

May 01, 2006

Identifying factors leading to uncontrolled diabetes mellitus in an outpatient clinic setting: a literature review and retrospective case-study

Alette E. Ellms
Northeastern University

Recommended Citation

Ellms, Alette E., "Identifying factors leading to uncontrolled diabetes mellitus in an outpatient clinic setting: a literature review and retrospective case-study" (2006). *Honors Junior/Senior Projects*. Paper 20. <http://hdl.handle.net/2047/d1000130x>

This work is available open access, hosted by Northeastern University.

Identifying factors leading to uncontrolled diabetes mellitus in an outpatient clinic setting: a literature review and retrospective case-study.

By: Alette Ellms, Pharm.D. Candidate

Preceptor: Michelle Jacobs, Pharm.D.

Introduction:

The prevalence and growth of diabetes mellitus (DM) in the United States has led to its designation as the fifth-deadliest disease. The American Diabetes Association (ADA) estimates that 20.8 million people, or 7% of the US population, currently have type 1 or type 2 diabetes and 1.3 million new cases are diagnosed each year.¹ There is no cure for this disease. The macro- and micro-vascular complications that develop from diabetes can be debilitating and life-threatening. The ADA estimates that over 224,000 deaths in the US in 2002 were related to DM complications. Patients with diabetes are two to four times more likely to die of heart disease or stroke than healthy patients of the same age. Diabetes is the leading cause of both blindness and kidney failure, and 60-70% of patients suffer from some severity of nerve damage.² Clinical trials have demonstrated that having tight glycemic control can slow the progression of micro-vascular complications,^{3,4} and recent evidence shows that long-term tight control can also improve macro-vascular complications, such as cardiovascular disease, for type 1 patients.⁵ This control, however, is not an easy task for many patients.

Proving exactly what factors lead to the loss of glycemic control can be challenging due to the multitude of elements that are potential causes. There has been some investigation in this subject. Studies with type 1 patients have found correlations between poor glucose control and factors such as poor dietary adherence, low socioeconomic status, and depression.^{6,7} Most studies done with type 2 patients have focused on one specific factor, such as depression or race, and its effects on glucose control. This study aimed to collectively consider the many factors present in a type 2 patient population that may lead to increased HgA1c values. By determining commonalities among uncontrolled patients, we identified possible risk factors that, if not managed appropriately, could contribute to loss of glucose control in other DM patients.

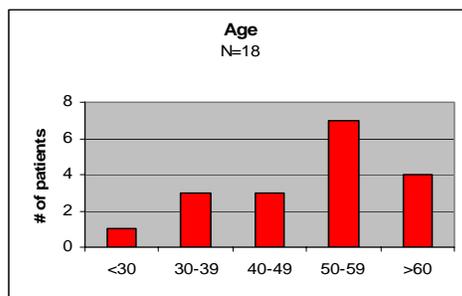
Methods:

The patient population studied with type 2 DM at an urban outpatient clinic, Whittier Street Health Center, in Roxbury, MA. Medical charts were retrospectively reviewed and data compiled for 18 patients that we identified as having uncontrolled DM, defined as most recent HgA1c >8.5%. Data collection took place between October 12 and November 7, 2005. Data was collected on demographics, co-morbid disease states, medications related to diabetes, hypertension, and lipid management, routine DM screening histories for retinopathy, nephropathy, and neuropathy, clinic visit histories, and any other patient-specific factors that we felt may have played a role in their uncontrolled diabetes. We then identified prevalent factors and investigated how they may have contributed to a high HgA1c in these patients.

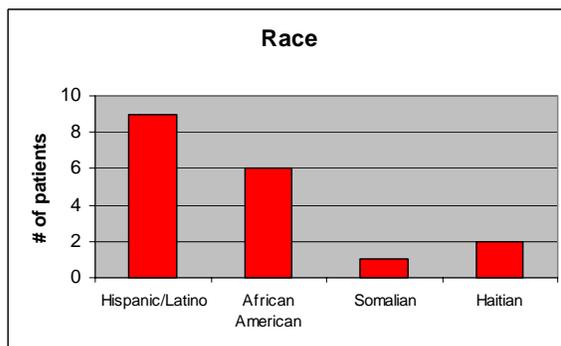
Results:

Demographic characteristics among study patients showed an equal distribution between gender, a majority in the age group of 50-59 (39%), and a majority of Hispanic/Latino race (50%) (Graph 1 and 2). The total population at the research site mainly consists of patients of Hispanic/Latino and African American race.

Graph 1



Graph 2

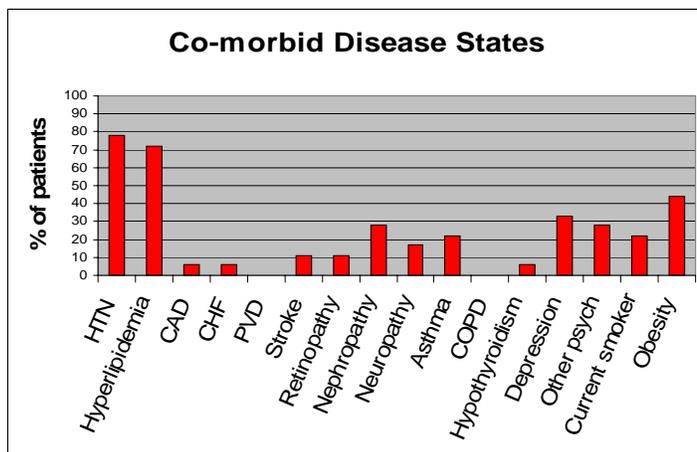


Sixteen patients (89%) had government-subsidized insurance plans, including seven patients with Massachusetts Medicaid and nine patients participating in the state's

Uncompensated Care Pool (UCP) insurance plan, where patients receive medical care and medications for free.

Results for co-morbid disease states indicate high prevalence of hypertension (78%), hyperlipidemia (72%), obesity (44%), depression (33%), and nephropathy (28%) (Graph 3). Of the 14 patients with hypertension, 43% were in control at the time of chart review. Control was defined as the most recent blood pressure reading <130/80 mmHg. Two patients were not taking any medication for this disease, seven patients took one medication, three patients took two, and two patients took three medications. Two patients utilized combination medication products. The most common antihypertensives used were ACE inhibitors and ARB's, followed by hydrochlorothiazide, then beta-blockers. None of our patients used a calcium channel blocker.

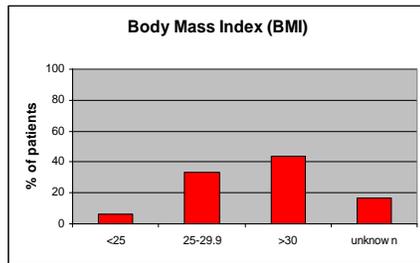
Graph 3



Thirteen patients (72%) had hyperlipidemia. Seven (54%) were controlled, defined as having a most recent LDL level of < 100 mg/dL. Four of these patients were not taking drug therapy for this condition and the remaining nine patients took one medication. Statins were used by eight of these patients for hyperlipidemia and one took a fibrate.

Eight patients (44%) were obese, defined as a Body Mass Index (BMI) ≥ 30 , six were overweight (BMI 25-29.5), one was of healthy weight (BMI < 25) and three patients had an unknown BMI, as that information was unavailable (Graph 4).

Graph 4

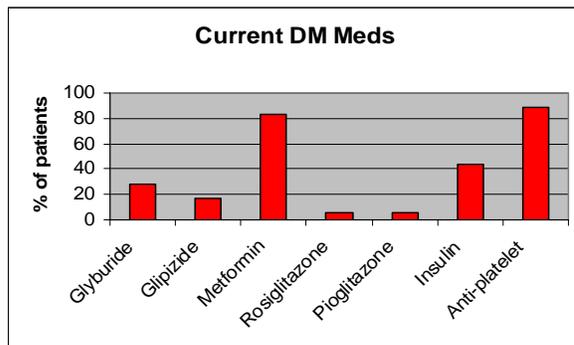


A total of six patients (33%) suffered from depression, three of whom were taking medication for this condition, and two sought active behavioral health appointments. Five of these patients had a clinical diagnosis of depression, while one patient had exhibited constant depressive symptoms throughout the last few months and we chose to include him in our analysis, despite a formal diagnosis included on his problem list. It was evident from his chart notes, the patient had diagnosable depression. Five patients suffered from another psychological disorder, anxiety or substance use disorder (28%).

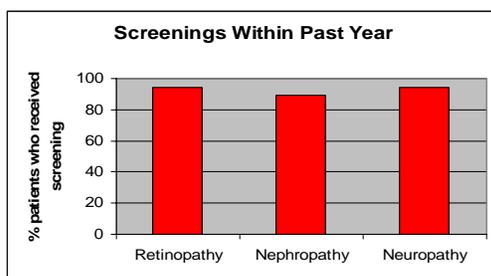
Five patients (28%) had nephropathy, defined as a most recent microalbuminuria level >30 . All patients with microalbuminuria were concurrently taking an ACE inhibitor or ARB.

In relation to diabetic disease, all 18 of our patients were uncontrolled ($A1c > 8.5\%$), hence the premise of our investigation. All except for two had been diagnosed with diabetes mellitus at least six months prior to chart review. Thirteen (72%) had at least two A1c readings within the past year. The number of DM medications that these patients took varied almost evenly from one to three, and only one patient utilized a combination medication product. The most commonly used DM medications (Graph 5) were metformin (83%), followed by insulin and sulfonylureas (44% each). Within the class of sulfonylureas, five patients took glyburide and three took glipizide. Only two patients used TZD's, one rosiglitazone and one pioglitazone. Most patients had received screenings within the past year for nephropathy (89%), neuropathy (94%), and retinopathy (94%) (Graph 6).

Graph 5



Graph 6



Discussion:

We found many similarities among our 18 patients with uncontrolled diabetes. The most prevalent of these included age 50-59, Hispanic or African American race, low-income eligible medical insurance, and the presence of hypertension, hyperlipidemia, depression, and obesity. It is very likely that the interaction of many factors collectively lead to the loss of DM control for these patients. For example, obesity can lead to depression, depression can compromise quality of self-care and promote non-adherence, and non-adherence can result in hyperglycemia. This is just one example of the many different combinations of factors that ultimately lead to uncontrolled DM. We investigated several of the most common contributing factors that we found among our patients.

Race:

Our study included nine Hispanic/Latino patients, six African Americans (AA), two Haitians, and one Somalian patient, a distribution that reflects the demographics of our health center. AA and Hispanic races have a higher risk of developing diabetes and complications than white people. In the US, it is estimated that 15% of AA's and 14% of Hispanics have DM, as opposed to 8% of whites.^{2,8} Race is also related to the control of

the disease. AA and Hispanics are more likely to have less control of their DM.^{9,10} Our study results support this conclusion in that all our uncontrolled patients were minorities. Minority patients also have greater risks of being obese, non-adherent, and developing depression with DM.^{11,12,13} Therefore, race is not only considered a risk factor for uncontrolled glucose in itself, but it also increases the likelihood of developing other conditions which are risk factors as well.

Tucker et al. observed that lack of control among minorities was mainly due to genetics,¹⁴ however it is more likely that environmental factors strongly contributed. One frequently researched factor is a lower socioeconomic status among AA's and Hispanics. A lower socioeconomic status negatively affects access to medical care and medications, and patients' quality of self-care.¹⁵ We looked at insurance status to measure the economic status of our patients. Five out of six AA's and all of Hispanics had low-income, or government-subsidized medical insurance, supporting the theory that lower economic status affects minorities' control. On the other hand, some studies have found that lack of DM control among minorities is independent of income level.^{9,16} Also, lack of glucose control has been linked to a lower education level, which minorities are more likely to have.¹⁷

Another possible reason that minorities have less DM control is due to the language barrier that may exist between patients and health care providers, although we did not make this association in our study. All our patients spoke English, except one who used a translator. A study conducted with both English and non-English speaking Hispanic DM patients also concluded that glycemic control was unrelated to Hispanic patients' ability to speak English.¹⁸ Nevertheless, language barriers have been linked to issues such as less self-monitoring, which then lead to less glucose control.¹⁹ Therefore, this factor should not be overlooked in other patients. It is the responsibility of both the patient and the health care professional to work to overcome these barriers by the use of interpreters or other ways.

Regardless of the cause, the results of minorities having worse glycemic control are higher rates of complications and deaths. The fact that minority DM patients are automatically at higher risk is a compelling indication for clinicians to initiate and continue aggressive therapy in these patients to control their glucose as well as possible.

Depression:

Six patients in our study suffered from co-morbid depression (33%), which is higher than the national prevalence of approximately 25%.²⁰ Most of these individuals used insulin, were non-Caucasian, had at least three co-morbid disease states, and BMI \geq 30. All these factors have been associated with increased depression in DM patients.²¹ In turn, depression can lead to hyperglycemia and an increased risk of micro- and macro-vascular complications.^{20,22} Lustman et al conducted a meta-analysis of published literature that looked for an association between depression and hyperglycemia, and concluded that a strong correlation does exist between the two.²³

We looked for factors that may have been responsible for developing or maintaining our patients' depression. Five out of six patients were using insulin. In fact, the majority of all our study patients who used insulin suffered from depression (5 out of 8). Insulin therapy has been linked to an increase in HgA1c in depression patients.²⁴ This could be due to a number of reasons, including the complexity and time requirement of self-administering such a treatment. For instance, Surwit et al found depression and poor glucose control to be related in patients using three or more insulin injections per day.²⁵ Our patients injected a maximum of twice per day, but even this regimen requires time and energy and can easily become an aggravating and inconvenient task. Also, all of our patients were taking metformin, except one who recently stopped due to intolerable side effects. Although we were unable to find any data relating metformin to depression, the finding remains noteworthy.

All of our depressed patients were of a minority race. Minorities are at an increased likelihood of developing depression with DM, although the exact reason remains unknown.^{21,26} Non-Caucasians are also less likely to be treated for their depression. As discussed previously, race itself (Hispanic or African American) is associated with an increased HgA1c. When combined with depression, the risk of uncontrolled DM is further increased.

All our patients all had at least three other disease states, which may contribute to depression due to the stresses and complications of having many medical conditions at once. Interestingly, 67% had a co-morbid psychiatric disorder (75% anxiety and 25% history of substance abuse). Among our patients, and in the published literature, many psychiatric illnesses have negative effects on glucose control.^{27,28} Also patients with these mental illnesses are less likely to receive optimal DM care, including routine testing.^{28,29,30}

Medical treatment of depression symptoms can improve glucose control. Fluoxetine and paroxetine are both effective medications in treating depression and subsequent glucose control improvement.^{31,32,33} Only 50% of our patients were taking antidepressant medication at the time of chart review. We also had two patients in our study receiving psychiatric counseling therapy. This treatment, specifically cognitive behavioral therapy (CBT), has been proven an effective treatment for depression and improves glucose control in DM patients.^{20,33} Also, poor glucose control has been shown to exacerbate depression symptoms, therefore intensive DM therapy may help to treat depression as well.

Given the strong relationship between depression and other psychiatric disorders and uncontrolled DM, it is imperative that we treat all conditions. Antidepressant therapy, CBT, and tight glucose control are all treatment options with proven benefits in controlling both DM and depression combined. Many of our patients have untreated depression and the addition of therapy would help to improve their glucose control.

Obesity:

Diabetes and obesity are closely related medical conditions. Of the millions of Americans with diabetes, 79% are either overweight or obese.³⁴ Eight of our patients were classified as obese with a BMI ≥ 30 . The remainder of patients were either overweight or their BMI was unknown, with the exception of one patient who was of healthy weight. Published clinical trials show a strong link between an increased BMI and an increased HgA1c.^{35,36,37} This finding remains true among many patient subgroups, including both sexes, the elderly, and minority races. Among our obese patients, 63% were female and all were under 65 years of age and belonging to a minority race. Only two of our patients reported consistent, effortful physical activity as part of their lifestyles. All study patients were routinely counseled at office visits on the importance of a healthy diet. Sixty-three percent of patients had medication regimens that included metformin, a drug proven to be of significant clinical benefit in obese diabetic patients. One patient recently discontinued metformin due to intolerable GI side effects. We also observed that 50% of our patients with obesity suffered from some type of co-morbid psychological illness, including depression, anxiety, or substance use disorder. In clinical trials, obesity has been strongly correlated with depression among DM patients.^{13,21} Again, we can see

that many factors interact with obesity and further increase the likelihood that these patients will develop uncontrolled blood glucose.

Several treatments, including pharmacological agents, have been clinically evaluated for their efficacy of decreasing patients' BMI, and, consequently increasing their glucose control. Sibutramine is shown to both decrease BMI and improve glucose control³⁸ and bromocriptine improves control, but the mechanism remains unknown.³⁹ Lifestyle modifications also have benefit in these patients. A low calorie diet and physical activity counseling both reduced patients' HgA1c in clinical trials.^{40,41} Besides affecting patients' physical health, obesity also has a negative impact on quality of life.⁴² Fortunately, although a widespread problem, obesity among DM patients is a treatable condition. It is an issue that clinicians must deal with each and every time they see their patients.

Hypertension:

Seventy-three percent of patients in the US who have diabetes also have hypertension. Controlling blood pressure in these patients is just as important as controlling blood glucose, but may be frequently overlooked. When uncontrolled, hypertension increases the risks of developing long-term diabetes complications.⁴³ Conversely, having controlled HTN can reduce the risk of developing complications, both micro- and macro-vascular, by 33-50%. Only six out of our 14 patients with HTN were currently controlled with drug therapy. Fifty percent of patients only took one HTN medication, which is frequently insufficient in controlling the blood pressure of diabetes patients.⁴⁴ The same factors that lead to uncontrolled glucose can also contribute to uncontrolled HTN, particularly minority race and depression.^{45,46} Given the increased risk of hyperglycemia in DM patients with uncontrolled HTN, blood pressure needs to be aggressively treated by clinicians.

Adherence:

Medication adherence is a problem that clinicians and patients face when treating virtually every disease state. Each patient has their own personal reasons for being non-adherent, which are not always obvious to health care professionals, making it very difficult to find effective methods of adherence improvement. We concluded from clinicians' chart notes that 56 % of our DM patients were non-adherent to either their

medications or self-monitoring, although, realistically, accurate rates of non-adherence are unobtainable by looking at medical charts alone. Common causes of medication non-adherence that our patients cited were running out of medication, lack of education in this area, and adverse drug effects.

Research into some of the factors that facilitate non-adherence in diabetes patients has been well documented. A recent review of many of the clinical trials in this area determined six factors shown to have the most influence on patient adherence; comprehension of regimen, perception of benefits, side effects, medication costs, regimen complexity, and emotional well-being.⁴⁷

Patients' comprehension of their treatments, perceptions of benefits, and impact of drug side effects are greatly influenced by the communication of clinicians. Decreases in HgA1c have been observed in patients whose physicians assessed their recall and comprehension of their treatments, and in those who reported good communication with their health care providers.^{48,49} Many patients are unaware of the long-term effects of their disease and do not notice any signs or symptoms of hyperglycemia. When unaware of the importance of adherence to long-term outcomes of their diabetes, patients may not take their medication as prescribed if they experience any unpleasant side effects. Therefore, it is extremely important for physicians to communicate the long-term benefits of therapy and to work with patients to minimize side effects.

Regimen complexity is a very strong predictor of medication adherence. Many studies have shown that as more medications are added to a patient's regimen, their adherence rate decreases.^{50,51,52} The same effect occurs when the doses per day are increased.^{50,51} The greatest percent of our patients were treated with only one hyperglycemic medication (39%), followed by two medications (33%), then three (28%). When looking at diabetes medications alone, 67% of our patients had a regimen with two dosing times throughout the day, regardless of the number of medications taken at those times. Most likely the patients have more than two dosing times per day when including all medications in their regimens. Simplifying patients' regimens will improve both adherence and control of their diabetes. The use of combination products is a convenient method to do this, but only one patient in our study utilized this type of medication.

Cost of medication is an influential factor on medication adherence in most health care settings. However, we did not consider it as one because 89% of our patients had insurance that did not require them to pay for their medications. It is possible that the

minimal use of combination products in our patients was due to the lack of insurance coverage of those medications.

The impact of emotional well-being on glucose control was discussed earlier in terms of the effects of depression and other psychological illnesses. These disorders, as well as emotional distress, also affect medication adherence. This finding further emphasizes the importance of appropriately treating these co-morbid conditions.

When adherence is improved, better glycemic control can be achieved. Addressing the six factors mentioned above is imperative. Other methods that have been shown effective include making telephone calls from the physicians' office, and the implementation of pharmacist-managed diabetes programs.^{53,54} The issue of medication adherence is an area that deserves much more attention from clinicians than it currently receives and can substantially improve DM glucose control when focused on.

Adherence to office visits is also a barrier to glucose control. When patients do not attend regular appointments with their physicians, it becomes even more difficult to manage their disease properly. Poor compliance with office visits has been associated with an increase in diabetic complications. We found that 67% of our patients had attended at least three appointments in the past six months. Also, a remarkable 94% of patients had been screened for both retinopathy and neuropathy in the past year and 89% for nephropathy. Overall, clinic attendance was not a big problem among our patients; however, a couple of individuals had extremely poor attendance. Many strategies have been proven effective in improving patients' appointment adherence and, subsequently, improving glucose control. This includes exit-interviews by clinicians, sending detailed appointment information to patients' homes and calling them prior to appointments.^{55,56} Therefore, appointment attendance is not completely out of the hands of clinicians.

Limitations:

Our study was based on data collected from physician chart notes. We did not include any information that the physician did not record. Some factors, such as adherence may not be accurately assessed in this way. Only patients with type 2 diabetes and a most recent HgA1c of >8.5% were included. We did not consider any previous HgA1c values in our data. The patient population of this study was entirely of minority race and primarily of low-income status. Factors affecting glucose control may differ among other patient populations in other geographical areas. Several of the patients

included have had HgA1c levels <8.5% taken since we ended the data collection period and are improving in glyceemic control.

Conclusions:

This study has collectively identified the factors most responsible for our patients' uncontrolled DM. Published literature strongly supports our findings in most cases. With this information we hope clinicians will expand their diabetes treatment to include other factors that would otherwise have seemed irrelevant. There are some risk factors, however, that are not treatable, including a patient's race or income level. These factors need to be acknowledged as warning signs that patients are at increased risk of having uncontrolled blood sugars. Other factors which are treatable, such as depression and medication adherence, have proven effective methods of treatment that should be utilized whenever possible. Overall, the goal of treatment in diabetes, and any other disease state, is to improve the patient's quality of life. To do this, treatment must go beyond controlling HgA1c levels to encompass every aspect of patient health.

-
- ¹ American Diabetes Association [homepage on the Internet]. Alexandria, VA. Accessed Sept 24-Dec 31, 2005.
- ² Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion. National Diabetes Fact Sheet. March 27, 2002.
- ³ U.K. Prospective Diabetes Study Group: Intensive blood-glucose control with sulfonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 352:837-853, 1998.
- ⁴ Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med*. 1993;329:977-986.
- ⁵ Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *New England Journal of Medicine*. 2005 Dec 22;353(25):2707-9.
- ⁶ Devries JH, Snoek FJ, Heine RJ. Persistent poor glycaemic control in adult type 1 diabetes. A closer look at the problem. *Diabet Med*. 2004 Dec;21(12):1263-1268.
- ⁷ Rosilio M, Cotton JB, Wieliczko MC, Gendrault B, Carel JC, Couvaras O. Factors associated with glycemic control. A cross-sectional nationwide study in 2,579 French children with type 1 diabetes. *Diabetes Care*. 1998;21(7):1146-1153.
- ⁸ Lanting LC, Joung IM, Mackenbach JP, Lamberts SW, Bootsma AH. Ethnic differences in mortality, end-stage complications, and quality of care among diabetic patients. *Diabetes Care*. 2005;28:2280-2288.
- ⁹ Harris MI, Eastman RC, Cowie CC, Flegal KM, Eberhardt MS. Racial and ethnic differences in glycemic control of adults with type 2 diabetes. *Diabetes Care*. 1999;22(3):403-408.
- ¹⁰ Summerson JH, Konen JC, Dignan MB. Race-related differences in metabolic control among adults with diabetes. *South Med J*. 1992 Oct;85(10):953-956.
- ¹¹ Cossrow N, Bonita F. Race/ethnic issues in obesity and obesity-related comorbidities. *The Journal of Clinical Endocrinology & Metabolism*. 2004;89(6):2590-2594.
- ¹² Schectman JM, Nadkarni MM, Voss JD. The association between diabetes metabolic control and drug adherence in an indigent population. *Diabetes Care*. 2002 June;25(6):1015-1021.
- ¹³ Blazer DG, Moody-Ayers S, Craft-Morgan J, Burchett B. Depression in diabetes and obesity: racial/ethnic/gender issues in older adults. *J Psychosom Res*. 2002 Oct;53(4):913-916.
- ¹⁴ Tucker KL, Bermudez OI, Castaneda C. Type 2 diabetes is prevalent and poorly controlled among Hispanic elders of Caribbean origin. *Am J Public Health*. 200 Aug;90(8):1288-1293.
- ¹⁵ Gonzalez VC, Stern MP, Arredondo PB, Martinez DS. The level of metabolic control in low income Mexico City diabetics. The Mexico City diabetes study. *Arch Med Res*. 1994 Winter;25(4):387-92.
- ¹⁶ de Rekeneire N, Rooks RN, Simonsick EM, Shorr RI, Kuller LH, Schwartz AV. Racial differences in glycemic control in a well-functioning older diabetic population. *Diabetes Care*. 2003;26:1986-92.
- ¹⁷ Larsson D, Lager I, Nilsson PM. Socio-economic characteristics and quality of life in diabetes mellitus--relation to metabolic control. *Scand J Public Health*. 1999 Jun;27(2):101-5.
- ¹⁸ Lasater LM, Davidson AJ, Steiner JF, Mehler PS. Glycemic control in English- vs Spanish speaking Hispanic patients with type 2 diabetes mellitus. *Arch Intern Med*. 2001 Jan 8;161(1):77-82
- ¹⁹ Karter AJ, Ferrara A, Darbinian JA, Ackerson LM, Selby JV. Self-monitoring of blood glucose: language and financial barriers in a managed care population with diabetes. *Diabetes Care*. 2000;23(4):477-483.

-
- ²⁰ Lustman PJ, Clouse RE. Depression in diabetic patients: the relationship between mood and glycemic control. *J Diabetes Complications*. 2005 Mar-April;19(2):113-122.
- ²¹ Katon W, Von Korff M, Ciechanowski P, Russo J, Lin E, Simon G. Behavioral and clinical factors associated with depression among individuals with diabetes. *Diabetes Care*. 2004;27:914-920.
- ²² Black S, Markides K, Ray L. Depression predicts increased incidence of adverse health outcomes in older Mexican Americans with type 2 diabetes. *Diabetes Care*. 2003;26:2822-2828.
- ²³ Lustman PJ, Anderson RJ, Freedland KE, de Groot M, Carney RM, Clouse RE. Depression and poor glycemic control. *Diabetes Care*. 2000 Jul;23(7):934-42.
- ²⁴ Bambauer KZ, Soumerai SB, Adams AS, Mah C, Zhang F, McLaughlin TJ. Does antidepressant adherence have an effect on glycemic control among diabetic antidepressant users? *Int J Psych Med*. 2004;34(4):291-304.
- ²⁵ Surwit RS, van Tilburg MA, Parekh PI, Lane JD, Feinglos MN. Treatment regimen determines the relationship between depression and glycemic control. *Diabetes Res Clinical Practice*. 2005 Jul;69(1):78-80.
- ²⁶ Diabetes Prevention Program Research Group. Depression symptoms and antidepressant use in diabetes prevention program participants. *Diabetes Care* 2005;28:830-837.
- ²⁷ Lustman PJ, Griffith LS, Clouse RE, Cryer PE. Psychiatric illness in diabetes mellitus. Relationship to symptoms and glucose control. *J Nerv Ment Dis*. 1986 Dec;174(12):736-42.
- ²⁸ *Diabetes Today*
- ²⁹ Peyrot M, Rubin R, Siminerio L. Physician and nurse use of psychosocial strategies and referrals in diabetes. *Diabetes*. 2002;51(suppl 2):A446.
- ³⁰ Rubin RR, Ciechanowski PS, Egede LE, Lin EHB, Lustman PJ. Recognizing and treating depression in patients with diabetes. *Curr Diab Rep*. 2004;4:119-125.
- ³¹ Lustman PJ, Freedland KE, Griffith LS, Clouse RE. Fluoxetine for depression in diabetes: a randomized double-blind placebo-controlled trial. *Diabetes Care*. 2000 May;23(5):618-623.
- ³² Paile-Hyvarinen M, Wahlbeck K, Eriksson JG. Quality of life and metabolic status in mildly depressed women with type 2 diabetes treated with paroxetine: a single-blind randomized placebo controlled trial. *BMC Fam Pract*. 2003 May;4:7.
- ³³ Lustman PJ, Griffith LS, Freedland KE, Kissel SS, Clouse RE. Cognitive behavioral therapy for depression in type 2 diabetes mellitus. *Ann Intern Med*. 1998 Oct;129(8):613-621.
- ³⁴ Prevalence of overweight and obesity among adults with diagnosed diabetes-United States, 1988-1994 and 1999-2002. *MMWR Morb Mortal Wkly Rep*. 2004;53:1066-1068.
- ³⁵ Bo S, Gentile L, Cavallo-Perin P, Vineis P, Ghia V. Sex- and BMI-related differences in risk factors for coronary artery disease in patients with type 2 diabetes mellitus. *Acta Diabetol*. 1999 Sep;36(3):147-53.
- ³⁶ Grylls WK, McKenzie JE, Horwath CC, Mann JI. Lifestyle factors associated with glycaemic control and body mass index in older adults with diabetes. *European Journal of Clinical Nutrition*. 2003 Nov;57(11):1386-1393.
- ³⁷ El-Kebbi IM, Cook CB, Ziemer DC, Miller CD, Gallina DL, Phillips LS. Association of younger age with poor glycemic control and obesity in urban african americans with type 2 diabetes. *Arch Intern Med*. 2003 Jan 13;163(1):69-75.
- ³⁸ Gokcel A, Karakose H, Ertorer EM, Tanaci N, Tutuncu NB, Guvener N. *Diabetes Care*. 2001 Nov;24(11):1957-60.

-
- ³⁹ Aminorroaya A, Janghorbani M, Ramezani M, Haghighi S, Amini M. *Horm Res.* 2004;62(2):55-9.
- ⁴⁰ Kirk A, Mutrie N, MacIntyre P, Fisher M. Effects of a 12-month physical activity counseling intervention on glycaemic control and on the status of cardiovascular risk factors in people with type 2 diabetes. *Diabetologia.* 2004 May;47(5):821-832.
- ⁴¹ Harder H, Dinesen B, Astrup A. The effect of a rapid weight loss on lipid profile and glycemic control in obese type 2 diabetic patients. *Int J Obes Relat Metab Disord.* 2004 Jan;28(1):180-2.
- ⁴² Hill-Briggs F, Gary TL, Hill MN, Bone LR, Brancati FL. Health-related quality of life in urban african americans with type 2 diabetes. *J Gen Intern Med.* 2002 Jan;17(6):412-9.
- ⁴³ Nicolucci A, Cavaliere D, Scorpiglione N, Carinci F, Capani F, Tognoni G, Benedetti MM. *Diabetes Care.* 1996;19(9):927-933.
- ⁴⁴ Cushman WC. The burden of uncontrolled hypertension: morbidity and mortality associated with disease progression. *Journal of Clinical Hypertension (Greenwich).* 2003 May-June;5(3 Suppl 2):14-22.
- ⁴⁵ Mainous AG, King DE, Garr DR, Pearson WS. Race, rural residence, and control of diabetes and hypertension. *Annals of Family Medicine.* 2004 Nov/Dec;2(6):563-8.
- ⁴⁶ Scalco AZ, Scalco MZ, Azul JB, Lotufo Neto F. Hypertension and depression. *Clinics.* 2005 Jun;60(3):241-50.
- ⁴⁷ Rubin RR. Adherence to pharmacologic therapy in patients with type 2 diabetes mellitus. *Amer J Med.* 2005;118(5A):27S-34S.
- ⁴⁸ Schillinger D, Piette JD, Grumbach K, et al. Closing the loop: physician communication with diabetic patients who have low health literacy. *Arch Intern Med.* 2003;163:83-90.
- ⁴⁹ Alazri MH, Neal RD. The association between satisfaction with services provided in primary care and outcomes in type 2 diabetes mellitus. *Diabet Med.* 2003;20:486-490.
- ⁵⁰ Paes AH, Bakker A, Soe-Agnie CJ. Impact of dosage frequency on patient compliance. *Diabetes Care.* 1997;20:1512-1517.
- ⁵¹ Bartels D. Adherence to oral therapy for type 2 diabetes: opportunities for enhancing glycemic control. *J Am Acad Nurse Pract.* 2004 Jan;16(1):8-16.
- ⁵² Schectman JM, Nadkarni MM, Voss JD. The association between diabetes metabolic control and drug adherence in an indigent population. *Diabetes Care.* 2002 Jun;25(6):1015-1021.
- ⁵³ Piette JD, Weinberger M, McPhee SJ, Crapo LA, Kraemer FB. Do automated calls with nurse follow-up improve self-care and glycemic control among vulnerable patients with diabetes? *Am J Med.* 2000;108:20-27.
- ⁵⁴ Nowak SN, Singh R, Clarke A, Campbell E, Jaber LA. Metabolic control and adherence to American Diabetes Association Practice Guidelines in a pharmacist-managed diabetes clinic. *Diabetes Care.* 2002;25:1479.
- ⁵⁵ Guse CE, Richardson L, Carle M, Schmidt K. The effect of exit-interview patient education on no-show rates at a family practice residency clinic. *Journal of the American Board of Family Practice.* 2003;16:399-404.
- ⁵⁶ Hardy KJ, O'Brien SV, Furlong NJ. Information given to patients before appointments and its effect on non-attendance rate. *BMJ.* 2001;323:1298-1300.