "Depression or anxiety" in D-SMART or had records of antidepressant use in D-ET.[41] To determine self-identified behavior change goals, patients chose the domains in which they would like to make changes including activity, eating, medication taking, monitoring, problem solving for blood sugars and sick days, reducing risks of diabetes complications, and living with diabetes. Patients also identified the level of each barrier that kept them from making the change. Among the four levels of each barrier to self-care, patients answering "A lot ", "some", "a little" were categorized as those who had barriers; patients answering "Not at all" were categorized as those who did not have barriers.

2.3 STATISTICAL ANALYSIS

Demographic and clinical data were reported using measures of central tendency (percentage or mean/medium). Comparisons between patients with and without depression or with and without antidepressant use were performed using the χ^2 test for categorical variables. Continuous variables were analyzed using the Student t or Wilcoxon rank sum test.

Multiple linear regression was employed for the number of self-identified behavior change goals and the number of barriers to self-care. Univariate modeling was performed followed by multivariable modeling. Those covariates whose p-values were < 0.10 were considered for multivariable models. Covariates for consideration included: depression status (Y/N), antidepressant use (Y/N), age (continuous), gender, race (white/black/others), education status (did not finish high school/high school/some college or greater), BMI (continuous), smoking (never/former/current), alcohol drinking (Y/N), family history of diabetes (Y/N), diabetes duration (continuous), diabetes education (Y/N), the number of diabetes complications (continuous), HbA1c level (continuous), insulin use (Y/N), and the number of barriers (7-13/0-6). Transformation of covariates was performed where necessary. P-values < 0.05 were considered significant. All analysis was completed using SAS 9.2. (SAS Institute Inc., Cary, North Carolina)

3.0 RESULTS

3.1 COMPARISONS BETWEEN PATIENTS INCLUDED AND EXCLUDED

Upon examination of those excluded from this analysis, we found that patients included were more likely to be white people with higher BMI, less alcohol drinking, family history of diabetes, insulin prescriptions, longer duration of diabetes, and more diabetes complications. There was no significant difference between patients included and excluded in depression status, age, gender, education status, smoking, diabetes education, and HbA1c level. (See Appendix A)

3.2 DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

Demographic and clinical characteristics of patients by depression/antidepressant status (ie. non-depressed patients, depressed patients with antidepressant, and depressed patients without antidepressant) are shown in Table 9. Between patients with and without depression, depressed patients were more likely to be younger (56 vs. 60 yr), obese (34.38 vs. 33.16 kg/m^2), female (71.96% vs. 55.03%), currently smoking (28.51% vs. 18.25%), to have more diabetes complications, and to suffer from kidney or bladder problems, numbness or pain, and vision problems, while they were less likely to drink alcohol (20.37% vs. 26.64%). Race, education status, family history of diabetes, duration of diabetes, diabetes education, HbA1c level, insulin

use, and the prevalence of some complications (such as high blood pressure, stroke, heart disease or chest pain, and problems with sexual function) were similar in patients with and without depression. Between patients with and without antidepressant use in the depressed subgroup, they were similar in most demographic and clinical characteristics except that those with antidepressant use were younger (55 vs. 57 yr) and were more likely to have diabetes education (29.44% vs. 14.44%) than those without antidepressant use.

3.3 UNADJUSTED SELF-IDENTIFIED BEHAVIOR CHANGE GOALS AND UNADJUSTED BARRIERS TO DIABETES SELF-CARE

By depression/antidepressant status, unadjusted self-identified behavior change goals and unadjusted barriers to diabetes self-care are presented in Table 10 and Table 11, respectively. Patients with and without depression were similar in the number of self-identified behavior change goals ($P = 0.11$). In the depressed subgroup, patients with and without antidepressant use were also similar in the number of goals ($P = 0.26$). For barriers to diabetes self-care, patients with depression had a greater number of barriers to self-care compared to those without depression (7 vs. 6, $P < .0001$), whereas in the depressed subgroup, patients with and without antidepressant use were similar in the number of barriers ($P = 0.75$).

3.4 LINEAR REGRESSION MODELS

Multiple linear regression was used to evaluate the effects of depression or antidepressant use on the number of goals or the number of barriers with controls for relevant covariates (Table 12). From the model 1, depression had no association with the number of goals after adjusting for age, race, education, and the number of barriers (P = 0.47). Patients who were young (P < .0001), white (black, P = 0.02; others, P = 0.01), educated (did not finish high school, P < .0001; high school diploma, P = 0.0002), and had a greater number of barriers (P = 0.03) were more likely to have a greater number of goals. From the model 2, patients with depression had 1.01 barriers greater than those without depression after controlling for BMI, race, education, age, and insulin prescription (P = 0.0001). Patients with a greater number of barriers were more likely to have higher BMI (P < .0001), to be black or other race (black, P = 0.05; others, P = 0.006), to have lower education (did not finish high school, P = 0.01; high school diploma, P = 0.11), and to have insulin prescription (P < .0001). From the model 3A, there was no relation between antidepressant use and the number of goals in the depressed subgroup after adjusting for age, race, education, insulin prescription, and family history of diabetes (P = 0.18). In the depressed subgroup, patients who were white people (black, P = 0.04; others, P = 0.001), had higher education (did not finish high school, P = 0.05; high school diploma, P = 0.13), did not use insulin (P = 0.07), and had family history of diabetes (P = 0.06) were more likely to have a greater number of goals. After excluding those covariates with borderline P value (such as education, insulin use, and family history of diabetes) (the model 3B), antidepressant use was still not significantly related to the number of goals after adjusting for age and race (P = 0.35). According to this model, white people (black, P = 0.05; others, P = 0.003) with younger age (P = 0.02) were more likely to have a greater number of goals in the depressed subgroup. From the

model 4, we found that depressed patients with and without antidepressants were similar in the number of barriers after controlling for age, BMI, education, and insulin use (P = 0.99). Patients with a greater number of barriers were more likely to have higher BMI (P = 0.0003), to have lower education (did not finish high school, P = 0.04; high school diploma, P = 0.24), and to use insulin (P = 0.004). The main findings remained the same even though additionally including HbA1c level, insulin use, or both as covariates in each model.

4.0 DISCUSSION

4.1 SUMMARY OF FINDINGS

In patients with type 2 diabetes enrolled in the AADE Outcomes System as part of their routine diabetes education, those with and without depression had a similar number of self-identified behavior change goals, whereas patients with depression had 1.01 barriers to diabetes self-care greater than those without depression. In the depressed subgroup, antidepressant use had no association with the number of goals they set and the number of barriers they identified.

4.2 SIGNIFICANCE OF THE STUDY

Goal setting and barrier identification play important roles in helping patients make behavior change and achieve better diabetes self-care ultimately. Depression is not only a common co-morbidity in patients with diabetes, but also a well-known barrier that affects diabetes self-care. Although several studies show negative effects of depression on diabetes self-care[37-43], whether depression has influences on goal setting and barrier identification has not been well-studied. The available study investigated the effects of depression on goal achievement for clinical outcomes,[51] rather than on goal setting for diabetes self-care. A number of studies explored barriers in patients with diabetes,[13, 25-28] rather than evaluated the effects of depression on

patients' barriers to diabetes self-care. Thus, our study is unique and provides important information for diabetes educators to help patients with diabetes and depression.

4.3 POSSIBLE EXPLANATIONS

Beyond our expectation that patients with depression have decreased interest in making behavior change due to associated characteristics (such as pessimism and fatigue), we found that there was no association between depression and the number of self-identified behavior change goals. One possible explanation is that the patient in our study was those who received routine diabetes education, and therefore these patients were more active to pursue intensive treatments to achieve better diabetes outcomes. This impetus to seek help to improve their disease may compromise their negative behavioral style, leading to the absence of an effect of depression on their goal setting.

Our study showed that patients with depression had a greater number of barriers to diabetes self-care than those without depression. However, there was no difference between those with and without antidepressant use in the depressed subgroup. This result is similar to previous findings that the treatment of depression (antidepressants and/or behavior therapies) had no effects on diabetes self-care behaviors (specifically, nutritional recommendations, smoking cessation, and foot care).[46, 48-50] Thus, these findings suggest that the treatment of depression alone may be not enough to address patients' barriers for them to achieve better diabetes self-care. Overcoming patients' barriers to diabetes self-care may require intensive interventions specific to each barrier. Another possibility is that complex diabetes regimens may reduce

patients' adherence to antidepressants[46, 50], leading to equal performance between patients with and without antidepressants.

4.4 LIMITATIONS

Our study has some limitations that warrant consideration. First, this study is cross-sectional, and therefore the temporal association cannot be established. For instance, we cannot determine whether depression increases the number of barriers to diabetes self-care, or a greater number of barriers to diabetes self-care make patients feel depressed, or both. Thus, future longitudinal studies are needed to examine all the cause-effect relationships in this study. Second, the goal setting and barrier identification were determined by patients in the D-SMART. Since there were 7 domains in goal setting and 13 items in barrier identification, some patients may feel burdened by completing all the questions and may not answer all questions for goal setting and barrier identification. Thus, among 1575 patients with type 2 diabetes in this system, 442 (28.06%) patients had missing data in goal setting and 428 (27.17%) patients in barrier identification. Furthermore, those who were excluded from this study due to missing values were different from those who were included in some demographic and clinical characteristics (such as race, BMI, alcohol drinking, family history of diabetes, insulin use, diabetes duration, and complications), which may restrict the generalizability of the results. Third, to identify those with depression, we relied on patients' self-report in D-SMART and their records of antidepressant use in D-ET. Since some patients may not reveal their depression tendency and not all depressed patients need to take antidepressants, the identification of depression on the basis of self-report and antidepressant use may underestimate the number of patients with depression. This

misclassification bias may account for inability to detect significant differences. To avoid this bias, structured interviews are preferred in future studies to make a diagnosis of major depression. In addition, formal psychiatric assessment is considered to be the gold standard in identifying depressed patients. Forth, the record of antidepressant use was obtained from the diabetes educator during the provision of DSME. However, the medication data indicated only medicines the patient prescribed, not medicines they actually took. Thus, the objective measurement (e.g., electronic monitoring caps[43]) is needed to monitor medication adherence in future studies. Fifth, some antidepressants are not only used to treat depression, but also taken to relieve other disorders. For example, duloxetine, a selective serotonin and norepinephrine reuptake inhibitor, is not only regarded as an antidepressant, but also wildly used to inhibit pain due to diabetic peripheral neuropathy. In our study, only 13 (2%) patients had records of duloxetine, and therefore this was not likely to affect our results.

4.5 FUTURE STUDIES

Based on our findings, patients with depression had about one barrier greater than those without depression. Although this difference between those with and without depression in the number of barriers is small, whether it may bring about significant influences on diabetes self-care is unanswered. It is possible that depressed patients are likely to have a certain item of barriers to diabetes self-care, and therefore they are likely to have poor adherence to the related domains of diabetes self-care. Thus, in future studies, it is necessary to examine the effects of depression on each item of barriers and also to evaluate the clinical significance of these effects on diabetes self-care.

Goal setting, skill acquisition, and maintenance of motivation are important components for diabetes patients to achieve successful self-care.[53, 54] It is well-known that depression is related to poor diabetes self-care.[37-43] In our study, we found that patients with and without depression had a similar number of self-identified behavior change goals. To confirm that patients with and without depression are similar in goal setting, investigating the effects of depression on identifying each domain of behavior change goals is needed. If patients with and without depression do perform similarly in goal setting, it suggests that depressed patients may have some problems to acquire coping skill or to maintain motivation so that they are less likely to have better diabetes self-care. Thus, exploring the factors that affect depressed patients in coping skill and maintenance of motivation is important in future studies.

4.6 PUBLIC HEALTH SIGNIFICANCE

Since depression was related to an increased number of barriers to diabetes self-care, depression screening is important in patients with diabetes. If depressed patients can be identified in the early stages, intensive interventions can be applied earlier to help them overcome potential barriers and then achieve better diabetes self-care. Although antidepressant use had no association with the number of goals or the number of barriers, it does not indicate that antidepressants are not useful in patients with diabetes and depression. Antidepressant use is still important in treating depression for patients with diabetes and depression.[48] Additionally, effective diabetes treatment may be compromised by depression-related characteristics (e.g., hopeless), while effective depression treatment may be diminished by diabetes complications (e.g., pain). Thus, collaborative treatment should be integrated to provide maximal benefit to

improve both diabetes and depression, and also to avoid adverse influences of one disease resulted from the treatment of the other disease.

5.0 TABLES AND FIGURE

Table 1: Characteristics of studies investigating goals in people with diabetes

AUTHOR	STUDY DESIGN	STUDY AIM	POPULATION	SAMPLE SIZE	METHODS/MEASUREMENTS
Rush WA et al. (2008)[51]	Prospective cohort study	To examine whether depressive symptoms are associated with achievement of recommended goals for control of glucose, lipids, and blood pressure among patients with diabetes.	Inclusion: type 1 or type 2 diabetes, and ≥ 18 y/o Exclusion: those without pharmacy coverage	1223 subjects	Depression • Survey at baseline • Self-reported • 2 questions from the PHQ-2 screening tool Goals for HbA1c (≤ 7.0), LDL (≤ 100), SBP (≤ 130), and DBP (≤ 80) • Medical record • 1-year period after the survey
Morrow AS et al. (2008)[13]	Cross-sectional study	To investigate the life and health goals of older adults with diabetes, and explore the factors that influence their diabetes self-management.	Inclusion: type 2 diabetes, ≥ 55 y/o, hypertension, and at least one other chronic comorbidity	24 subjects	Qualitative in-depth interviews • Prior to the interview, information about the patient's medical history, ability to perform activities of daily living, and demographic characteristics was collected using questionnaires administered by investigators. • Health care goals, effects of diabetes and other chronic conditions on daily life, self-management practices, and communication with health care providers were asked using interview guide.
Ismail K et al. (2008)[55]	Randomized controlled trial	To determine whether motivational enhancement therapy with or without cognitive behavior therapy improves glycemic control in type 1 diabetes compared with usual care.	Inclusion: type 1 diabetes for ≥ 2 years, with HbA1c levels of 8.2% ~ 15%, and without complications or severe comorbid disease.	344 subjects	HbA1c (primary outcome) Depression (secondary outcomes) • Self-report • Patient Health Questionnaire-9 (score range, 0 to 27; scores ≥ 10 represent major depressive disorder) Diet, exercise, and blood sugar testing (secondary

Table 1: Characteristics of studies investigating goals in people with diabetes (cont.)

					outcomes) • Revised Summary of Diabetes Self-Care • Days in the last 7 days the participant engaged in self-care (score range, 0 to 7 days) Hypoglycemia (secondary outcomes) • Hypoglycemia Fear Survey • 10 behavior items (score range, 0 to 40) and 13 worry items (score range, 0 to 52) self-rated on 5-point Likert scales. Quality of life (secondary outcomes) • Satisfaction and impact subscales of the Diabetes • Quality of Life scale (score range per subscale, 1 to 5) Body mass index (secondary outcomes)
Estabrooks PA et al. (2005)[15]	Randomized controlled trial	To determine the frequency and effectiveness of behavioral goal choices in the self-management of diabetes and to test goal-setting theory hypotheses that self-selection and behavioral specificity of goals are key to enhancing persistence.	Inclusion: type 2 diabetes, and ≥ 25 y/o	422 subjects	Physical activity • 11-item Behavioral Risk Factor Surveillance System (BRFSS) • A brief screener on frequency and duration of vigorous and moderate-level activities Dietary fat • 17-item Block Dietary Data Systems (BDDS) • A brief calculation of the participant's dietary fat Fruits and vegetables intake • 7-item BDDS "Fruit/Vegetable Screener" • A brief scanner on current number of fruit and vegetable portions consumed each day
Huang ES et al. (2005)[14]	Qualitative study	To examine how older patients define their healthcare goals, what factors shape their goals, and the extent to which their goals relate to self-care behavior.	Inclusion: type 2 diabetes, and ≥ 65 y/o	28 subjects	Semi-structured interviews • The questions of the interview guide were designed to explore patients' healthcare goals, diabetes mellitus care goals, experiences with diabetes mellitus, priorities for self-care strategies, and daily self-care tasks
Rachmani R et al. (2005)[17]	Randomized controlled trial	To examine whether motivating patients to gain expertise and closely following their risk parameters will attenuate the course of microvascular and cardiovascular sequelae of diabetes.	Inclusion: type 2 diabetes < 10 yr, 40-70 y/o, BMI ≤ 35 kg/m^2, BP ≥ 140/90 mmHg; LDL ≥ 120 mg/dl, serum creatinine ≤ 2 mg/dl (176 µmol/L), albumin/creatinine ratio < 200 mg/g; and no history of myocardial infarction, angina pectoris,	141 subjects	Cardiovascular parameters (MI, stroke, CABG+PCI, Nonfatal CV events, CV mortality, Non-CV mortality) • From the letters of the primary care physicians, hospital discharge summaries, or other consultants' reports. Lab data (HbA1c, SBP, DBP, LDL, GFR, and albumin/creatinine)

Table 1: Characteristics of studies investigating goals in people with diabetes (cont.)

			vascular surgery, stroke, or any systemic or malignant disease.		
Olivarius NF et al. (2001)[18]	Randomized controlled trial	To assess the effect of a multifaceted intervention directed at general practitioners on six year mortality, morbidity, and risk factors of patients with newly diagnosed type 2 diabetes.	Includion: newly diagnosed type 2 diabetes who survived until 6 year follow up , and > 40 y/o	874 subjects	Predefined primary outcomes: overall mortality and incidences of diabetic retinopathy, urinary albumin concentration >15 mg/l, myocardial infarction, and stroke in patients without these outcomes at baseline. Secondary outcomes: new peripheral neuropathy, angina pectoris, intermittent claudication, and amputation. Tertiary outcomes: levels of risk factors included in patients' goals.

HbA1c: Glycosylated Hemoglobin
LDL: Low-Density Lipoprotein
BP: Blood Pressure
SBP: Systolic Blood Pressure
DBP: Diastolic Blood Pressure
MI: Myocardial Infarction
CABG: Coronary Artery Bypass Graft
PCI: Percutaneous Coronary Intervention
CV: Cardiovascular.
GFR: Glomerular Filtration rate

Table 2: Major findings of studies investigating goals in people with diabetes

AUTHOR	MAJOR FINDING(S) / RESULTS (PRIMARILY WITH RESPECT TO DEPRESSION)	STUDY NOVELTY / COMMENTS
Rush WA et al. (2008)[51]	• Diabetes patients with depression symptoms were less likely to be at their glucose goal (43% vs 50%; P = .0176) but more likely to be at their SBP goal (57% vs 51%; P = .0435). • The association between lipids and depression symptoms was related to a lower rate for low-density lipoprotein testing (56% vs 68%; P < .0001). • Treatment with antidepressants resulted in a greater percentage achieving glucose and blood pressure goals but not lipid goals.	• Depression seems to have a variable impact on achieving these clinical goals, perhaps because the goals have differing measurement logistics and biological profiles. • Depression symptoms make it harder to reach glucose goals but that treatment with an antidepressant may ameliorate this effect.
Morrow AS et al. (2008)[13]	• Primary life and health goals reported by participants: Longevity, spend time with family, improve or maintain physical functioning, maintain independence, improve diabetes care (improve lifestyle (diet, exercise, weight), control sugars, avoid complications) • Factors influencing diabetes self-care goals: Health care providers, ancillary and outside resources, family, diabetes discordant illnesses, and retirement. • Functional capabilities and social support were key factors in the ways that older adults described the relationship between self-management of diabetes and their broader goals.	• Limitation: 1) generalizability • The language used to describe health goals was often indistinguishable from that used to describe life goals. • For goal-setting to be effective, patients and caregivers must feel confident in performing the necessary self-management steps and must feel that the specific self-management goal is related to one's overall life goals as well.
Ismail K et al. (2008)[55]	• In an analysis including all randomly assigned patients, the 12-month change in HbA1c levels compared with usual care was -0.46% (95% CI, -0.81% to -0.11%) in the motivational enhancement therapy plus cognitive behavior therapy group and -0.19% (CI, -0.53% to 0.16%) in the motivational enhancement therapy group alone. • There was no evidence of treatment effects on secondary outcomes.	• Nurse-delivered motivational enhancement therapy and cognitive behavior therapy is feasible for adults with poorly controlled type 1 diabetes.
Estabrooks PA et al. (2005)[15]	• At baseline, participants who selected goals to increase physical activity, to reduce fat consumption, or to increase fruits and vegetables intake were significantly less active, consumed more dietary fat, and ate fewer fruits and vegetables, respectively . • Participants who selected a reduced-fat goal showed a significantly larger decrease than did those who selected a goal for physical activity or for fruits and vegetables. • Participants who selected a goal for fruits and vegetables showed significant increase in fruits and vegetables consumption. • Participants who selected a goal for physical activity demonstrated significant increase in days of moderate and vigorous physical activity.	• When participants are provided with information on health behavior status and an option of behavioral goals for managing type 2 diabetes, they will select personally appropriate goals, resulting in significant behavioral changes over a 6-month period
Huang ES et al. (2005)[14]	• The majority of patients expressed their healthcare goals in a social and functional language, in contrast to the biomedical language of risk factor control and complication prevention, even when specifically asked about goals for diabetes mellitus care. • Patient's predominant healthcare goals centered on maintaining their independence and their activities of daily living (71%). • Medical experiences of friends and family (50%), social comparison with peers (7%), and medical professionals (43%) shaped patients' goals. • Self-reported medication adherence and glucose monitoring was high, but more than	• Providers could enhance their communication about such medical decisions by exploring patients' specific circumstances and reframing diabetes mellitus treatment goals in patients' own language. These may be crucial steps to developing successful individualized care plans.

Table 2: Major findings of studies investigating goals in people with diabetes (cont.)

	one-quarter of patients failed to adhere to any dietary recommendations, and one-third failed to adhere to their exercise regimens.	
Rachmani R et al. (2005)[17]	• There were 80 cardiovascular events (8 deaths) in the control group versus 47 events (5 deaths) in the intervention group (P = 0.001). The relative risk (RR) over 8 yr for a cardiovascular event in the intervention group versus the control group was 0.65 (95% confidence interval, 0.89 to 0.41). • There were 17 and 8 cases of stroke in the control and intervention groups, respectively (P = 0.05). RR for stroke was 0.47 (95% confidence interval, 0.85 to 0.32). • In the control group, 14 patients developed overt nephropathy (4 ESRD) versus 7 (1 ESRD) in the intervention group (P = 0.05). • Throughout the study period, BP, LDL cholesterol, and HbA1c were significantly lower in the intervention group than in the control patients.	• Well informed and motivated patients were more successful in obtaining and maintaining good control of their risk factors, resulting in reduced cardiovascular risk and slower progression of microvascular disease.
Olivarius NF et al. (2001)[18]	• Predefined non-fatal outcomes and mortality were the same in both groups. • The following risk factor levels were lower for intervention patients than for comparison patients (median values): fasting plasma glucose concentration (7.9 vs. 8.7 mmol/l, P = 0.0007), HbA1c (8.5% vs. 9.0%, P < 0.0001; reference range 5.4-7.4%), systolic blood pressure (145 vs. 150 mm Hg, P = 0.0004), and cholesterol concentration (6.0 vs. 6.1 mmol/l, P = 0.029, adjusted for baseline concentration). • Both groups had lost weight since diagnosis (2.6 v 2.0 kg). • Metformin was the only drug used more frequently in the intervention group (24% (110/459) vs. 15% (61/415)). • Intervention doctors arranged more follow up consultations, referred fewer patients to diabetes clinics, and set more optimistic goals.	• In primary care, use of the model (individualised goals with educational and surveillance support) may reduce risk factors to a level that has been shown to have a beneficial effect on the development of diabetic complications without adverse weight gain.

HbA1c: Glycosylated Hemoglobin
LDL: Low-Density Lipoprotein
BP: Blood Pressure
SBP: Systolic Blood Pressure
DBP: Diastolic Blood Pressure
ESRD: End Stage Renal Disease

Table 3: Characteristics of studies investigating barriers to self-care behaviors in people with diabetes

AUTHOR	STUDY DESIGN	STUDY AIM	POPULATION	SAMPLE SIZE	MEASUREMENTS
Vijan S et al. (2005)[25]	Cross-sectional study	To evaluate, both quantitatively and qualitatively, barriers to following dietary recommendations in people with type 2 diabetes	People were recruited from the primary care population of a large academic medical centre and two VA hospitals. Exclusion: those were diagnosed with diabetes prior to 30 y/o	197 subjects	Quantitative phase Patient attitudes towards hypoglycaemic treatments • A mailed, self-administered 50-question survey • Ratings of the burden of diabetes therapies on a seven-point scale (from 0 = do not dislike at all to 6 = dislike very much) Qualitative phase Patient views towards diabetes care and barriers to follow interventions • Six focus group with 6-12 participants in each
Wagner J et al. (2005)[26]	Cross-sectional study	To test the hypothesis that invasiveness is a barrier to SMBG	Adults with diabetes attending the 2002, 2003, and 2004 American Diabetes Association "Diabetes Expos" (health fairs) held at convention centers of large, northeastern cities.	339 subjects (subsample= 32 subjects)	Anxiety regarding insulin injecting and SMBG • The Diabetes Fear of Injecting and Self-Testing Questionnaire (D-FIST) Hassle/burden regarding SMBG • The Diabetes Hassles Scale • SMBG routine burden and non-routine burden Knowledge about the link between glycemic control and long-term vascular complications of diabetes. • The Diabetes Heart Disease Facts Questionnaire Percentage of SMBG adherence • Self-reported No. of SMBG / recommended No. of SMBG • Meter-recorded No. of SMBG / recommended No. of SMBG Invasiveness as a barrier to SMBG • Measure of Invasiveness as a reason for Skipping SMBG (MISS) • A higher score on the MISS reflects the tendency to miss or skip SMBG because of the invasiveness of the procedure.
Nagelkerk J et al. (2006)[27]	Cross-sectional study	To describe the perceived barriers to self-management of adults with type 2 diabetes in a rural setting and to identify effective strategies in self-management to highlight infrastructure needs or changes in	Inclusion: type 2 diabetes, ≥ 21 y/o, having a telephone, and being able to read, write and speak English.	24 subjects	The focus group interview schedule was developed using the key-informant technique, where three individuals with a special interest in diabetes were interviewed using open-ended questions. Key concepts emerged which were included in the focus group scheme.

Table 3: Characteristics of studies investigating barriers to self-care behaviors in people with diabetes (cont.)

		clinical practice that would facilitate the integration of diabetes self-management.			
Morrow AS et al. (2008)[13]	Cross-sectional study	To investigate the life and health goals of older adults with diabetes, and explore the factors that influence their diabetes self-management.	People from outpatient clinics in the Houston area Inclusion: type 2 diabetes, ≥ 55 y/o, hypertension, and at least one other chronic comorbidity	24 subjects	Qualitative in-depth interviews • Prior to the interview, information about people's medical history, ability to perform activities of daily living, and demographic characteristics was collected using questionnaires administered by investigators. • Health care goals, effects of diabetes and other chronic conditions on daily life, self-management practices, and communication with health care providers were asked using interview guide.
Daly JM et al. (2009)[28]	Cross-sectional study	To determine (1) which barriers to diabetes management were associated with the problem behaviors and (2) which patient behaviors and barriers are associated with diabetes control as measured by glycosylated hemoglobin (HbA1c).	People being followed in primary care outpatient clinics at a midwestern medical center Inclusion: type 2 diabetes, regular clinic patients (≥ 2 outpatient visits within the previous 12 months), and having HbA1c test within the previous 3 months	253 subjects	Diabetes self-care behaviors and barriers • 141 questions in 7 domains • Self-report • Self-care behaviors were classified in 2 ways: (1) percentage of time the people adhered to medication, meal plan, exercise, and glucose testing plans during the past month, and (2) the level of satisfaction with each of the preceding domains. From these 2 measures, a combined dichotomous adherence-satisfaction score for each domain was created. • Barriers to each self-care behavior were dichotomous. • Depressive symptoms were evaluated using self-reported 9-item Patient Health Questionnaire (PHQ-9) • Physical and mental health was evaluated using 12-item Short-Form Health Survey (SF-12) HbA1c • Chart review

SMBG: Self-Monitoring of Blood Glucose

Table 4: Major findings of studies investigating barriers to self-care behaviors in people with diabetes

AUTHOR	MAJOR FINDING(S) / RESULTS (PRIMARILY WITH RESPECT TO DEPRESSION)	STUDY NOVELTY / COMMENTS
Vijan S et al. (2005)[25]	Quantitative phase • Moderate diet was seen as a greater burden than oral agents (median 1 vs. 0, P = 0.001), but less of a burden than insulin (median 1 vs. 4, P < 0.001). • A strict diet aimed at weight loss was rated as being similarly burdensome to insulin (median 4 vs. 4, P = NS). • Self-reported adherence was much higher for both pills and insulin than it was for a moderate diet. Qualitative phase • The most commonly identified barrier was the cost (14/14 reviews), followed by small portion sizes (13/14 reviews), support and family issues (13/14 reviews), and quality of life and lifestyle issues (12/14 reviews). • People in the urban site, who were predominantly African-American, noted greater difficulties in communicating with their provider about diet and social circumstances, and also that the rigid schedule of a diabetes diet was problematic.	• Limitation: 1) selected populations used, 2) low (54%) response rate of survey, and 3) no causal inference due to cross-sectional study. • Interventions aimed at improving people's ability to modify their diet need to take account of people's preferences and cultural, racial, or economic variation. • Treatment guidelines need to consider people's preferences and barriers when setting goals for treatment.
Wagner J et al. (2005)[26]	• 63% of respondents reported skipping SMBG because of the invasiveness of the procedure. • MISS scores were negatively related to percent adherence to healthcare provider SMBG recommendations as measured by memory function of automated meters (Spearman's r = 0.47, P < 0.01) and absolute SMBG frequency regardless of SMBG recommendations (Spearman's r = 0.11, P < 0.05) • MISS scores were positively correlated with SMBG anxiety (Spearman's r = 0.50, P < 0.01) even though high anxious participants were deleted (Spearman's r = 0.28, P < 0.01). • MISS scores were also correlated with the degree to which people find routine and non-routine SMBG checks a burden (routine r = 0.38, P < 0.01; non-routine r = 0.45, P < 0.01). • Participants with less knowledge about the importance of glycemic control in the development of diabetes vascular complications had higher MISS scores.	• Limitation: Since participants may have higher adherence to SMBG compared to general diabetes patients (volunteer bias), it would be harder to find an effect for invasiveness as a barrier to SMBG.
Nagelkerk J et al. (2006)[27]	• Perceived barriers to self-management in rank order 1. Lack of knowledge and understanding of a specific diet plan 2. Lack of individualized and coordinated care 3. Helplessness and frustration from lack of glycaemic control despite adherence 4. Limited resources to obtain recommended equipment, medicines, laboratory tests and provider services 5. Inconvenient, costly and non-specific group education sessions 6. Difficulty in remembering to take medications, lack of knowledge about medication action, side effects, schedules, and adjustments	• Limitation: 1) one clinical practice with a fairly homogeneous sample, and 2) no causal inference due to cross-sectional study. • Identifying individual barriers, facilitating the acquisition of a support network, developing collaborative relationships with healthcare providers and maintaining a positive attitude are key strategies in facilitating integration.

Table 4: Major findings of studies investigating barriers to self-care behaviors in people with diabetes (cont.)

	• Effective strategies in self-management by rank order 1. Developing a collaborative relationship with a healthcare provider 2. Maintaining a positive attitude that prompts proactive learning 3. Having a support person who gives encouragement and assistance and facilitates self-management 4. Acquiring adequate resources for self-management 5. Maintaining routine medication administration times and routines 6. Participating in group education that encourages questions and discussion of feelings and fears	
Morrow AS et al. (2008)[13]	• Factors influencing diabetes self-care goals: Health care providers, ancillary and outside resources, family, diabetes discordant illnesses (barrier), and retirement (barrier). • Functional capabilities and social support were key factors in the ways that older adults described the relationship between self-management of diabetes and their broader goals.	• Limitation: 1) generalizability
Daly JM et al. (2009)[28]	• The main barriers across most self-care behaviors were cost (most common) and depression. • Higher HbA1c levels were strongly associated with the belief that type 2 diabetes is a serious problem (P = 0.049) and depression (P = 0.005). Lower HbA1c levels were significantly associated with being married (P = 0.016) and greater self-reported adherence-satisfaction with taking medication (P = 0.001) and testing blood glucose (P = 0.042). • The PHQ-9 depression score was significantly correlated with financial barriers, with a coefficient of 0.45 (P = 0.0001). In the t test, PHQ-9 mean score was 11.51 for people with financial barriers compared with 5.33 for those without financial barriers (P = 0.0001).	• Limitation: 1) small sample size, 2) no causal inference due to cross-sectional study, 3) self-report measurement

SMBG: Self-Monitoring of Blood Glucose

Table 5: Characteristics of studies investigating effects of depression on self-care behaviors in people with diabetes

AUTHOR	STUDY DESIGN	STUDY AIM	POPULATION	SAMPLE SIZE	DEPRESSION ASSESSMENT	SELF-CARE ASSESSMENT
Ciechanowski PS et al. (2000)[37]	Cross-sectional study	To explore the impact of depressive symptoms in primary care patients with diabetes on diabetes self-care, adherence to medication regimens, functioning, and health care costs.	Patients from 2 primary care clinics of the Group Health Cooperative (GHC) in Puget Sound, Washington. Inclusion: types 1 and 2 diabetes, > 18 years old, and ≥ 2 years enrollment. Exclusion: severe cognitive deficit.	367 subjects	Hopkins Symptom Checklist-20, Revised (HSCL-20) • 20-item questionnaire • Depression and additional symptom subscales • 3 tertiles of depression: low, medium, and high • Self-report	Diet (amount and type), exercise, and SMBG • 12-item questionnaire • Percentage of activities recommended by the physician that were actually performed. • Self-report Adherence to oral hypoglycemic regimens • Automated data • Percentage of days in oral hypoglycemic therapy interruption
Ciechanowski PS et al. (2003)[38]	Cross-sectional study	To determine if diabetes self-care behaviors, physical functioning, diabetes symptom reporting, and glucose control are significantly associated with depressive symptoms in both type 1 and 2 diabetes.	This study was carried out in a tertiary care specialty clinic at the University of Washington Diabetes Care Center (DCC), Seattle, Washington. Inclusion: type 1 or type 2 diabetes, enrollment in both 1998 and 1999, ≥ 18 years old Exclusion: severe cognitive deficits	Type 1 = 276 subjects Type 2 = 199 subjects	Hopkins Symptom Checklist-20, Revised (HSCL-20) • 20-item questionnaire • Depression and additional symptom subscales • Self-report	Diet (amount and type), exercise, and SMBG • 12-item questionnaire • Percentage of activities recommended by the physician that were actually performed. • Self-report
Lin EH et al. (2004)[39]	Cross-sectional study	To assess whether diabetes self-care, medication adherence, and use of preventive services were associated with depressive illness.	Nine Group Health Cooperative primary care clinics in western Washington were selected for the study. Inclusion: type 1 or type 2 diabetes Exclusion: cognitive impairment	4463 subjects (Type 1 = 95.6% Type 2 = 4.4%)	Patient Health Questionnaire • According to DSM-IV criteria • A continuous severity score. • Structured interviews (78% sensitivity and 98% specificity). • Self-report	Diet, exercise, SMBG, foot checks, and smoking status • Recently revised version of the Summary of Diabetes Self-Care Activities (SDSCA) • Number of days in the prior week subject engaged in a certain activity • Self-report Adherence to oral hypoglycemic medicines • GHC automated pharmacy database • Percentage of non-adherence days Preventive services (HbA1c test, retinal exam, and microalbumin urine test)

Table 5: Characteristics of studies investigating effects of depression on self-care behaviors in people with diabetes (cont.)

						• Automated diagnostic and laboratory data
Park HS et al. (2004)[40]	Cross-sectional study	To determine whether depressive symptoms are associated with poor self-care behaviors among people with type 2 diabetes	People who visited the Ewha Womans University Hospital, Seoul, Republic of Korea, Inclusion: type 2 diabetes history of 1-15 years, and > 30 years old. Exclusion: Advanced diabetic complications, or a history of psychiatric treatment.	168 subjects	Centers for Epidemiologic Studies-Depression (CES-D) scales. • Self-report	Medication adherence, SMBG, diet, exercise, and participation in patient education programs • Self-report • Dichotomized into adherent or non-adherent categories.
Kilbourne AM et al. (2005)[43]	Prospective cohort study	To assessed the association between depression and diabetes medication adherence	Veterans receiving primary care at an urban Veterans Administration facility in US Inclusion: type 2 diabetes, and taking oral hypoglycemic therapy medication Exclusion: taking insulin only	203 subjects	Patient Health Questionnaire (PHQ-9) • At baseline • Self-report • The presence of the nine symptoms of depression corresponding to DSM-IV criteria • Dichotomized variable (sensitivity = 0.73 and specificity = 0.94)	Adherence to oral hypoglycemic therapy • Four sources: patient report, provider report, electronic monitoring caps (EMCs), and pharmacy data
Kalsekar ID et al. (2006)[42]	Retrospective cohort study	To examine the impact of depression on adherence to oral hypoglycemic agents in people newly diagnosed with type 2 diabetes	People newly diagnosed with type 2 diabetes during a 4 year period (1998-2001) were identified from a Medicaid claims database. Exclusion: ≥ 65 years old, people who took troglitazone, people with schizophrenia, bipolar disorder, dementia, and Alzheimer's disease	1326 subjects	Medical claim data • Single-episode major depressive disorder (ICD-9-CM codes 296.20-296.26), recurrent-episode major depressive disorder (ICD -9-CM code 296.3), neurotic depression/ chronic depression /dysthymia (ICD -9-CM code 300.4), and depression not otherwise specified (ICD -9-CM code 311).	Adherence to oral hypoglycemic agents • Prescription refill data • 12 month follow-up period from the index prescription • MPR-1: a measure of medication adherence in the period between the first and last prescription fills • MPR-2: a measure of medication adherence in the period between the index prescription and the end of the follow-up period. People who discontinued therapy after a single prescription were included
Gonzalez JS et al. (2007)[41]	Cross-sectional study	To examine the association between	People who were followed in one of two outpatient primary	879 subjects	Harvard Department of Psychiatry/National	Diet, exercise, SMBG, and foot care

Table 5: Characteristics of studies investigating effects of depression on self-care behaviors in people with diabetes (cont.)

		depression, measured as either a continuous symptom severity variable or a clinical categorical variable, and self-care behaviors in type 2 diabetes.	care medical clinics in Massachusetts Inclusion: type 2 diabetes, and at least one primary care visit		Depression Screening Day Scale (HANDS) • 10-item questionnaire • Total score: 0 to 30 • A score of ≥ 9 for depression (sensitivity > 0.95 and specificity = 0.60–0.94) • Self-report	• Recently revised version of the Summary of Diabetes Self-Care Activities (SDSCA) • Number of days of non–adherence over the previous 7 days • Self-report Medication adherence • Self-report • Dichotomized responses into "any missed doses" and "no missed doses" in the past 7 days

SMBG: Self-Monitoring Of Blood Glucose
MPR: Medication Possession Ratio

Table 6: Major findings of studies investigating effects of depression on self-care behaviors in people with diabetes

AUTHOR	MAJOR FINDING(S) / RESULTS (PRIMARILY WITH RESPECT TO DEPRESSION)	STUDY NOVELTY / COMMENTS
Ciechanowski PS et al. (2000)[37]	• Compared with people in the low-severity depression symptom tertile, those in the medium- and high severity tertiles of depression were significantly less adherent to dietary recommendations (diet amount or diet type). • People in the high-severity tertile were significantly distinct from those in the low severity tertile by having a higher percentage of days in non-adherence to oral hypoglycemic regimens (7.1% vs. 14.9%, P = 0.04). • There is no effect of depression on exercise and glucose monitoring.	• This study was probably the first one investigating the association between depression and self-care behaviors. • The severity of depression was divided into four level: none, low, medium, and high
Ciechanowski PS et al. (2003)[38]	• Among people with type 1 and 2 diabetes, depressive symptoms were significantly associated with lower adherence to diet amount (P < 0.001), diet type (P < 0.05), and exercise regimens (P < 0.01), but not significantly associated with glucose monitoring.	• These associations were robust after controlling for diabetes type and complications. • This study was conducted in a tertiary care specialty clinic, which may limit the generalizability to a typical primary care population.
Lin EH et al. (2004)[39]	• Major depression was associated with unhealthy diet, less physical activity, smoking, and lower adherence to oral hypoglycemic, antihypertensive, and lipid-lowering medications. • A slightly higher proportion of people with depression received no HbA1c test in the prior year compared to those without depression. • Depressed people and non-depressed people did not significantly differ from each other with regard to home-glucose tests, foot checks, and other preventive diabetes services.	• Depression appeared to influence patient-initiated activities (e.g., exercise, diet, and medication adherence) more than physician-initiated services (e.g., HbA1c test, retinal test, and microalbumin test).
Park HS et al. (2004)[40]	• Higher depressive-symptom scores were significantly associated with poor participation in education programs (OR = 1.21, 95% CI = 1.06–1.38), poor diet (OR = 1.11, 95% CI = 1.01–1.22), and marginally with poor medication taking (OR = 1.14, 95% CI = 1.00–1.31). • Depressive symptoms were not significantly associated with either SMBG or exercise.	• This study was the only one conducted in Korea. • This study also investigated the association between depression and participation in education programs, which is one of the most important behaviors for diabetes care. • The lower rates of glucose monitoring in this study can be explained by cost for glucometers, which was not covered by insurance in Korea.
Kilbourne AM et al. (2005)[43]	• Depressed people were less likely to self-report good adherence (P = 0.03) and had a lower median percentage of days with adequate medication coverage on the basis of pharmacy refill data. • After adjustment for alcohol use, cognitive impairment, age, and other medication use, depression was still negatively associated with adequate adherence according to patient report and pharmacy data. • Depression showed no association with medication adherence on the basis of provider or EMC data.	• The generalizability of this study was limited because 1) the VA healthcare system had unique features, such as the mail-order pharmacy system and a comprehensive pharmacy database 2) it only included the elder veteran population without female people.
Kalsekar ID et al. (2006)[42]	• People with depression had significantly lower adherence (MPR-1 86%; MPR-2 66%) to oral hypoglycemic agents compared with people without depression (MPR-1 89%; MPR-2 73%). • Depressed people were 3–6% less adherent to oral hypoglycemic agents than non-	• This study only recruited younger people with newly diagnosed type 2 diabetes. • The magnitude of difference in adherence was not large in this study.

Table 6: Major findings of studies investigating effects of depression on self-care behaviors in people with diabetes (cont.)

	depressed people, after controlling for confounding factors.	
Gonzalez JS et al. (2007)[41]	• After controlling for covariates, people with probable major depression reported significantly fewer days' adherent to diet, exercise, and glucose self-monitoring regimens ($P < 0.01$) and 2.3-fold increased odds of missing medication doses in the previous week (95% CI 1.5–3.6, $P < 0.001$) compared with all other respondents. • Among the two-thirds of people not meeting the criteria for major depression (HANDS score < 9, n = 709), increasing HANDS scores were incrementally associated with poorer self-care behaviors ($P < 0.01$).	• These findings challenged the conceptualization of depression as a categorical risk factor for non-adherence. • Even low levels of depressive symptomatology were associated with non-adherence to important aspects of diabetes self-care.

SMBG: Self-Monitoring Of Blood Glucose
MPR: Medication Possession Ratio

Table 7: Characteristics of studies investigating depression treatment in people with diabetes and depression

AUTHOR	STUDY DESIGN	STUDY AIM	POPULATION	SAMPLE SIZE	MEASUREMENTS
Lustman PJ et al. (1997)[48]	Randomized controlled trials	To evaluate the effects of nortriptyline on depression and glycemic control to see whether depression in diabetes is treatable and whether restoring mental health contributes to improved medical outcome. Intervention: nortriptyline Control: placebo	Inclusion: 21 to 65 y/o, type 1 or type 2 diabetes, and relatively poor control of diabetes (HbA1c ≥ 9%) Exclusion: having history of bipolar depression or any psychotic disorder, and currently taking psychoactive medications.	28 depressed subjects (14 subjects in nortriptyline group and 14 subjects in placebo group); 40 non-depressed subjects (12 subjects in nortriptyline group and 28 subjects in placebo group)	Depression: • The major Axis I clinical syndromes were assessed using the DIS (revised three version) and diagnosed according to the criteria of the DSM-IIIR • The severity of current depression symptoms was measured using the BDI Diabetes outcome: • HbA1c Adherence to medication: • An electronic monitoring device was used • Adherence = (the number of days the patient removed the prescribed number of medication dosages) ÷ (the total number of days in treatment) Adherence to self-monitoring of blood glucose: • An memory glucometer was used • Weekly adherence = (the number of samples measured) ÷ (the number of tests requested)
Lustman PJ et al. (1998)[49]	Randomized controlled trials	To determine the antidepressant efficacy of cognitive behavior therapy (CBT) added to supportive diabetes education, and whether remission of depression is associated with improved glycemic control. Intervention: CBT plus diabetes education Control: diabetes education	Inclusion: type 2 diabetes, 21 to 70 y/o, and major depression Exclusion: having a history of panic disorder, bipolar depression, or any psychotic disorder, currently taking psychoactive medications. Depression Identification: ≥ 14 on BDI	20 subjects receiving CBT plus diabetes education; 22 subjects receiving diabetes alone	Depression: • The major Axis I clinical syndromes were assessed using the DIS (revised three version) and diagnosed according to the criteria of the DSM-IIIR • The severity of current depression symptoms was measured using the BDI Adherence to self-monitoring of blood glucose: • An memory glucometer was used • Weekly adherence = (the number of samples measured) ÷ (the number of tests requested)
Williams JW et al. (2004)[50]	Randomized controlled trials	To determine whether enhancing care for depression improves affective and diabetic outcomes in older adults with diabetes and depression.	Inclusion: ≥ 60 y/o, type 1 or type 2 diabetes, and major depression or dysthymic disorder Exclusion: having a history of bipolar disorder or psychosis, ongoing treatment with a psychiatrist, or severe cognitive	205 subjects in intervention group; 212 subjects in usual group	Depression: • The severity of depressive symptoms were assessed using the SCL-20 • The diagnoses of major depression or dysthymia were evaluated using the structured clinical interview for DSM-IV

Table 7: Characteristics of studies investigating depression treatment in people with diabetes and depression (cont.)

		Intervention: enhanced depression care (education, problem solving, and antidepressant) Control: usual care	impairment Depression Identification: According to the criteria of the DSM-IV		Diabetes self-care (diet, exercise, glucose testing, diabetes medication, and foot care): • The 12-item SDSCA, augmented by an item to assess foot care Diabetes outcome: • HbA1c
Lin EH et al. (2006)[46]	Randomized controlled trials	To examine the impact of improved depression treatment on self-care behaviors Intervention: improved depression care (pharmacotherapy and/or problem solving) Control: usual care	Inclusion: ≥ 18 y/o, diagnosed with type 1 or type 2 diabetes and depression Exclusion: having gestational diabetes, psychotic disorder, bipolar disorder, use of mood-stabilizing or antipsychotic medication, and current care by a psychiatrist Depression Identification: A score of 10 or higher on the PHQ-9 at the initial screening and evidence of persistent depression as measured by a mean item score of 1.1 or higher on the SCL-20 2 weeks later.	164 subjects in intervention group; 165 subjects in usual group	Diet, exercise, blood glucose testing, foot checks, and smoking • The 12-item SDSCA Medication adherence • Automated pharmacy refill data of oral hypoglycemic agents, lipid-lowering agents, and angiotensin-converting enzyme inhibitors

DIS: National Institute of Mental Health Diagnostic Interview Schedule
DSM: Diagnostic and Statistical Manual of Mental Disorders
BDI: Beck Depression Inventory
PHQ-9: Patient Health Questionnaire-9
SCL-20: Hopkins Symptom Checklist-20
SDSCA: Summary of Diabetes Self-Care Activities

Table 8: Major findings of studies investigating depression treatment in people with diabetes and depression

AUTHOR	MAJOR FINDING(S) / RESULTS (PRIMARILY WITH RESPECT TO DEPRESSION)	STUDY NOVELTY / COMMENTS
Lustman PJ et al. (1997)[48]	• The reduction in depression symptoms was significantly greater in depressed people treated with nortriptyline compared with those receiving placebo (-10.2 vs -5.8, p = .03). • Nortriptyline was not statistically superior to placebo in reducing glycated hemoglobin of the depressed subjects (p = .5). • For people in the nortriptyline and placebo groups, the compliance with the medication regimen and with blood glucose monitoring did not differ as a function of treatment received during the 8-week trial. • Path analysis indicated that the direct effect of nortriptyline was to worsen glycemic control whereas depression improvement had an independent beneficial effect on glycated hemoglobin. These findings were not explained by the relationships of nortriptyline treatment to weight change (r = -0.21, p = .31) or depression improvement to compliance with the protocol for self-monitoring of blood glucose (r = 0.01, p = .97).	• The HbA1c level cannot appropriately be used to evaluate the effects of treatment on glucose control during the study (8 weeks) since this measurement reflects average blood glucose levels over the preceding 90-120 days.
Lustman PJ et al. (1998)[49]	• The percentage of people achieving remission of depression (Beck Depression Inventory score ≤ 9) was greater in the CBT group than in the control group: post-treatment, 85.0% of people in the CBT group compared with 27.3% of controls achieved remission (difference, 57.7 percentage points [95% Cl, 33 to 82 percentage points]) (P< 0.001); at follow-up, 70.0% of people in the CBT group compared with 33.3% of controls achieved remission (difference, 36.7 percentage points [Cl, 9 to 65 percentage points]) (P = 0.03). • Post-treatment glycosylated hemoglobin levels were not different in the two groups, but follow-up mean glycosylated hemoglobin levels were significantly better in the CBT group than in the control group (9.5% compared with 10.9%; P= 0.03). • Covariate-adjusted mean GHb levels were lower in the nondepressed group at both the post-treatment (8.5% compared with 10.9%; P = 0.003) and follow- up (9.2% compared with 12.1%; P = 0.006) evaluations compared to depressed group at the both time points. • Over the 10-week treatment period, compliance with self-monitoring of blood glucose levels declined in the CBT group compared with the control group (P = 0.01).	• The explanation for decreased adherence to glucose monitoring in CBT group may be that participation of the CBT group in diabetes education complicated an already complex regimen and was more than the people could handle. It is a well-established principle of compliance that any action that complicates a treatment regimen (such as adding a medication or using divided rather than single-dose schedules) usually decreases compliance with other components of treatment.
Williams JW et al. (2004)[50]	• At 12 months, diabetic patients who were assigned to intervention had less severe depression (range, 0 to 4 on a checklist of 20 depression items; between-group difference, –0.43 [95% CI, –0.57 to –0.29]; P < 0.001) than did participants who received usual care. • In the intervention group, weekly exercise days increased (between-group difference, 0.50 day [CI, 0.12 to 0.89 day]; P = 0.001); other self-care behaviors were not affected. • At baseline, mean (±SD) hemoglobin A1c levels were 7.28% ± 1.43%; follow-up values were unaffected by the intervention (P > 0.2).	• In this study, subjects were significantly older, less likely to receive hypoglycemic medications, and had much better mean hemoglobin A1c levels at baseline than did subjects in other studies.
Lin EH et al.	• During the 12-month intervention period, enhanced depression care and outcomes were	• Perhaps 1) the seemingly logical assumption reflects too

Table 8: Major findings of studies investigating depression treatment in people with diabetes and depression (cont.)

(2006)[46]	not associated with improved diabetes self-care behaviors (healthy nutrition, physical activity, or smoking cessation). • Relative to the usual care group, the intervention group reported a higher rate of nonadherence to oral hypoglycemic agents (mean difference = –6.3%, 95% CI, –11.91% to –0.71%). Adherence to lipid-lowering agents and to antihypertensive medicines was similar for the 2 groups.	simplistic an understanding of the relation between depression and behavior changes or/and 2) the modest effects of the intervention on depression outcomes may not have been powerful enough to increase optimism and motivation, prerequisites for good self-care. • Intervention patients showed lower adherence to oral hypoglycemic medicines may highlights the complexity and challenge people face in managing multiple medical conditions on a daily basis.

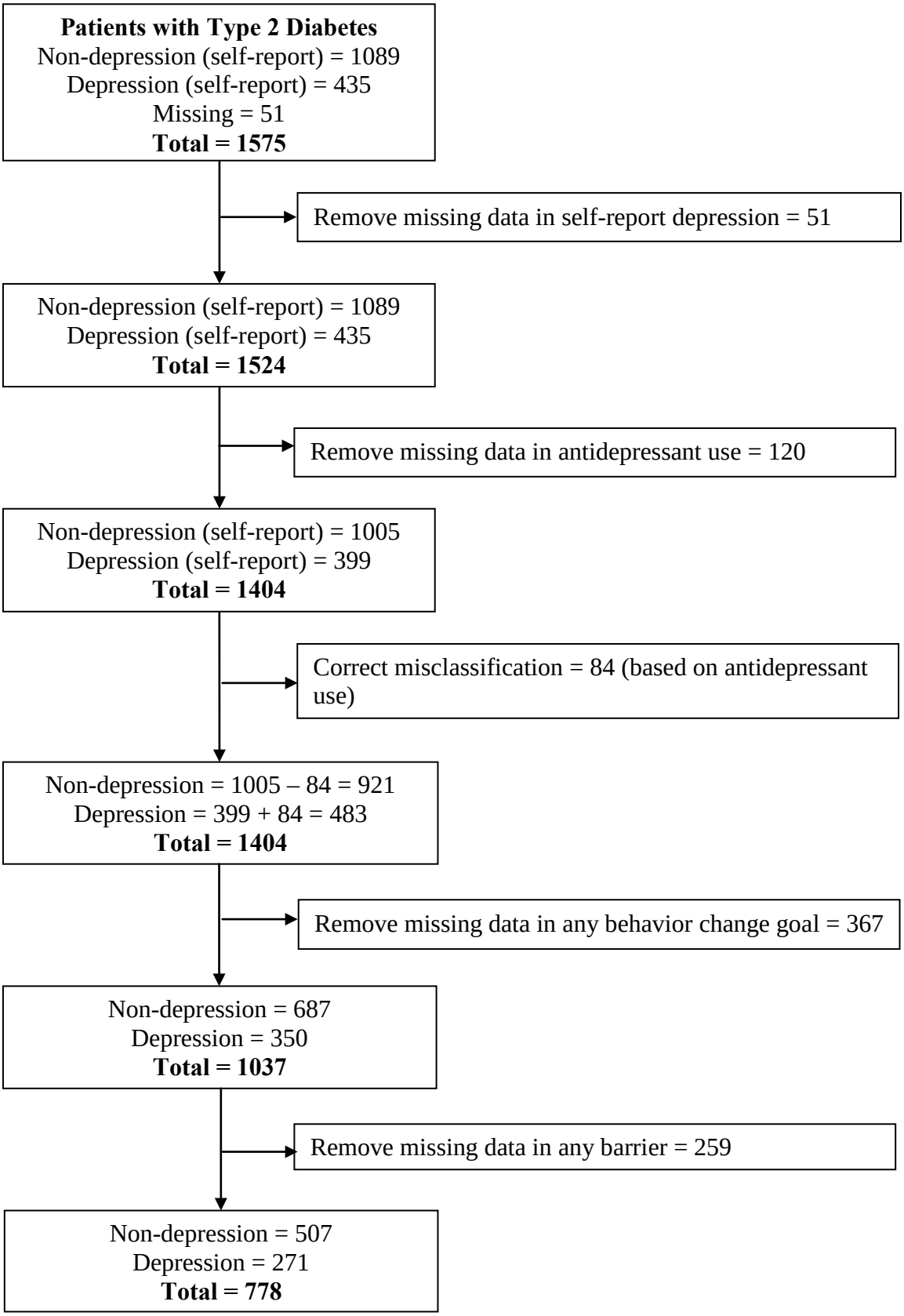

Figure 1: Flowchart of patients in this analysis

Table 9: Demographic and clinical characteristics of patients with type 2 diabetes by depression/antidepressant status

	Non-depression (n = 507)	Depression with Antidepressant (n = 181)	Depression without Antidepressant (n = 90)	No. of Missing Value	P value[a]	P value[b]
Age, median (q1-q3),y	60 (52 – 69)	55 (49 – 62)	57 (49 – 70)	0, 0, 1	<.0001	0.04
BMI, median (q1-q3), kg/m^2	33.16 (28.78–39.14)	34.75 (30.90–40.14)	33.03 (28.37–39.49)	46, 30, 11	0.03	0.14
Gender, N (%)						
Men	228 (44.97)	49 (27.07)	27 (30.00)	0	<.0001	0.61
Women	279 (55.03)	132 (72.93)	63 (70.00)			
Race, N (%)						
White	437 (86.71)	155 (85.64)	76 (86.36)	3, 0, 2	0.79	0.96
Black	41 (8.13)	14 (7.73)	7 (7.95)			
Others	26 (5.16)	12 (6.63)	5 (5.68)			
Educational status, N (%)						
Did not finish high school	59 (11.68)	21 (11.67)	6 (6.67)	2, 1, 0	0.66	0.35
High school	232 (45.94)	84 (46.67)	48 (53.33)			
Some college or greater	214 (42.38)	75 (41.67)	36 (40.00)			
Smoking, N (%)						
Never	324 (76.78)	109 (68.99)	49 (63.64)	85, 23, 13	0.01	0.64
Former	21 (4.98)	7 (4.43)	3 (3.90)			
Current	77 (18.25)	42 (26.58)	25 (32.47)			
Alcohol drinking, N (%)	134 (26.64)	35 (19.34)	20 (22.47)	4, 0, 1	0.05	0.55
Family history of diabetes, N (%)	365 (72.71)	140 (78.65)	67 (74.44)	5, 3, 0	0.17	0.44
Years with diabetes, median (q1-q3)	2 (0–10)	3 (0–10)	1 (0–9)	91, 36, 15	0.84	0.17
Diabetes education, N (%)	120 (23.81)	53 (29.44)	13 (14.44)	3, 1, 0	0.84	0.007
HbA1c, median (q1-q3),%	7.7 (6.7–9.3)	7.7 (6.8–9.3)	7.7 (6.7–9.5)	168, 51, 25	0.80	0.80
Complications, N (%)						
High blood pressure	355 (70.02)	131 (72.38)	58 (64.44)	0	0.94	0.18
Stroke	22 (4.34)	11 (6.08)	6 (6.67)	0	0.24	0.85
Heart disease / Chest pain	140 (27.61)	50 (27.62)	30 (33.33)	0	0.57	0.33
Kidney / Bladder problems	76 (14.99)	43 (23.76)	18 (20.00)	0	0.009	0.49

Table 9: Demographic and clinical characteristics of patients with type 2 diabetes by depression/antidepressant status (cont.)

	Numbness / Pain / Tingling of hands/feet	200 (39.45)	88 (48.62)	50 (55.56)	0	0.002	0.28
	Eye or vision problems	155 (30.57)	75 (41.44)	45 (50.00)	0	0.0001	0.18
	Problems with sexual function	75 (14.79)	31 (17.13)	17 (18.89)	0	0.29	0.72
No. of complications, median (q1-q3)		2 (1–3)	2 (1–3)	2 (1–3)	0	0.0002	0.58
With any complication, N (%)		468 (92.31)	171 (94.48)	83 (92.22)	0	0.47	0.47
With ≥ 3 complications, N (%)		160 (31.56)	79 (43.65)	44 (48.89)	0	0.0001	0.41
Insulin, N (%)		128 (25.25)	58 (32.04)	22 (24.44)	0	0.20	0.20

[a]The P value is used to make comparisons between patients with and without depression. For categorical variables, the P value is generated from the χ^2 test. For continuous variables, the P value is generated from the Wilcoxon rank sum test since all the variables are not normally distributed.

[b]The P value is used to make comparisons between patients with and without antidepressant in the depressed subgroup. For categorical variables, the P value is generated from the χ^2 test. For continuous variables, the P value is generated from the Wilcoxon rank sum test since all the variables are not normally distributed.

Table 10: Self-identified behavior change goals of patients with type 2 diabetes by depression/antidepressant status

	Non-depression (n = 507)	Depression with Antidepressant (n = 181)	Depression without Antidepressant (n = 90)	P value[a]	P value[b]
No. of self-identified behavior change goals, median (q1-q3)	2 (1 – 4)	2 (1 – 4)	2 (1 – 3)	0.11	0.26
Activity, N (%)	265 (52.27)	111 (61.33)	48 (53.33)	0.09	0.21
Eating, N (%)	370 (72.98)	139 (76.80)	64 (71.11)	0.56	0.31
Medication taking, N (%)	90 (17.75)	34 (18.78)	20 (22.22)	0.46	0.50
Monitoring, N (%)	112 (22.09)	46 (25.41)	22 (24.44)	0.34	0.86
Problem solving for blood sugars and sick days, N (%)	81 (15.98)	42 (23.20)	17 (18.89)	0.05	0.42
Reducing risks of diabetes complications, N (%)	252 (49.70)	89 (49.17)	38 (42.22)	0.45	0.28
Living with diabetes, N (%)	170 (33.53)	70 (38.67)	30 (33.33)	0.35	0.39

[a]The distributions between patients with and without depression are compared using the χ^2 tests for categorical variables and the Wilcoxon rank sum test for continuous variables since the number of behavior change goals is not normally distributed.

[b]The distributions between patients with and without antidepressant in the depressed subgroup are compared using the χ^2 tests for categorical variables and the Wilcoxon rank sum test for continuous variables since the number of behavior change goals is not normally distributed.

Table 11: Barriers to diabetes self-care of patients with type 2 diabetes by depression/antidepressant status

	Non-depression (n = 507)	Depression with Antidepressant (n = 181)	Depression without Antidepressant (n = 90)	P value[a]	P value[b]
No. of barriers, median (q1-q3)	6 (3 – 8)	7 (5 – 10)	7 (5 – 9)	<.0001	0.75
I don't know what to do or how to do it, N (%)	405 (79.88)	155 (85.64)	77 (85.56)	0.05	0.99
It's too hard, N (%)	330 (65.09)	134 (74.03)	70 (77.78)	0.004	0.50
I don't have the time, N (%)	282 (55.62)	101 (55.80)	52 (57.78)	0.82	0.76
My health is not good, N (%)	264 (52.07)	123 (67.96)	62 (68.89)	<.0001	0.88
I can't see well enough to do it, N (%)	99 (19.53)	46 (25.41)	30 (33.33)	0.007	0.17
I can't afford it, N (%)	201 (39.64)	98 (54.14)	40 (44.44)	0.003	0.13
No place to do it, N (%)	132 (26.04)	57 (31.49)	23 (25.56)	0.30	0.31
I don't have the will power, N (%)	317 (62.52)	142 (78.45)	63 (70.00)	0.0002	0.13
My family / friends don't support me, N (%)	153 (30.18)	76 (41.99)	30 (33.33)	0.01	0.17
I can't remember to do it, N (%)	190 (37.48)	88 (48.62)	39 (43.33)	0.01	0.41
It's too uncomfortable, N (%)	198 (39.05)	93 (51.38)	41 (45.56)	0.005	0.37
It's not that important, N (%)	117 (23.08)	48 (26.52)	26 (28.89)	0.19	0.68
I don't enjoy it, N (%)	299 (58.97)	114 (62.98)	60 (66.67)	0.15	0.55

[a]The distributions between patients with and without depression are compared using the χ^2 tests for categorical variables and the Wilcoxon rank sum test for continuous variables since the number of barriers is not normally distributed.

[b]The distributions between patients with and without antidepressant in the depressed subgroup are compared using the χ^2 tests for categorical variables and the Wilcoxon rank sum test for continuous variables since the number of barriers is not normally distributed.

Table 12: Multivariable Models

Model 1: Association between depression and the number of goals (n = 769)			Adjusted R-Square = 0.0789
Variables	Coefficient Estimate	P value	95% Confidence Interval
Depression (yes/no)	0.10	0.47	(-0.16, 0.35)
Age (year)	-0.02	<.0001	(-0.03, -0.01)
Race (ref = White)			
Black	-0.56	0.02	(-1.01, -0.10)
Others	-0.68	0.01	(-1.22, -0.15)
Educational status (ref = Some college or greater)			
Did not finish high school	-0.88	<.0001	(-1.30, -0.46)
High school diploma	-0.51	0.0002	(-0.77, -0.25)
No. of barriers (7-13/0-6)	0.28	0.03	(0.04, 0.53)
Model 2: Association between depression and the number of barriers (n = 683)			Adjusted R-Square = 0.1166
Variables	Coefficient Estimate	P value	95% Confidence Interval
Depression (yes/no)	1.01	0.0001	(0.50, 1.52)
BMI (kg/m^2)	3.40	<.0001	(2.26, 4.54)
Race (ref = White)			
Black	0.92	0.05	(0.01, 1.83)
Others	1.70	0.006	(0.50, 2.90)
Educational status (ref = Some college or greater)			
Did not finish high school	1.11	0.01	(0.27, 1.95)
High school diploma	0.41	0.11	(-0.10, 0.92)
Age (year)	-0.009	0.38	(-0.03, 0.01)
Insulin (yes/no)	1.10	<.0001	(0.56, 1.65)
Model 3A: Association between antidepressant use and the number of goals in the depressed subgroup (n = 264)			Adjusted R-Square = 0.0854
Variables	Coefficient Estimate	P value	95% Confidence Interval
Antidepressant (yes/no)	0.31	0.18	(-0.15, 0.77)
Age (year)	-0.01	0.17	(-0.03, 0.006)
Race (ref = White)			
Black	-0.82	0.04	(-1.62, -0.02)
Others	-1.43	0.001	(-2.31, -0.56)
Educational status (ref = Some college or greater)			
Did not finish high school	-0.74	0.05	(-1.49, 0.01)
High school diploma	-0.36	0.13	(-0.82, 0.10)
Insulin (yes/no)	-0.43	0.07	(-0.91, 0.04)
Family history of diabetes (yes/ no)	0.49	0.06	(-0.03, 1.02)

Table 12: Multivariable Models (cont.)

Model 3B: Association between antidepressant use and the number of goals in the depressed subgroup (n = 268)			Adjusted R-Square = 0.0539
Variables	Coefficient Estimate	P value	95% Confidence Interval
Antidepressant (yes/no)	0.22	0.35	(-0.24, 0.68)
Age (year)	-0.02	0.02	(-0.04, -0.004)
Race (ref = White)			
Black	-0.79	0.05	(-1.59, 0.01)
Others	-1.34	0.003	(-2.23, -0.46)
Model 4: Association between antidepressant use and the number of barriers in the depressed subgroup (n = 228)			Adjusted R-Square = 0.0955
Variables	Coefficient Estimate	P value	95% Confidence Interval
Antidepressant (yes/no)	0.005	0.99	(-0.85, 0.86)
Age (year)	0.01	0.52	(-0.02, 0.05)
BMI (Kg/m^2)	3.71	0.0003	(1.74, 5.68)
Educational status (ref = Some college or greater)			
Did not finish high school	1.53	0.04	(0.08, 2.99)
High school diploma	0.52	0.24	(-0.34, 1.38)
Insulin (yes/no)	1.38	0.004	(0.45, 2.30)

APPENDIX A: DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS IN STUDY AND OUT OF STUDY

		Out of Study (n = 797)	In Study (n = 778)	No. of Missing	P value[a]
Depression status, N (%)		212 (33.87)	271 (34.83)	171, 0	0.70
Age, median (q1-q3), y		60 (51–69)	58 (51–68)	6, 1	0.17
BMI, median (q1-q3), kg/m^2		32.84 (28.15–38.20)	33.67 (29.32–39.42)	164, 87	0.02
Gender, N (%)					
	Men	343 (43.04)	304 (39.07)	0	0.11
	Women	454 (56.96)	474 (60.93)		
Race, N (%)					
	White	647 (81.69)	668 (86.42)	5, 5	0.03
	Black	78 (9.85)	62 (8.02)		
	Others	67 (8.46)	43 (5.56)		
Educational status, N (%)					
	Did not finish high school	95 (12.55)	86 (11.10)	40, 3	0.18
	High school	379 (50.07)	364 (46.97)		
	Some college or greater	283 (37.38)	325 (41.94)		
Smoking, N (%)					
	Never	534 (76.83)	482 (73.36)	102, 121	0.32
	Former	31 (4.46)	31 (4.72)		
	Current	130 (18.71)	144 (21.92)		
Alcohol drinking, N (%)		241 (30.98)	189 (24.45)	19, 5	0.004
Family history of diabetes, N (%)		544 (69.74)	572 (74.29)	17, 8	0.05
Years with diabetes, median (q1-q3)		1 (0–8)	2 (0–10)	186, 142	0.01
Diabetes education, N (%)		166 (21.15)	186 (24.03)	12, 4	0.17
HbA1c, median (q1-q3),%		7.5 (6.6–9.5)	7.7 (6.7–9.4)	316, 244	0.32

Complications, N (%)					
	High blood pressure	513 (68.77)	544 (69.92)	51, 0	0.62
	Stroke	38 (5.09)	39 (5.01)	51, 0	0.94
	Heart disease / Chest pain	188 (25.20)	220 (28.28)	51, 0	0.18
	Kidney / Bladder problems	88 (11.80)	137 (17.61)	51, 0	0.001
	Numbness / Pain / Tingling of hands/feet	260 (34.85)	338 (43.44)	51, 0	0.0006
	Eye or vision problems	271 (36.33)	275 (35.35)	51, 0	0.69
	Problems with sexual function	123 (16.49)	123 (15.81)	51, 0	0.72
No. of complications, median (q1-q3)		2 (1–3)	2 (1–3)	51, 0	0.005
With any complication, N (%)		675 (90.48)	722 (92.80)	51, 0	0.10
With ≥ 3 complications, N (%)		224 (30.03)	283 (36.38)	51, 0	0.009
Insulin, N (%)		147 (21.88)	208 (26.74)	125, 0	0.03

[a]For categorical variables, the P value is generated from the χ^2 test. Since all the continuous variables are not normally distributed, the P value is generated from the Wilcoxon rank sum test.

APPENDIX B: ANTIDEPRESSANT

TCA (Tricyclic Antidepressant)

Amitriptyline (Elavil)
Nortriptyline (Pamelor)
Imipramine (Tofranil)
Desipramine (Norpramin)
Clomipramine (Anafranil)
Protriptyline (Vivactil)
Lofepramine (Gamanil, Lomont)
Trimipramine (Surmontil)
Mianserin (Bolvidon)
Doxepin (Sinequan)
Amoxapine (Asendin)
Dosulepin (Prothiaden)

SSRI (Selective Serotonin Reuptake Inhibitor)

Fluoxetine (Prozac)
Paroxetine (Paxil)
Sertraline (Zoloft)
Fluvoxamine (Luvox)
Citalopram (Celexa)
Escitalopram (Lexapro)

SNERI (Serotonin/Norepinephrine Reuptake Inhibitor)

Reboxetine (Edronax)
Venlafaxine (Effexor)
Desvenlafaxine (Pristiq)
Duloxetine (Cymbalta)
Bupropion (Wellbutrin)
Nafazodone or Nafezodone or Nefazodone (Serzone)
Trazodone (Desyrel)
Maprotiline (Ludiomil)
Mirtazapine (Remeron)

MAO (Monoamine Oxidase Inhibitor)

Phenelzine (Nardil)
Meclobemide (moclobemide) (Aurorix, Manerix)
Selegiline (l-deprenyl)
Tranylcypromine (Parnate)
Isocarboxazid (Marplan)

Miscellaneous

St. John's wort
Flupentixol or flupenthixol (Depixol and Fluanxol)
Ademetionine (Gumbaral)

APPENDIX C: INSULIN

Rapid-acting insulins
- Humalog (insulin lispro)
- Novolog (insulin aspart)
- Apidra (insulin glulisine)

Short-acting insulins
- Humulin R (regular)
- Novolin R (regular)

Intermediate-acting insulins

NPH
- Humulin N
- Novolin N

Lente
- Humulin L

Long-acting insulins
- Humulin U (ultralente)
- Lantus (insulin glargine)

Pre-mixed insulin

Pre-mixed insulin analogs
- Humalog Mix 75/25 (insulin lispro)
- Novolog Mix 70/30 (insulin aspart)

NPH-regular combinations
- Humulin 70/30
- Novolin 70/30
- Humulin 50/50

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