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Comparison of demographic factors and cardiovascular risk factor control among U.S. adults with type 2 diabetes by insulin treatment classification

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Abstract

Aims—Data on glucose and cardiovascular disease (CVD) risk factor control among persons with type 2 diabetes mellitus (DM) according to insulin treatment status are lacking. We examined DM control, risk factors, and comorbidities among U.S. persons according to insulin treatment status.

Methods—In the U.S. National Health and Nutrition Examination Surveys 2003–2006, we examined in 10,637 adults aged ≥30 with type 2 DM the extent of control of A1c, LDL-C, HDL-C, triglycerides, and blood pressure (BP) and composite goal attainment by insulin use status.

Results—6.6% ($n=889$, projected to 14.3 million) had type 2 DM; of these, 22.9% were insulin users and 57.2% were treated only by other diabetes medications. Overall, 58.2% had an A1c<7% (53 mmol/mol) (insulin users 33.1%, non-insulin treated 66.1%, and 77.9% of those not on medication, $p<0.0001$). Overall, 44.2% were at a BP goal of <130/80 mmHg, 43.8% had an LDL-C<100 mg/dl (2.6 mmol/L), and 13.9% a BMI<25 kg/m². Only 10.2% were simultaneously at A1c, LDL, and BP goals (5.4% of those on insulin).

Conclusions—U.S. adults with type 2 DM, especially those treated with insulin remain inadequately controlled for A1c and CVD risk factors and have a high prevalence of comorbidities.

Keywords

Diabetes mellitus; Epidemiology; Cardiovascular risk factors; Insulin; Control

Latest statistics from the American Diabetes Association (ADA) indicate 7.8% of the total U.S. population has diabetes mellitus (DM); among adults aged 20 and over it is 12.9%, of which 40% are undiagnosed, with an additional 30% having either impaired fasting glucose or glucose in tolerance (Cowie et al., 2009; National Diabetes Fact Sheet, 2007). Only a small proportion are at goal for recommended levels of A1c, blood pressure (BP), and lipids (Bertoni et al., 2008; Cheung et al., 2009; Imperatore, Cadwell, & Geiss, 2004; Kemp et al., 2005; Malik, Lopez, Chen, Wu, & Wong, 2007; Saydah, Fradkin, & Cowie, 2003; Shaya et al., 2010). Notably, studies of large cohorts show one-tenth or fewer persons with DM to be at goal for A1c, BP, and LDL-cholesterol (LDL-C) (Bertoni et al., 2008; Cheung et al.,

2009; Kemp et al., 2005; Malik et al., 2007). Control of these factors, particularly blood pressure and LDL-C, is well-documented to reduce the risk of CVD events in persons with diabetes, and control of blood sugar results in substantial reductions in microvascular complications (Buse et al., 2007; Colhoun et al., 2004; Collins et al., 2003; Keech et al., 2003; Vijan and Hayward, 2004; Zerber & Parchman, 2010). Guidelines have been issued for the management of key CVD risk factors for the primary prevention of CVD in persons with diabetes; however, adherence to these guidelines is less than optimal (Koopman, Mainous, Diaz, & Geesey, 2005).

Data on CVD risk factor control, treatment, and associated comorbidities in recent cohorts of persons with DM are lacking, especially according to treatment status—e.g, being on insulin or other medications, or among those not on medication. Accordingly, this study examined, in a contemporary cohort of U.S. persons with type 2 DM in 2003–2006 CVD risk factor control and associated comorbidities overall, by gender, and according to those being treated by insulin, other anti-diabetes medications, and those not on medication. Such information is important for the proper targeting of efforts to optimize control of CVD risk factors in those with type 2 DM.

1. Materials and methods

1.1. Subjects

Using the National Health and Nutrition Surveys (NHANES) 2003 to 2006, we identified 889 adults ages 30 years and older (projected to 14.3 million, 53.8% females) with type 2 DM. Among those with type 2 DM, 22.9% were insulin users, 57.2% were non-insulin users, and 19.9% were not on medication.

1.2. Definitions

The definition of type 2 DM in this study is consistent with published literature (Buse et al., 2007) and was on the basis of whether one or more of the following four conditions were met: 1) if fasting glucose ≥ 7.0 mmol/l (126 mg/dL) after a 12 h fast, 2) non-fasting glucose ≥ 11.1 mmol/L (200 mg/dL) (if not fasting), 3) use of oral anti-diabetes agents, or 4) a self-reported diagnosis of DM, as well as having an age of being told they had DM at age 30 and older as previously defined in prior NHANES work (Koopman et al., 2005). Treatment categories were based upon self-reported use of anti-diabetes agents at the time of the interview and three categories were identified: 1) those reporting any use of insulin (Insulin users); 2) those reporting taking any-other anti-diabetes agent but no insulin use (treated non-insulin users); 3) those reporting no use of either insulin or any other anti-diabetes agent (not on hypoglycemic medication). Duration of DM was defined as age when first told of having DM subtracted from the current age.

1.3. Risk factor measures

Lipid (triglyceride, total cholesterol [TC], high density lipoprotein cholesterol [HDL-C], in mg/dL) and glucose levels were based on serological tests, and urinalysis defined urine levels of albumin and creatinine. LDL-C was defined on the basis of Friedwald's equation ($LDL-C = TC - HDL-C - 1/5$ triglycerides). Target control levels for the different serologic/biochemical markers were defined as follows: 1) LDL-C < 100 mg/dL (2.6 mmol/L) if triglyceride levels were < 400 mg/dL (4.5 mmol/L) after an 8-h fast, 2) HDL-C cholesterol as HDL-C > 40 mg/dL (1.1 mmol/L) (males) and > 50 mg/dL (1.3 mmol/L) (females), 3) triglycerides < 150 mg/dL, and 4) glycemic control defined as an A1c level of $< 7\%$ (53 mmol/mol). Microalbuminuria was defined as an albumin–creatinine ratio (ACR) of 30–300 mg/g for both males and females (National Kidney Foundation, 2002), with macroalbuminuria was defined as ACR of > 300 mg/g for both females and males (National

Kidney Foundation, 2002). Blood pressure (BP) was defined as an average of up to four measurements taken in the sitting position; a BP of <130/80 mmHg was the defined goal for DM patients. A1c, lipid, and BP target recommendations have been previously described by the American Diabetes Association (ADA) (American Diabetes Association, 2011) and as performance measures by the National Committee for Quality Assurance (Ahmann, 2007).

We also present proportions at waist circumference levels of <102 cm for males and <88 cm for females. A body mass index (BMI) <25 kg/m² was defined on the American Association of Clinical Endocrinologists recommendations (Rodbard et al., 2007), although those at <30 kg/m² are also presented. Smoking was defined by self-report of cigarette use, history of use, starting age of use, amount used, past 30-day prevalence of cigar, pipe, chewing tobacco, snuff, and brand of cigarette; and was also defined by measured cotinine level >25. Self-reported questions of being ever told of having coronary heart disease (CHD), stroke, or heart failure were also included to define pre-existing CVD. Modification of Diet in Renal Disease (MDRD) equation calculated estimated glomerular filtration rates (eGFR)=175× [(calibrated serum creatinine (mg/dl)^{-1.154}](age^{-0.203})×0.742 (if female)×1.210 (if African American). The National Kidney Foundation classified estimated eGFR into kidney damage stages (renal disease as GFR <60 mL/min, stage 3 as GFR 30–59 mL/min, stage 4 as 15–30 mL/min, and stage 5 as <15 mL/min)(Levey et al., 1999). Chronic kidney disease (CKD) was defined as stages 3 or greater by this formula. Health insurance information type (private, Medicare, uninsured, or other) was also available.

1.4. Medications

Anti-diabetes medications included: metformin, sulfonylureas, thiazolidinediones, alpha-glucosidase, meglitinides, miscellaneous antidiabetes agents, and antidiabetes combinations. Anti-hypertensive medications included: angiotensin 2 inhibitors, angiotensin converting enzyme inhibitors (ACE), beta-adrenergic blocking agents, calcium channel blocking agents, diuretics, antiadrenergic agents peripherally acting, antiadrenergic agents centrally acting, aldosterone receptor antagonists, methyldopa, and fixed dose combinations. Lipid-lowering medications included: HMG-CoA reductase inhibitors, miscellaneous antihyperlipidemic agents, fibric acid derivatives, bile acid sequestrants, cholesterol absorption inhibitors, and antihyperlipidemic combinations. Medication treatment information of survey participants was obtained by self-reported answers of yes or no for taking any of the listed medications within the past 30 days. If answered yes for taking any of the listed medications, the participant was asked to show the interviewer the medication containers for all the products used. If there was no medication container available, the participant was asked to verbally report the name of the medication.

1.5. Statistical analysis

Data analyses were performed with SUDAAN statistical software, version 9.0.1 (Research Triangle Park, North Carolina) and SAS version 9.1.3 (SAS Institute, Cary, NC), allowing for obtaining population weighted estimates and means for projection to the U.S. population. More specifically, Chi-square test of proportions and analysis of covariance were used to determine the prevalence of individual, composite, and co-morbidity risk factors in males, females, and age groups. Cross-tabulations determined the prevalence of anti-diabetes, anti-hypertensive, and lipid-lowering agents across treatment status (insulin users, non-insulin treated, not on medication), gender, ethnicity (African American, non-Hispanic white, and Hispanic), and age groups (<65 years and ≥ 65 years).

2. Results

Table 1 shows in our overall sample and according to gender and treatment groups (insulin, non-insulin, or not on medication), demographic factors, age, smoking, and comorbidities. Overall, our sample comprised of 68.3% non-Hispanic White, 13.7% Hispanic, and 18.0% non-Hispanic Blacks, the proportions of which were similar by gender and ethnicity. The distribution of treatment categories were as follows: insulin users (22.9%); non-insulin users (57.2%); and not on hypoglycemic medication (19.9%). Overall, 62.7% had a duration of DM <10 years, 31.1% had a duration of DM of 10 to 25 years, and 6.2% had a duration of DM of 25+ years. This was similar across gender but varied significantly by treatment group, with significantly fewer insulin users (25%) having a diabetes duration of <10 years ($p<0.0001$). Overall, 17.1% of those with type 2 diabetes were uninsured, 30.6% had private insurance, 31.5% had Medicare, and 20.9% have some other type of insurance; there was a trend to females and those not on medication being more uninsured.

Overall, 18.8% had prevalent CHD, 11.5% and 13.1% stroke and heart failure respectively, and 31.4% overall had CVD, which encompassed CHD, stroke, and heart failure (Table 1). Twenty-two percent of type 2 DM had stage 3 or greater CKD. Insulin users had higher prevalence for CHD, heart failure ($p<0.0001$), overall CVD ($p<0.0001$), and CKD ($p<0.0001$) in comparison to non-insulin users and those not on medication. Males had a higher prevalence than females of CHD and heart failure while women had higher prevalence of stroke and renal disease (GFR<60 ml/min). Overall, 24.3% of type 2 diabetes had microalbuminuria (ACR 30–300 mg/L) which was most common in those not on medication; overall 6.9% had macroalbuminuria (ACR >300 mg/L), which was most common in insulin users (17.8%) ($p<0.0001$).

In Table 2, individual and composite risk factors (A1c, BP, HDL-C, LDL-C, BMI, waist circumference, and triglycerides) were examined stratified across gender and treatment groups. The prevalence of being at goal for A1c<7% (53 mmol/mol) was lowest among those with insulin (33.1%) and higher in those on other medications or not on hypoglycemic medication ($p<0.0001$). Non-insulin users had a higher incidence of being at goal for BP<130/80 mmHg, while insulin users were more likely to be at goal for LDL-C. The proportions at recommended HDL-C levels were similar across treatment groups; however, insulin users had the lowest prevalence for being at goal for triglycerides levels (17.5%) ($p<0.05$ across treatment groups), and body mass index (8.4% at BMI<25 kg/m² and 32.7% at BMI<30 kg/m²). Attainment of individual risk factor goals did not differ significantly by gender. For the whole population, simultaneous attainment of A1c, BP, and LDL-C goals was only 10.2%; and for A1c, BP, and BMI<30 kg/m² was 10.7% (but only 2.9% if BMI goal<25 kg/m²). Insulin users were significantly less likely to be at goal for any of these measures than non-insulin users or those not on hypoglycemic medication ($p<0.05$ to $p<0.001$).

We also examined the proportion of DM patients at goal for 0 to 4 risk factor measures concurrently (A1c <7% [53 mmol/mol], BMI<25 kg/m², LDL-C<100 mg/dl (2.6 mmol/L), and BP<130/80 mmHg). Overall, only 0.3% were concurrently at goal for all four measures, 8.5% for some combination of 3 measures, and 34% for some combination of two measures. Insulin users tended to be less likely to be at goal; 0%, 3.2%, and 24.7%, for four, three, and two measures respectively (Table 3).

Diabetes medication use was examined in Table 4 across insulin status groups and gender only for the most recent survey phase (2005–2006); 80.3% of type 2 DM patients were taking antidiabetes medications. Of those taking insulin during this period, 34.5% were on insulin only, 17.6% on insulin+thiazolidinediones, and 10.8% on insulin+sulfonylureas. Of

the non-insulin group, 27.3% were on metformin only, 21.3% on metformin+sulfonylureas, and 14.8% on sulfonylureas only. Males and females had higher proportions of taking single types of diabetes medications in comparison to taking multiple, other, and fixed dose combinations diabetes medications. Regarding antihypertensive therapy (data not shown), 71% reported some type of BP medication, with insulin users most likely to be on diuretics (39.7%) and non-insulin users most likely on ACE inhibitors (41.9%). Moreover, type 2 DM subjects not on insulin were much less likely to be on combination antihypertensive therapy, with more than 50% on monotherapy, compared to only 25% of insulin users.

3. Discussion

Our report of U.S. adults with type 2 diabetes shows only one-tenth to be at goal for A1c, BP, and LDL-cholesterol, and among insulin users, only 5% are at goal for these parameters. Moreover, less than one-sixth of persons with diabetes are at an ideal body mass index <25 kg/m². Our data from 2005–2006 show virtually no improvement in control for A1c, BP, and LDL-cholesterol since our earlier report based on US adults with DM in 2001–2002 (Malik et al., 2007), and further demonstrate the important gap between treatment recommendations and goal achievement, with the situation dramatically worse among more severe persons with diabetes relying on insulin use. Earlier reports also document similarly poor achievement of glycemic, BP, and lipid goals (Imperatore et al., 2004; Saydah et al., 2003), as well as a high burden of comorbidities, particularly in older persons (Shaya et al., 2010). Our results are comparable with those from other studies. A large population-based survey in Australia found that only 2% of persons with diabetes were at lipid, BP, and glycemic control targets (Kemp et al., 2005) and in the Look Ahead randomized trial of overweight and obese individuals with diabetes, only 10.1% met A1c, BP, and LDL-C goals (Bertoni et al., 2008). Also, Cheung et al. recently showed only 12% of adults aged 20 and over with diabetes (Type 1 and 2 combined) were at all three targets (Cheung et al., 2009). In addition, in a study examining CVD attributable risk due to modifiable risk factors in type 2 diabetes, the A1c level was the primary variable driving risk reduction, followed by smoking status and lipid levels, indicating the importance of these three modifiable factors, in particular, for reducing CVD risk in persons with diabetes (Zeber & Parchman, 2010). Well-established from clinical trials is the efficacy of both antihypertensive and statin therapy in reducing CVD event risk in diabetes. (Chobanian et al., 2003; Colhoun et al., 2004; Collins et al., 2003; Keech et al., 2003; Hansson et al., 1998; Vijan and Hayward, 2004).

Our finding of substantially poorer glycemic control (and therefore overall composite risk factor control) among insulin users compared to other persons with type 2 diabetes requires some explanation. First and not unexpected, those with worse glycemic control to begin with were more likely to be put on insulin (and still have the poorest control). Also, insulin users, while of similar age, had a substantially longer duration of diabetes, greater prevalence of cardiovascular disease (in particular heart failure), chronic kidney disease, macroalbuminuria, as well as obesity and hypertriglyceridemia as compared to subjects not requiring insulin use. While insulin may be useful for improving glycemic control, often worse in those with these comorbidities, it is also possible insulin itself may be atherogenic (Breen and Giacca, 2010), possibly driving in part the greater prevalence of CVD observed, although we cannot conclude this from our cross-sectional data. Also, the greater prevalence of macroalbuminuria among insulin users is noteworthy in that macroalbuminuria is strongly associated with chronic kidney disease (CKD) which in turn confers greater risks for CHD (Bouchi et al., 2010). Finally, while those not on hypoglycemic medication had better glycemic control, this most likely was due to a high proportion of these individuals having less severe diabetes. While these individuals also tended to be less overweight/obese, they were more likely not to be controlled for blood pressure or LDL-C than other persons with

diabetes in our study. Polypharmacy is frequently required to achieve the A1c goal level <7% (53 mmol/mol). In one study, 42% of persons with type 2 diabetes taking metformin, sulfonylureas, or a combination with insulin have been observed to not be at goal for A1c <7% (53 mmol/mol) (Nichols, Glauber, Javor, & Brown, 2000). Our data show many of our insulin treated subjects are not on additional medications to control their glucose; therefore, greater physician and patient education regarding the use of combination therapy, particularly in this more difficult to manage group, is needed. Also, the suboptimal control rates for both lipids and BP are due to the inadequacy of appropriately aggressive therapy (e.g. including use of combination therapy) to achieve target levels. We have previously shown high risk persons, including those with DM, have substantially poorer goal attainment for lipids and BP despite being on treatment (Ghandehari, Kamal-Bahl, & Wong, 2008; Wong et al., 2007).

Most important is that our goals are based on those in effect during the time course of this study (2003–2006) and it is important to realize that there is constant evolution in guidelines; for instance, the most recent ADA recommendations for an A1c <7% (53 mmol/mol) are considered reasonable for nonpregnant adults with DM, but less stringent goals may be appropriate for certain patients such as those with a history of severe hypoglycemia or those with advanced micro or macrovascular disease (American Diabetes Association, 2011). Given recent studies, such as ACCORD which have failed to show in adults with DM the benefits of intensive glucose lowering (The Action to Control Cardiovascular Risk in Diabetes Study Group, 2008) or blood pressure control (The Action to Control Cardiovascular Risk in Diabetes Study Group, 2010), there may continue to be evolution in the guidelines in the years ahead.

Our study has important strengths and limitations. An important strength is the generalizability of our study sample to the general U.S. population of adults with diabetes which is possible from the NHANES sample weighting methodology. In addition, there was systematic methodology for the collection of all data, including questionnaire self-report information and laboratory measures. An important limitation to this study is the cross-sectional design, in which information on treatment, risk factors, and comorbidities were collected at the same time; thus, one is unable to ascertain the temporal nature between these factors. Further, as there is no definitive diagnosis of type 2 DM, this study defines this as being told of having DM at the age of 30 and older by a physician; however, in recent years there are more persons with type 2 DM that are being diagnosed at a younger age. Thus, while our age requirement for type 2 diabetes diagnosis will likely have eliminated all of those with type 1 DM, it is possible we may have excluded some with type 2 DM diagnosed at an earlier age. Finally, while subjects brought in medication containers to verify use of specific medications, there was no means to ascertain dosage of or adherence to any particular medication in NHANES.

In conclusion, our report demonstrates that as recently as 2003–2006, less than half of type 2 DM persons were at goal for A1c, BP, LDL-C, or BMI individually and one-tenth or less are at composite goals (A1c, BP and LDL-C (or BMI)), with insulin-treated DM patients showing much poorer control. Despite clear treatment recommendations for A1c, BP and lipids, and the negative impact of obesity on disease progression in type 2 DM patients, a substantial unmet need still exists in US type 2 DM patients. Whereas education and lifestyle changes are crucial in addressing the obesity epidemic in type 2 DM patients, adherence to lifestyle changes remains very difficult. While some key trials (Knowler et al., 2002; Tuomilehto et al., 2001) have documented the value of lifestyle changes to prevent DM in those with pre-diabetes, the counseling and monitoring that were available in these trials are not typical of what is normally available in clinical practice, thus resources need to be provided to ensure there is adequate support for lifestyle modification efforts to be

successful. Finally, it will be important to demonstrate that composite goal achievement will result in reduced morbidity and mortality and ultimately benefit population health.

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References

- Ahmann AJ. Guidelines and performance measures for diabetes. *The American Journal of Managed Care*. 2007; 13:S41–S46. [PubMed: 17417932]
- American Diabetes Association. Executive summary: standards for medical care in diabetes—2011. *Diabetes Care*. 2011; 34(suppl 1):s4–s10. [PubMed: 21193627]
- Bertoni AG, Clark JM, Feeney P, Yanovski SZ, Bantle J, Montgomery B, et al. Suboptimal control of glycemia, blood pressure, and LDL cholesterol in overweight adults with diabetes: the Look AHEAD Study. *Journal of Diabetes and its Complications*. 2008; 22(1):1–9. [PubMed: 18191071]
- Bouchi R, Babazono T, Yoshida N, Nyumura I, Toya K, Hayashi T, et al. Association of albuminuria and reduced estimated glomerular filtration rate with incident stroke and coronary artery disease in patients with type 2 diabetes. *Hypertension Research: Official Journal of the Japanese Society of Hypertension*. 2010;10.1038/hr.2010.170
- Breen DM, Giacca A. Effects of insulin on the vasculature. *Current Vascular Pharmacology*. 2011; 9(3):321–332. [PubMed: 20807190]
- Buse JB, Ginsberg HN, Bakris GL, Clark NG, Costa F, Eckel R, et al. Primary prevention of cardiovascular disease in people with diabetes mellitus: a scientific statement from the American Heart Association and the American Diabetes Association. *Diabetes Care*. 2007; 30(1):162–172. [PubMed: 17192355]
- Cheung BM, Ong KL, Cherny SS, Sham PC, Tso AW, Lam KS. Diabetes prevalence and therapeutic target achievement in the United States, 1999–2006. *The American Journal of Medicine*. 2009; 122:443–453. [PubMed: 19375554]
- Chobanian AV, Bakris GL, Black HR, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *JAMA: The Journal of The American Medical Association*. 2003; 289:2560–2571. [PubMed: 12748199]
- Colhoun HM, Betteridge DJ, Durrington PN, Hitman GA, Neil HA, Livingstone SJ, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomized placebo-controlled trial. *Lancet*. 2004; 364(9435):685–696. [PubMed: 15325833]
- Collins R, Armitage J, Parish S, Sleight P, Peto R. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomized placebo-controlled trial. *Lancet*. 2003; 361(9374):2005–2016. [PubMed: 12814710]
- Cowie CC, Rust KF, Ford ES, Eberhardt MS, Byrd-Holt DD, Li C, et al. Full accounting of diabetes and pre-diabetes in the US population in 1988–1994 and 2005–2006. *Diabetes Care*. 2009; 32(2): 287–294. [PubMed: 19017771]
- Ghandehari H, Kamal-Bahl S, Wong ND. Prevalence and extent of dyslipidemia and recommended lipid levels in U.S. adults with and without cardiovascular co-morbidities: the National Health and Nutrition Examination Survey 2003–2004. *American Heart Journal*. 2008; 156:112–119. [PubMed: 18585505]
- Hansson L, Zanchetti A, Carruthers SG, Dahlöf B, Elmfeldt D, Julius S, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. *HOT Study Group. Lancet*. 1998; 351:1755–1762. [PubMed: 9635947]

- Imperatore G, Cadwell BL, Geiss L. Thirty-year trends in cardiovascular risk factor levels among US adults with diabetes: National Health and Nutrition Examination Surveys, 1971–2000. *American Journal of Epidemiology*. 2004; 160:531–539. [PubMed: 15353413]
- Keech A, Colquhoun D, Best J, et al. Secondary prevention of cardiovascular events with long-term pravastatin in patients with diabetes or impaired fasting glucose: results from the LIPID trial. *Diabetes Care*. 2003; 26:2713–2721. [PubMed: 14514569]
- Kemp TM, Barr ELM, Zimmet PZ, Cameron AJ, Welborn TA, Colagiuri S, et al. Glucose, lipid, and blood pressure control in Australian adults with type 2 diabetes. *Diabetes Care*. 2005; 28(6):1490–1492. [PubMed: 15920075]
- Knowler WC, Barrett-Conner E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *The New England Journal of Medicine*. 2002; 346:393. [PubMed: 11832527]
- Koopman RJ, Mainous AG III, Diaz VA, Geesey ME. Changes in age at diagnosis of type 2 diabetes mellitus in the United States, 1988 to 2000. *Annals of Family Medicine*. 2005; 3:60–63. [PubMed: 15671192]
- Levey AS, Bosch JP, Lewis JB, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. *Annals of Internal Medicine*. 1999; 130:461–470. [PubMed: 10075613]
- Malik S, Lopez V, Chen R, Wu W, Wong ND. Untreatment of cardiovascular risk factors among persons with diabetes in the United States. *Diabetes Research and Clinical Practice*. 2007; 77(1): 126–133. [PubMed: 17118478]
- National Diabetes Fact Sheet. National Institute of Diabetes and Digestive and Kidney Diseases. 2007
- National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *American Journal of Kidney Diseases: the Official Journal of the National Kidney Foundation*. 2002; 14:s198–s203. (part 7) guideline.
- Nichols GA, Glauber HS, Javor K, Brown JB. Achieving further glycemic control in type 2 diabetes mellitus. *The Western Journal of Medicine*. 2000; 173:175–179. [PubMed: 10986179]
- Rodbard HW, Blonde L, Braithwaite SS, Brett EM, Cobin RH, Yandelsman Y, et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the management of diabetes mellitus. *Endocrine Practice: Official Journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*. 2007; 13(suppl 1):1–68. [PubMed: 17613449]
- Saydah SH, Fradkin J, Cowie CC. Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. *JAMA: the Journal of the American Medical Association*. 2003; 26:2713–2721.
- Shaya FT, Yan X, Lin PJ, Simoni-Wastila L, Bron M, Baran R, et al. US trends in glycemic control, treatment, and comorbidity burden in patients with diabetes. *Journal of Clinical Hypertension*. 2010; 12:826–832. [PubMed: 21029348]
- The Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in type 2 diabetes. *The New England Journal of Medicine*. 2008; 358:2545–2559. [PubMed: 18539917]
- The Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive blood pressure control in type 2 diabetes mellitus. *The New England Journal of Medicine*. 2010; 362:1575–1585. [PubMed: 20228401]
- Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *The New England Journal of Medicine*. 2001; 344:1343. [PubMed: 11333990]
- Vijan S, Hayward RA. Pharmacologic lipid-lowering therapy in type 2 diabetes mellitus: background paper for the American College of Physicians. *Annals of Internal Medicine*. 2004; 140:650–659. [PubMed: 15096337]
- Wong ND, Lopez VA, L'Italien G, Chen R, Kline S, Franklin SS. High prevalence and treatment rates, but inadequate control of hypertension in U.S. persons in 2003–2004 with cardiovascular disease comorbidities. *Archives of Internal Medicine*. 2007; 167(22):2437–2442. [PubMed: 18071165]

Zeber J, Parchman ML. Cardiovascular disease in type 2 diabetes: attributable risk due to modifiable risk factors. *Canadian Family Physician Medecin de Famille Canadien*. 2010; 56:e302–e307. [PubMed: 20705869]

Table 1
Demographics and co-morbidities of type 2 diabetes subjects by gender and treatment (NHANES 2003–2006).

| <i>n</i> (%) | Overall | Males | Females | Insulin | Non-insulin | No hypoglycemic medication |
|---|---------------|----------------------------|------------|-----------------------------|-------------|----------------------------|
| <i>Demographics</i> | | | | | | |
| Overall | <i>n</i> =889 | 440 (46.2) | 449 (53.8) | 227 (22.9) | 500 (57.2) | 162 (19.9) |
| Mean Age (years) | 60.6 | 59.4 ^{††} | 61.8 | 62.1 [†] | 60.7 | 58.8 |
| % Smoking | 155 (17.5) | 89 (18.9) ^{†††††} | 66 (16.4) | 33 (14.7) | 85 (16.2) | 37 (24.8) |
| Race (<i>n</i> =852) | | | | | | |
| Non-Hispanic White | 354 (68.3) | 184 (70.3) | 170 (66.6) | 77 (64.1) | 209 (70.4) | 68 (67.3) |
| Hispanics | 250 (13.7) | 119 (12.8) | 131 (14.4) | 61 (12.4) | 142 (13.2) | 47 (16.5) |
| Non-Hispanic Black | 248 (18.0) | 123 (16.9) | 125 (18.9) | 79 (23.5) | 130 (16.4) | 39 (16.2) |
| Duration of Diabetes (<i>n</i> =879) | | | | | | |
| <10 years | 510 (62.7) | 253 (63.7) | 257 (61.8) | 59 (25.0) ^{*****} | 330 (72.3) | 121 (78.5) |
| 10–<25 years | 300 (31.1) | 153 (30.7) | 147 (31.4) | 126 (59.3) | 140 (24.4) | 34 (17.8) |
| 25+ years | 79 (6.2) | 34 (5.6) | 45 (6.7) | 42 (15.7) | 30 (3.3) | 7 (3.7) |
| Insurance (<i>n</i> =484) | | | | | | |
| Un-insured | 88 (17.1) | 36 (12.7) [†] | 52 (20.5) | 16 (10.7) [*] | 44 (15.4) | 28 (29.2) |
| Private | 112 (30.6) | 65 (40.1) [†] | 47 (23.1) | 25 (25.5) | 68 (34.5) | 19 (25.9) |
| Medicare | 173 (31.5) | 84 (28.3) [†] | 89 (34.0) | 53 (40.1) | 91 (29.5) | 29 (26.8) |
| Other | 111 (20.9) | 51 (18.9) [†] | 60 (22.4) | 33 (23.8) | 62 (20.7) | 16 (18.1) |
| <i>Co-morbidities</i> | | | | | | |
| Coronary Heart Disease (CHD) (<i>n</i> =889) | 178 (18.8) | 112 (24.2) ^{†††} | 66 (14.1) | 60 (23.7) | 85 (15.8) | 33 (21.6) |
| Stroke (<i>n</i> =889) | 112 (11.5) | 54 (9.5) | 58 (13.2) | 36 (13.9) | 52 (9.5) | 24 (14.9) |
| Heart Failure (<i>n</i> =889) | 129 (13.1) | 69 (13.9) | 60 (12.3) | 64 (27.5) ^{*****} | 44 (7.1) | 21 (13.6) |
| Cardiovascular Disease (CVD) (<i>n</i> =889) | 296 (31.4) | 154 (31.4) | 142 (31.3) | 110 (47.7) ^{*****} | 138 (24.8) | 48 (31.3) |
| Renal Disease (<i>n</i> =787) | | | | | | |
| GFR<60 mL/min | 202 (22.3) | 98 (20.8) | 104 (23.7) | 77 (40.0) ^{*****} | 96 (16.9) | 29 (18.5) |
| Stage 5 | 8 (0.7) | 4 (0.7) | 4 (0.7) | 5 (2.5) | 2 (0.1) | 1 (0.6) |
| Stage 4 | 24 (2.4) | 11 (2.2) | 13 (2.6) | 14 (5.8) | 8 (1.2) | 2 (2.0) |
| Stage 3 | 170 (19.3) | 83 (18.0) | 87 (20.4) | 58 (31.7) ^{**} | 86 (15.7) | 26 (15.9) |
| Microalbuminuria (<i>n</i> =850) | 226 (24.3) | 126 (28.4) [†] | 100 (20.9) | 62 (25.4) | 122 (24.6) | 42 (22.5) |
| Macroalbuminuria (<i>n</i> =850) | 79 (6.9) | 43 (7.9) | 36 (6.1) | 44 (17.8) ^{*****} | 30 (4.5) | 5 (1.9) |

Comparing differences between gender or between age groups:

† p<0.05
†† p<0.01,
††† p<0.001,
†††† p<0.0001.

Comparing proportion between insulin users, non-users, and those not on hypoglycemic medication:

* p<0.05,
** p<0.01,
*** p<0.001,
**** p<0.001.

/ p<0.05 when compared to those not on hypoglycemic medication.

Denominator sample size is shown in parenthesis in row columns; weighted total sample size=14.3 million.

Table 2
Control of individual and composite risk factors among type 2 diabetes subjects by gender and treatment group (NHANES 2003–2006).

| n (%) | Overall | Males | Females | Insulin | Non-insulin | No hypoglycemic medication |
|--|------------|-----------------|------------|----------------|-------------|----------------------------|
| A1c Goal:<7% (53 mmol/mol) (n=838) | 444 (58.2) | 215 (54.8) | 229 (61.3) | 58 (33.1) **** | 276 (61.0) | 110 (77.9) |
| Blood Pressure Goal:<130/80 mmHg (n=804) | 350 (44.2) | 200 (50.2) † | 150 (38.4) | 86 (41.3) | 211 (47.1) | 53 (38.9) |
| LDL-C Goal:<100 mg/dl (2.6 mmol/L) (n=449) | 202 (43.8) | 108 (46.6) | 94 (41.5) | 52 (53.3) | 116 (44.0) | 34 (34.7) |
| Proportion at Goal for A1c, BP, and LDL-c (n=411) | 41 (10.2) | 24 (10.5) | 17 (9.9) | 4 (5.4) | 26 (10.6) | 11 (12.9) |
| Proportion at Goal for A1c, BP, and BMI<30 kg/m ² (n=749) | 82 (10.7) | 53 (13.5) | 29 (8.2) | 8 (4.8) * | 54 (11.2) | 20 (15.7) |
| Proportion at Goal for A1c, BP, and BMI<25 kg/m ² (n=749) | 23 (2.9) | 13 (3.2) | 10 (2.6) | 0 (0.0) *** | 16 (2.7) | 7 (6.2) |
| HDL-C Goal: 40 mg/dL (1.1 mmol/L) (M), 50 mg/dL (1.3 mmol/L) (W) (n=827) | 499 (56.4) | 266 (57.9) | 233 (55.0) | 119 (60.0) | 275 (53.5) | 105 (60.9) |
| Triglycerides Goal: <150 mg/dL (1.7 mmol/L) (n=819) | 228 (25.8) | 118 (25.7) | 110 (25.8) | 40 (17.5) * | 144 (27.9) | 44 (28.3) |
| Body Mass Index Goal: <25 kg/m ² (n=858) | 137 (13.9) | 69 (11.8) | 68 (15.6) | 22 (8.4) * | 79 (13.7) | 36 (20.3) |
| Body Mass Index Goal: <30 kg/m ² (n=858) | 410 (43.1) | 222 (44.7) | 188 (41.8) | 82 (32.7) ** | 235 (43.0) | 93 (54.9) |
| Waist Circumference Goal: 88 cm (W), 102 cm (M) (n=805) | 180 (17.7) | 134 (25.7) †††† | 46 (10.6) | 34 (14.1) | 100 (17.4) | 46 (22.3) |

Comparing differences between gender or between age groups:

† p<0.05

†† p<0.01,

††† p<0.001,

†††† p<0.0001.

Comparing proportion between insulin users and non-users:

* p<0.05,

** p<0.01,

*** p<0.001,

**** p<0.0001.

Denominator sample size is shown in parenthesis in row columns.

Table 3

Proportion at Control by Number of Risk Factor Measures among Type 2 Diabetic Subjects by Gender and Age Group within Treatment Group (NHANES 2003–2006).

| n (%) | Measures include: A1c<7% (53 mmol/mol), BMI<25 kg/m ² , BP<130/80 mmHg, LDL-C<100 mg/dL (2.6 mmol/L) | Gender | | Age Groups | | |
|--------------------|---|------------|------------|------------|------------|------------|
| | | Overall | Females | Males | <65 Years | 65+ Years |
| Overall | Controlled on 0 measures | 137 (14.2) | 74 (14.1) | 63 (14.2) | 77 (16.3) | 60 (11.3) |
| | Controlled on 1 measure | 380 (43.0) | 207 (45.6) | 173 (40.1) | 186 (41.1) | 194 (45.7) |
| | Controlled on 2 measures | 286 (34.0) | 127 (31.2) | 159 (37.2) | 137 (35.5) | 149 (31.8) |
| | Controlled on 3 measures | 81 (8.5) | 39 (8.9) | 42 (8.0) | 31 (6.8) | 50 (10.7) |
| | Controlled on 4 measures | 5 (0.3) | 2 (0.3) | 3 (0.4) | 2 (0.2) | 3 (0.5) |
| Insulin | Controlled on 0 measures | 48 (23.5) | 27 (23.9) | 21 (23.1) | 30 (27.2) | 18 (18.9) |
| | Controlled on 1 measure | 117 (48.6) | 69 (53.3) | 48 (42.5) | 54 (42.9) | 63 (55.8) |
| | Controlled on 2 measures | 53 (24.7) | 18 (18.9) | 35 (32.0) | 23 (25.5) | 30 (23.6) |
| | Controlled on 3 measures | 9 (3.2) | 5 (3.9) | 4 (2.4) | 5 (4.4) | 4 (1.7) |
| | Controlled on 4 measures | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Non insulin (((500 | Controlled on 0 measures | 71 (12.4) | 40 (12.8) | 31 (11.8) | 33 (13.9) | 38 (10.2) |
| | Controlled on 1 measure | 196 (40.4) | 103 (42.1) | 93 (38.5) | 93 (37.8) | 103 (44.0) |
| | Controlled on 2 measures | 179 (38.0) | 82 (34.9) | 97 (41.5) | 86 (41.4) | 93 (33.4) |
| | Controlled on 3 measures | 50 (8.8) | 25 (9.7) | 25 (7.8) | 17 (6.5) | 33 (11.9) |
| | Controlled on 4 measures | 4 (0.4) | 2 (0.5) | 2 (0.4) | 2 (6.5) | 2 (0.5) |
| Not on med | Controlled on 0 measures | 18 (8.7) | 7 (6.0) | 11 (11.7) | 14 (11.2) | 4 (4.6) |
| | Controlled on 1 measure | 67 (44.2) | 35 (46.1) | 32 (42.0) | 39 (48.3) | 28 (37.5) |
| | Controlled on 2 measures | 54 (33.1) | 27 (35.3) | 27 (30.5) | 28 (30.2) | 26 (37.6) |
| | Controlled on 3 measures | 22 (13.6) | 9 (12.6) | 13 (14.8) | 9 (10.2) | 13 (19.1) |
| | Controlled on 4 measures | 1 (0.4) | 0 (0.0) | 1 (0.9) | 0 (0.0) | 1 (1.1) |

There were no significance differences between measures and gender and age groups.

Table 4
Diabetes Medication Use by Treatment Group and Gender among Type 2 Diabetes Subjects (NHANES 2005–2006).

| <i>n</i> (%) | Overall <i>n</i> =445 | Insulin users (<i>n</i> =122) | Non-insulin users (<i>n</i> =241) | No hypoglycemic Medication (<i>n</i> =82) | Males (<i>n</i> =218) | Females (<i>n</i> =227) |
|-------------------------------|-----------------------|--------------------------------|------------------------------------|--|------------------------|--------------------------|
| Diabetes Medications | 363 (80.3) | 122 (100.0)**** | 241 (100.0) | 0 (0.0) | 176 (80.6) | 187 (80.0) |
| Any Diabetes Medication | | | | | | |
| Insulin Only | 56 (10.5) | 56 (34.5)**** | 0 (0) | 0 (0) | 27 (8.7) | 29 (12.0) |
| Metformin | 73 (21.7) | 10 (9.0) | 63 (27.3) | 0 (0) | 35 (22.5) | 38 (21.1) |
| Sulfonylureas | 66 (13.6) | 16 (10.8) | 50 (14.8) | 0 (0.0) | 33 (12.0) | 33 (15.0) |
| Thiazolidinediones | 31 (12.4) | 15 (17.6) | 16 (10.1) | 0 (0.0) | 14 (11.7) | 17 (13.0) |
| Metformin+Sulfonylureas | 54 (16.4) | 6 (5.2) | 48 (21.3) | 0 (0) | 24 (16.0) | 30 (16.7) |
| Metformin +Thiazolidinediones | 15 (3.9) | 4 (5.5) | 11 (3.3) | 0 (0) | 8 (5.6) | 7 (2.6) |
| Sulf + Thiaz | 11 (4.1) | 3 (5.7) | 8 (3.4) | 0 (0) | 4 (2.6) | 7 (5.4) |
| Metformin + Sulf + Thiaz | 18 (6.6) | 3 (2.5) | 15 (8.4) | 0 (0) | 11 (9.0) | 7 (4.5) |
| Other | 9 (2.8) | 5 (5.4) | 4 (1.6) | 0 (0) | 1 (0.8) | 8 (4.4) |
| Fixed Dose Combinations | 30 (8.0) | 4 (3.8) | 26 (9.8) | 0 (0.0) | 19 (11.1) | 11 (5.3) |
| 1 medication | 186 (47.1) | 56 (34.5) | 130 (52.6) | 0 (0.0) | 91 (44.1) | 95 (49.6) |
| 2 medications | 131 (37.1) | 44 (40.9) | 87 (35.4) | 0 (0.0) | 57 (34.0) | 74 (39.7) |
| 3 medications | 46 (15.8) | 22 (24.6) | 24 (12.0) | 0 (0.0) | 28 (21.9) | 18 (10.7) |

Other Diabetes Medications include: Non-Sulfonylureas, Alpha-Glucosidase Inhibitors, Meglitinides, and miscellaneous anti-diabetes agents;

* $p < 0.05$,

** $p < 0.01$,

*** $p < 0.001$,

**** $p < 0.0001$

$p < 0.0001$ across medication prevalence, classes, or number of medications between insulin users and non-users or gender; weighted total sample size=14.8 million.