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Rates of Complications and Mortality in Older Diabetes Patients: The Diabetes and Aging Study

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Abstract

Importance—In the coming decades, the population of older adults with diabetes is expected to grow substantially. Understanding the clinical course of diabetes in this population is critical for establishing evidence-based clinical practice recommendations, research priorities, allocating resources, and setting health policies.

Objective—Contrast rates of diabetes complications and mortality across age and diabetes duration categories.

Design, Setting, Participants—This cohort study (2004–2010) included 72,310 older (≥60 years of age) patients with type 2 diabetes enrolled in a large, integrated healthcare delivery system. Incidence densities (events per 1000 person-years (pys)) were calculated for each age category (60s, 70s, 80+ years) and duration of diabetes (shorter: 0–9 years vs. longer: 10+ years).

Main Outcome Measures—Incident acute hyperglycemic events, acute hypoglycemic events (hypoglycemia), microvascular complications [end-stage renal disease (ESRD), peripheral

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vascular disease, lower extremity amputation, advanced eye disease], cardiovascular complications [coronary artery disease (CAD), cerebrovascular disease (CVD), congestive heart failure (CHF)], and all-cause mortality.

Results—Among older adults with diabetes of short duration, cardiovascular complications followed by hypoglycemia were the most common non-fatal complications. For example, among 70–79 year olds with short duration of diabetes, CAD and hypoglycemia rates were higher (11.5 and 5.0/1000 pys respectively), compared to ESRD (2.6/1000), amputation (1.3/1000), and acute hyperglycemic events (0.8/1000). We observed a similar pattern among subjects in the same age group with long diabetes duration where CAD and hypoglycemia had some of the highest incidence rates (19.0 and 15.9 /1000 pys respectively), compared to ESRD (7.6/1000), amputation (4.3/1000), and acute hyperglycemic events (1.8/1000). For a given age group, rates of each outcome, particularly hypoglycemia and microvascular complications, increased dramatically with longer duration. However, for a given duration of diabetes, rates of hypoglycemia, cardiovascular complications, and mortality increased steeply with advancing age, while rates of microvascular complications remained stable or declined.

Conclusion—Duration of diabetes and advancing age independently predict diabetes morbidity and mortality rates. As long-term survivorship with diabetes increases and as the population ages, more research and public health efforts to reduce hypoglycemia will be needed, to complement ongoing efforts to reduce cardiovascular and microvascular complications.

Nearly half of the 24 million patients currently living with diabetes in the U.S. are over 60 years of age. In the next two decades, their numbers are expected to double and their direct medical costs are expected to triple, due to the combined effects of an aging population and high rates of overweight and obesity.[1] The clinical heterogeneity of these patients, in terms of characteristics such as duration of diabetes and comorbid illnesses greatly, increases the challenge of caring for older patients.[2] Many older patients are living longer with their diabetes. Longer duration of diabetes is associated with more complications and more difficulty with maintaining glycemic control.[3,4] Understanding the contemporary clinical course of diabetes in older patients is the critical first step needed to individualize and prioritize care, and target support for future research efforts.

The clinical course of diabetes in older patients of today is presumably quite different from that reported in previous studies due to the rapid evolution of diabetes care. Most of our current understanding about the clinical course of diabetes in older patients is based on studies of populations from the 1990s.[5,6] These studies found that Medicare patients with diabetes had elevated risks of complications (microvascular and cardiovascular) and mortality compared to patients without diabetes[5] and that cardiovascular events (ischemic heart disease (181.5 events/1000 person-years) and stroke (126.2/1000 person-years)) were by far the most common complications, while hypoglycemia was much less common (28.3/1000 person-years).[6] Following the publication of the United Kingdom Prospective Diabetes Study (UKPDS) findings in the late 1990s, clinicians have pursued more aggressive risk factor control[7,8] and have more treatment options at their disposal.[9] For example, clinicians dramatically increased their prescribing of ACE inhibitors and statins following the release of evidence demonstrating the benefits of these drugs[10,11] for preventing diabetes complications.[12]

Apart from not reflecting the influence of recent changes in clinical practice, prior studies of older patients did not systematically examine how the course of diabetes differs by age and duration of diabetes. These variables have been proposed as two key potential guides to the individualization of care goals and treatments.[13] In a study by Bethel and colleagues, investigators followed a diabetes population from a 5% sample of the Medicare population newly diagnosed in 1994 and did not provide data on patients with longer standing

diabetes.[5] Bertoni and colleagues utilized the same Medicare sample to look at rates of complications by different age categories but did not evaluate differences in the course of disease by duration of diabetes.[6] A more nuanced description of the clinical course of diabetes is needed to inform medical decision making in older diabetes patients. In this paper, we describe contemporary rates of diabetes complications and mortality and contrast them across categories of age and duration of diabetes, in a population of older adults with uniform access to integrated care.

Methods and Design

Source Population

The Kaiser Permanente Northern California ("Kaiser") Diabetes Registry ("Registry") is a well-characterized population, maintained continuously since 1993.[14–16] Registry inclusion is based on a validated algorithm incorporating multiple sources of data including pharmacy records, laboratory data, and outpatient, emergency room and hospitalization diagnoses of diabetes.[17] Data from clinical information systems (electronic medical records) are downloaded annually.

Our sampling frame included subjects with type 2 diabetes from the Registry who were 60 years or older on January 1, 2004 (baseline) with continuous Kaiser membership, and available clinical data. Starting with the full Registry (n=228,740), we excluded 75,673 under the age of 60, 61,284 lacking continuous Kaiser membership or pharmacy benefits in the 12 months prior to baseline, 11,107 with type 1 diabetes or unknown type of diabetes,[18] and 8366 individuals with no A1C test result during the year prior to baseline or no date of diabetes diagnosis (used to estimate duration). The remaining 72,310 subjects were the basis for these analyses.

Timeframe for analysis

We followed subjects for a 7-year observation window, assigning person-time at risk starting on January 1, 2004 and censoring follow-up at the first occurrence of the following: any of the non-fatal outcomes of interest, death, discontinuation of Kaiser membership or pharmacy benefits (gap of at least 3 months in coverage), or the end of followup (December 31, 2010). The mean follow-up time for mortality was 5.44 years.

Exposures

Patients were divided into six major subgroups defined jointly by age (60–69, 70–79, and 80+ years) and duration of diabetes (0–9 years, 10+years of diabetes) as of baseline January 1, 2004. Date of initial diagnosis of diabetes was based preferentially on self-report (38.5%) and, when missing, on administrative records (61.5%).

Outcomes

The occurrence and timing of each event were based on a combination of outpatient, emergency department, or inpatient primary diagnostic codes (ICD-9), or procedure codes (CPT-4) (see Appendix Table 1).

Acute hyperglycemic event was defined as hospitalizations for diabetes with hyperosmolarity, diabetes with ketoacidosis, or uncontrolled diabetes. *Acute hypoglycemic* event (hypoglycemia) was defined based on hospitalization or emergency department diagnostic codes for hypoglycemia.

Microvascular complications included end-stage renal disease (ESRD), severe diabetic eye disease, peripheral vascular disease, and amputation. Incident *ESRD* was defined as

initiating chronic dialysis therapy or kidney transplantation identified through hospitalizations or Kaiser's reporting systems for the United States Renal Data System. Severe *diabetic eye disease* was identified based on outpatient diagnostic codes for blindness, proliferative retinopathy, macular edema, or outpatient photocoagulation procedures. The presence of *peripheral vascular disease* was based on inpatient codes for the disease as well as lower extremity angioplasty. *Amputation* was identified through inpatient diagnostic and procedure codes.

Non-fatal cardiovascular complication was identified via hospitalization and/or emergency department records. These included *coronary artery disease* (CAD: myocardial infarction, coronary artery bypass surgery, angioplasty), *cerebrovascular disease* (CVD: ischemic or hemorrhagic stroke, carotid endarterectomy), and *congestive heart failure* (CHF).

Mortality and date of death were captured from the California State Mortality File, Social Security Death Records, or Kaiser administrative records when the death occurred within the health system.

Other variables

Covariates, ascertained at baseline, included demographics (sex and race/ethnicity), latest laboratory results within one year prior to baseline (A1C, LDL, GFR), prevalent complications (acute hyperglycemic or hypoglycemic event within previous year, or any history of ESRD, peripheral vascular disease, amputation, eye disease, coronary artery disease, cerebrovascular disease, and congestive heart failure), and baseline dispensing of diabetes-related medications.

Statistical Analysis

All analyses were performed with SAS version 9.1 (SAS Institute, Cary, North Carolina) and associations were considered statistically significant at the 0.05 level. However, given the large sample size, we also considered clinical significance in addition to statistically significant contrasts. We calculated crude and sex-race adjusted incidence densities for each outcome (number of events/1,000 person-years (pys)), based on the sub-population at risk, i.e., after excluding subjects with a prevalent history of each outcome of interest. We also conducted tests of trend to determine if the incidence significantly increased or decreased by age group or duration of diabetes.

In sensitivity analyses, rather than exclude those with a prevalent history of only the outcome of interest, we repeated the above analyses in the healthy subpopulation with no history of any of our outcomes of interest at baseline.

Results

The mean age of the subjects was 71 years with 15% of the study population 80 years of age or older. For each age group, the majority of patients had shorter duration (0–9 years) of diabetes (Table 1). There were 2.4 times more patients with shorter than longer duration of diabetes for patients in their 60s and 1.5 times more patients with shorter duration for patients 80+ years of age.

There were a number of noteworthy baseline differences between patients with shorter versus longer duration of diabetes. Within each age category, patients with longer duration of diabetes were more likely to have poorer glycemic control compared to those with shorter diabetes duration. For example, 14.3% of patients 80+ years of age with longer duration of diabetes had a baseline A1C >8.0% compared to only 6.4% for those in the same age group but with shorter duration of diabetes. Compared to patients with shorter duration of diabetes,

patients with longer duration of diabetes also had higher baseline prevalence rates of microvascular and cardiovascular complications and were more likely to use each class of glucose lowering medication, particularly insulin. For example, the proportion of patients 80+ years with longer duration using insulin was 34.8% compared to 5.0% for those in the same age group with shorter duration of diabetes. Most patients were on statins and ACE inhibitors, but the prevalence varied across age and duration subgroups (range: 56.9–70.8% for statins, 50.6–63.5% for ACE inhibitors).

Rates of complications and mortality with shorter duration of diabetes

In general, the non-fatal complications with the highest incidence were cardiovascular complications (coronary artery disease, CHF, and cerebrovascular disease) followed by diabetic eye disease and acute hypoglycemic events (Table 2). Congestive heart failure and cerebrovascular disease increased most dramatically with advancing age (255% and 229% increase between ages 60–69 and 80+, respectively), while the other outcomes increased less markedly. ESRD, amputation, and acute hyperglycemic events were consistently rare complications. Among individual microvascular complications, diabetic eye disease had the highest incidence in all age groups. For example, in 70–79 year olds, the incidence of eye disease was 6.2/1000 person-years (pys) while the incidence of ESRD and amputation were 2.6/1000 pys and 1.3/1000 pys, respectively.

Not unexpectedly, the mortality rates increased steeply with advancing age among those with shorter duration of diabetes (19.6/1000 pys for 60 year olds, 42.7/1000 pys for 70 year olds, and 105.2/1000 pys for those 80+ years of age). In patients 80+ years of age, the mortality rate was 4.3 times the rate of CHF, the most common non-fatal event.

Rates of complications and mortality with longer duration of diabetes

The incidence rates in older patients with longer duration of diabetes (10+ years) shared some similarities with rates of those with shorter duration of diabetes with some exceptions (Table 3). For patients with longer duration of diabetes, hypoglycemia had incidence rates that were similar to those of coronary artery disease and cerebrovascular disease. As a result, hypoglycemia had the fourth highest incidence of all individual non-fatal complication among patients 60–69 years of age and the third highest incidence among patients 70 and older. Rates of incident coronary artery disease, cerebrovascular disease, congestive heart failure, and hypoglycemic events increased more steeply with advancing age than the other non-fatal outcomes. Unlike those with shorter duration diabetes, patients with longer duration had modest declines in the rates of microvascular complications (ESRD, eye disease, and lower extremity amputation) with advancing age (−27%, −27%, and −1% between ages 60–69 and 80+, respectively). The rarest complications were lower extremity amputation and acute hyperglycemic events among all age groups.

The largest difference across age groups among those with longer duration was in the mortality rates. The mortality rates were significantly higher among patients 80+ years of age in comparison to patients in their 60s and 70s (33.2/1000 pys (60–69), 65.9/1000 pys (70–79), 132.9/1000 pys(80+)). In patients 80+ years of age, the mortality rate was almost 4.0 times the rate of CHF, the most common non-fatal event.

Rates of complications and mortality across duration of diabetes

For a given age-group, incidence rates were consistently higher for all outcomes (non- fatal complications as well as mortality) in subjects with longer compared to those with shorter duration of diabetes. This pattern was most evident in the 60–69 year olds. Incidence of microvascular outcomes was much greater among those with longer duration of diabetes compared to those with shorter duration. For example, ESRD, eye disease and lower

extremity amputation incidence was 296%, 248% and 290% greater, respectively, comparing longer to shorter duration among 60–69 year olds. Much smaller differences (142%, 86%, and 128%, respectively) were observed in the 80+ age group. The other complications differed less dramatically by duration. Among patients in the 80+ age group, the non-fatal complication with the greatest elevated risk with longer duration was hypoglycemia (215%).

Findings for the healthier subpopulation without prior complications

For patients with no prevalent history of any complications, we found that, in general, complication rates were markedly lower compared to the overall cohort (See Appendix Table 2 and 3). However, we found very similar rankings of individual complications, similar patterns between patients with shorter and longer duration of diabetes, and across age groups.

Discussion

Recent recommendations regarding diabetes care in older patients[19,20] have emphasized the importance of individualization of treatment , although this remains poorly defined. Based on clinical trial results,[13,21] some experts suggest the importance of considering age and duration of diabetes as criteria for risk stratification when individualizing care.[13] However, the contemporary epidemiologic patterns have not been adequately documented in usual care settings.

In this evaluation of subjects with type 2 diabetes, we found that age and duration of diabetes were independent predictors of the clinical course of diabetes. Moreover, their interaction (i.e., age*duration) was significant for end-stage renal disease, eye disease, lower extremity amputation, stroke, heart failure, and mortality, albeit not for hyperglycemia. The significant interactions justified evaluating effect sizes separately for each stratum. For consistency, we used the stratified approach for all outcomes.

Depending on the subgroup, the 4-year incidence of cardiovascular complications and hypoglycemia traded positions (depending on age and duration) among most frequent non-fatal complication of diabetes, while microvascular complications and acute hyperglycemic events occurred at much lower rates. Most notably, the risk of hypoglycemia rose markedly and independently with advancing age and duration of diabetes, and hypoglycemia was the third most frequent complication among patients age 70 or older with longer duration of diabetes. Within specific age groups, microvascular complications increased most dramatically with longer duration of diabetes. It is important to note that selected groups, particularly those 80 or older with longer duration of diabetes, were at the highest risk for developing almost all individual complications and consequently, also, multiple complications.

These findings should be informative for the management of diabetes in older people. Diabetes management has been classically centered on glycemic control. Moderately glycemic control (A1C of 7.0%) most clearly prevents microvascular complications and potentially reduces long-term cardiovascular complications in middle-aged patients.[7,22] However, very intensive glycemic control (i.e., with targets for A1C<6.0%) has been found to increase mortality risk in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial in older patients with long-standing diabetes.[23] In addition, the collective experience from ACCORD, ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation), and VADT (Veterans Affairs Diabetes Trial) suggests that very intensive control does not appear to provide significant benefits for cardiovascular outcomes [24,25] in older patients, especially those with or at high

risk for heart disease. There are also doubts regarding the effect of intensive glucose control on preventing end-stage renal disease.[26] Our observations that cardiovascular complications and hypoglycemia are common complications provides additional support for the re-orientation of care of older diabetes patients away from intensive glycemic control as the core focus of management. The distinctive clinical course of different patient strata supports recommendations to individualize glycemic targets among older people.[19]

These findings are based on observations in a contemporary, ethnically diverse population of older diabetes patients with uniform access to care in a large, integrated healthcare delivery system. The incidence rates of acute hyperglycemic events, microvascular complications, and cardiovascular complications in our study are all dramatically lower than those reported previously. In the Bertoni study of Medicare recipients enrolled in 1995[6], the incidence density of diabetic ketoacidosis was 24.3/1000 pys, the incidence of ischemic heart disease was 181.5/1000 pys, and the incidence of amputation was 9.8/1000 pys. We observed much lower rates of those complications in this study. For example, among the oldest patients (80+ years) with longer duration, the rates for acute hyperglycemic events, CAD and amputation were only 2.4, 24.1, and 3.9/1000 pys respectively. Our lower rates of cardiovascular events are consistent with a general decline in these events in the last 30 years for both diabetes and non-diabetes patients.[27] Our hypoglycemia rates varied from a low of 3.0/1000 pys for those 60–69 years of age with diabetes duration less than 10 years to 19.6/1000 pys for those 80+ years of age with 10 or more years of diabetes. Because these rates were very sensitive to age and diabetes duration, it is difficult to contrast the hypoglycemia rates we observed with those previously reported from the Bertoni study (28.3/1000 pys).

Progression of diabetes complications is influenced by a myriad of factors including delays in diagnosis, the natural history of type 2 diabetes, evolving diabetes care, patient self-management and genotypic variation. For example, the incidence of hypoglycemia among the elderly may increase due to defective counterregulation and hypoglycemic unawareness that occurs with aging and longer duration of diabetes[28], or it may be the result of increased reliance on specific agents (e.g., insulin, sulfonylureas), associated with a higher risk of hypoglycemia, to achieve lower glycemic targets. Psychosocial factors and functional limitations are also likely to be important determinants of hypoglycemia risk..[29] Hypoglycemia may also occur more frequently than traditional diabetes complications because the rates of microvascular and cardiovascular complications have declined from historic highs due to more effective primary prevention efforts and better risk factor control. The use of more intensive diabetes treatments, which has became more common from the 1990s to the 2000s[30], may put patients at greater risk of hypoglycemia. As we grow more successful at increasing long-term survivorship with type 2 diabetes, hypoglycemia may emerge as a dominant non-fatal complication of older patients. To the extent that hypoglycemia is a side effect of treatment, its emergence as a dominant “complication” raises serious concerns about the acceptable limits of iatrogenesis; it has been suggested that, for some patients, preventing hypoglycemia is more important than tight glycemic control.[31]

It is important to remember that the event rates of outcomes observed in this study are impacted not only by short-term clinical exposures and treatments, but also those received over a lifetime. For example, the older patients in our sample with duration of diabetes of over 10 years may have received their initial treatments during the early 1990s and thus their early treatment may have been less intensive since they predated the influence of UKPDS and Diabetes Control and Complications Trial[32] findings. In accordance with the concept that early control of glucose has long-lasting effects (legacy effect or metabolic memory),[22,33] it is likely that the rates of complications observed in those with longer

duration of diabetes will be quite different in the coming decade due to changes that have occurred in treatment patterns.

The clinical course of disease among patients in the Registry is also, in part, a product of the access and quality of diabetes care delivered within an integrated healthcare delivery system. In this population, the blood sugar levels were, on average, well-controlled (which may have influenced hypoglycemia rates) and the utilization of statins and ACE inhibitors was high. The patterns observed in this setting may differ from those in other clinical settings and populations, particularly the uninsured and underinsured. Although there are geriatric diabetes populations with limited access to quality diabetes care (e.g., geographically isolated patients), our findings should be broadly applicable to many older people living with diabetes since the vast majority receive Medicare-supported coverage. It is also important to note that the event rates in this study are based on a particular coding strategy which we applied systematically to all patient subgroups (Appendix 1).

This 4-year cohort study describes the clinical course of diabetes in older adults. These findings will be relevant and informative for clinicians, researchers, and policy makers. For clinicians, the study details how the expected course of diabetes may differ by age and duration of diabetes. While we have witnessed great advances in the prevention of microvascular and cardiovascular disease among patients with diabetes, our findings suggest the need for increased clinical and research focus on reducing and understanding the incidence of hypoglycemia for older adults with diabetes. For policymakers, the study provides important data that may be used for projecting health care expenditures for a large and growing segment of the Medicare population.[1] More importantly, the data from this study may inform the design and scope of public policy interventions that meet the unique needs of those who live with the disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Huang ES, Basu A, O'Grady M, Capretta JC. Projecting the future diabetes population size and related costs for the U.S. Diabetes Care. Dec; 2009 32(12):2225–2229. [PubMed: 19940225]
2. Huang ES, Zhang Q, Gandra N, Chin MH, Meltzer DO. The effect of comorbid illness and functional status on the expected benefits of intensive glucose control in older patients with type 2 diabetes: a decision analysis. Ann Intern Med. Jul 1; 2008 149(1):11–19. [PubMed: 18591633]
3. Nathan DM, Singer DE, Godine JE, Perlmuter LC. Non-insulin-dependent diabetes in older patients. Complications and risk factors. Am J Med. Nov; 1986 81(5):837–842. [PubMed: 3535494]
4. Turner RC, Cull CA, Frighi V, Holman RR. Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). UK Prospective Diabetes Study (UKPDS) Group. JAMA. Jun 2; 1999 281(21):2005–2012. [PubMed: 10359389]

5. Bethel MA, Sloan FA, Belsky D, Feinglos MN. Longitudinal incidence and prevalence of adverse outcomes of diabetes mellitus in elderly patients. Arch Intern Med. May 14; 2007 167(9):921–927. [PubMed: 17502533]
6. Bertoni AG, Krop JS, Anderson GF, Brancati FL. Diabetes-related morbidity and mortality in a national sample of U.S. elders. Diabetes Care. Mar; 2002 25(3):471–475. [PubMed: 11874932]
7. U K. Prospective Diabetes Study Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet. 1998; 352(9131):837–853. [PubMed: 9742976]
8. U K. Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. BMJ. 1998; 317:703–713. [PubMed: 9732337]
9. Hirsch IB. Insulin analogues. N Engl J Med. Jan 13; 2005 352(2):174–183. [PubMed: 15647580]
10. Heart Outcomes Prevention Evaluation Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Lancet. Jan 22; 2000 355(9200):253–259. [PubMed: 10675071]
11. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20536 high-risk individuals: a randomised placebo-controlled trial. Lancet. 2002; 360:7–22. [PubMed: 12114036]
12. Huang ES, Basu A, Finch M, Frytak J, Manning W. The complexity of medication regimens and test ordering for patients with diabetes from 1995 to 2003. Curr Med Res Opin. Jun; 2007 23(6): 1423–1430. [PubMed: 17559738]
13. Ismail-Beigi F, Moghissi E, Tiktin M, Hirsch IB, Inzucchi SE, Genuth S. Individualizing glycemic targets in type 2 diabetes mellitus: implications of recent clinical trials. Ann Intern Med. Apr 19; 2011 154(8):554–559. [PubMed: 21502652]
14. Karter AJ, Parker MM, Moffet HH, et al. Missed appointments and poor glycemic control: an opportunity to identify high-risk diabetic patients. Med Care. Feb; 2004 42(2):110–115. [PubMed: 14734947]
15. Karter AJ, Ferrara A, Liu JY, Moffet HH, Ackerson LM, Selby JV. Ethnic disparities in diabetic complications in an insured population. JAMA. May 15; 2002 287(19):2519–2527. [PubMed: 12020332]
16. Iribarren C, Karter AJ, Go AS, et al. Glycemic control and heart failure among adult patients with diabetes. Circulation. Jun 5; 2001 103(22):2668–2673. [PubMed: 11390335]
17. Karter AJ, Schillinger D, Adams AS, et al. Elevated Rates of Diabetes in Pacific Islanders and Asian Subgroups: The Diabetes Study of Northern California (DISTANCE). Diabetes Care. Oct 24.2012
18. Karter AJ, Ackerson LM, Darbinian JA, et al. Self-monitoring of blood glucose levels and glycemic control: the Northern California Kaiser Permanente Diabetes registry. Am J Med. Jul; 2001 111(1):1–9. [PubMed: 11448654]
19. Kirkman MS, Briscoe VJ, Clark N, et al. Diabetes in older adults. Diabetes Care. Dec; 2012 35(12):2650–2664. [PubMed: 23100048]
20. Sinclair A, Morley JE, Rodriguez-Manas L, et al. Diabetes mellitus in older people: position statement on behalf of the International Association of Gerontology and Geriatrics (IAGG), the European Diabetes Working Party for Older People (EDWPOP), and the International Task Force of Experts in Diabetes. J Am Med Dir Assoc. Jul; 2012 13(6):497–502. [PubMed: 22748719]
21. Brown AF, Mangione CM, Saliba D, Sarkisian CA. California Healthcare Foundation/American Geriatrics Society Panel on Improving Care for Elders with D. Guidelines for improving the care of the older person with diabetes mellitus. J Am Geriatr Soc. May; 2003 51(5 Suppl Guidelines):S265–280. [PubMed: 12694461]
22. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med. Oct 9; 2008 359(15):1577–1589. [PubMed: 18784090]
23. Gerstein HC, Miller ME, Byington RP, et al. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. Jun 12; 2008 358(24):2545–2559. [PubMed: 18539917]

24. Patel A, MacMahon S, Chalmers J, et al. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med. Jun 12; 2008 358(24):2560–2572. [PubMed: 18539916]
25. Duckworth W, Abraira C, Moritz T, et al. Glucose control and vascular complications in veterans with type 2 diabetes. N Engl J Med. Jan 8; 2009 360(2):129–139. [PubMed: 19092145]
26. Coca SG, Ismail-Beigi F, Haq N, Krumholz HM, Parikh CR. Role of intensive glucose control in development of renal end points in type 2 diabetes mellitus: systematic review and meta-analysis intensive glucose control in type 2 diabetes. Arch Intern Med. May 28; 2012 172(10):761–769. [PubMed: 22636820]
27. Preis SR, Hwang SJ, Coady S, et al. Trends in all-cause and cardiovascular disease mortality among women and men with and without diabetes mellitus in the Framingham Heart Study, 1950 to 2005. Circulation. Apr 7; 2009 119(13):1728–1735. [PubMed: 19307472]
28. Bolli G, de Feo P, Compagnucci P, et al. Abnormal glucose counterregulation in insulin-dependent diabetes mellitus. Interaction of anti-insulin antibodies and impaired glucagon and epinephrine secretion. Diabetes. Feb; 1983 32(2):134–141. [PubMed: 6337896]
29. Sarkar U, Karter AJ, Liu JY, Moffet HH, Adler NE, Schillinger D. Hypoglycemia is more common among type 2 diabetes patients with limited health literacy: the Diabetes Study of Northern California (DISTANCE). J Gen Intern Med. Sep; 2010 25(9):962–968. [PubMed: 20480249]
30. Saydah SH, Fradkin J, Cowie CC. Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. JAMA. Jan 21; 2004 291(3):335–342. [PubMed: 14734596]
31. Slomski A. Avoiding hypoglycemia at all costs is crucial for some with diabetes. JAMA : the journal of the American Medical Association. Jun 26; 2013 309(24):2536–2537. [PubMed: 23800913]
32. The 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. Sep 30; 1993 329(14):977–986. [PubMed: 8366922]
33. Nathan DM, Cleary PA, Backlund JY, et al. Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. N Engl J Med. Dec 22; 2005 353(25):2643–2653. [PubMed: 16371630]

Table 1

Characteristics of a cohort of 72,310 older (≥60 years of age) adults with type 2 diabetes, by age and duration of diabetes. Kaiser Permanente Northern California. 2004–2010.

Age groups (years)	**60–69**		**70–79**		**80+**	
Duration of diabetes category (years)	0–9	10+	0–9	10+	0–9	10+
N	23,899	10,088	18,018	9,786	6,325	4,194
Demographics, %						
Male	54.7	53.6	52.4	51.5	46.8	49.1
Race/ethnicity, %						
Non-Hispanic White	50.5	43.5	58.6	51.4	68.4	58.4
Non-Hispanic Black	9.9	14.1	7.2	10.0	6.3	13.7
Hispanic	10.9	13.9	10.1	12.9	6.3	8.5
Asian	4.2	4.3	6.0	5.7	5.1	4.7
South Asian	0.3	1.0	0.1	0.4	0.03	0.1
Filipino	6.5	6.3	4.4	4.5	2.1	2.0
Other Asian	2.6	1.6	1.5	1.0	0.7	0.4
Pacific Islander	0.1	0.4	0.03	0.2	0.02	0.02
Other/Mixed	10.4	14.5	10.3	13.9	10.4	12.1
Missing	4.9	0.4	1.8	0.2	0.7	0.1
Systolic blood pressure						
<130 mm Hg	37.5	36.4	35.2	35.3	35.7	36.0
>=130 mmg Hg	55.5	57.9	59.1	59.4	59.7	59.7
Missing	7.0	5.7	5.8	5.3	4.7	4.3
LDL cholesterol						
<100 mg/dl	41.9	49.5	46.4	52.9	41.0	48.9
>=100 mg/dl	53.4	45.8	48.6	42.0	47.9	40.6
Missing	4.7	4.7	5.0	5.1	11.1	10.5
A1C Categories, %						
<=5.9	17.5	6.2	20.2	8.6	23.2	11.4
6.0–6.9	45.4	32.3	51.6	40.5	53.9	44.5

Age groups (years)	60–69		70–79		80+	
7.0–7.9	22.2	34.0	19.2	32.8	16.7	29.8
8.0–8.9	7.7	15.4	5.3	11.4	3.6	9.4
>=9.0	7.3	12.2	3.8	6.8	2.8	4.9
Estimated Glomerular Filtration Rate, %						
>=90	15.0	12.1	5.2	4.6	3.0	3.4
60–89	50.2	43.0	48.6	39.5	39.5	34.9
30–59	21.3	29.6	33.5	40.3	46.5	47.7
15–29	0.7	3.8	1.8	5.0	3.3	6.4
<15	0.3	2.2	0.4	2.0	0.5	1.4
Missing	12.4	9.3	10.5	8.6	7.2	6.2
Baseline History of Complication, %						
Acute hyperglycemic event, previous year	0.4	0.7	0.4	0.8	0.6	1.0
Acute hypoglycemic event, previous year	0.2	0.6	0.3	0.9	0.6	1.3
End-stage renal disease	0.5	2.7	0.4	2.1	0.3	1.2
Amputation	0.4	2.8	0.5	2.7	0.7	2.7
Eye disease	5.4	40.6	6.4	41.6	7.3	38.9
Coronary artery disease	10.0	18.7	14.4	22.3	17.9	24.1
Cerebrovascular disease	3.2	6.2	5.8	9.5	9.6	11.4
Peripheral vascular disease	2.8	8.0	5.5	11.3	8.6	13.6
Congestive heart failure	6.4	14.4	11.2	18.9	19.7	25.6
Medications, %						
Taking no glucose lowering medications	32.7	5.2	41.2	7.3	48.8	10.9
Insulin	7.5	44.6	5.7	39.2	5.0	34.8
Sulfonylurea	47.4	59.7	44.4	60.9	41.2	60.2
Metformin	41.1	54.7	28.5	43.9	16.3	29.6
Thiazolidinedione	7.1	19.9	5.0	15.0	3.5	9.8
Acarbose	0.5	1.6	0.3	1.2	0.4	0.7
Regpaglinide	0.1	0.3	0.1	0.2	0.1	0.1
≥2 glucose lowering drugs	29.4	63.2	21.3	53.3	13.1	38.0

Age groups (years)	**60–69**		**70–79**		**80+**	
≥3 glucose lowering drugs	6.1	20.1	3.5	13.1	2.0	7.3
Insulin and oral therapy	5.3	27.0	3.6	19.9	3.0	13.5
Statin	64.8	70.8	66.7	70.8	56.9	60.5
Other lipid lowering agent	7.4	8.1	6.2	7.0	3.4	4.0
ACE inhibitor	54.2	63.5	53.6	62.3	50.6	59.7
Other anti-hypertensive	67.2	74.1	76.6	80.4	81.3	83.0

Table 2

Sex and Race-Adjusted incidence of Diabetes Complications in Older Adults with Shorter Duration of Type 2 Diabetes (Events/1000 person-years) (95%CI). Kaiser Permanente Northern California. 2004–2010.

0–9 Years Duration	Ages: 60–69	Ages: 70–79	Ages: 80+	P-Value
Acute Hyperglycemic Events	0.78 (0.61–1)	0.82 (0.63–1.06)	1.11 (0.76–1.61)	0.11
Acute Hypoglycemic Events	3.03 (2.72–3.39)	5.03 (4.55–5.55)	6.22 (5.35–7.23)	<0.01
End Stage Renal Disease	2.00 (1.76–2.27)	2.60 (2.29–2.95)	2.38 (1.91–2.96)	0.15
Eye Disease	5.82 (5.31–6.37)	6.16 (5.59–6.78)	7.99 (6.94–9.19)	<0.01
Peripheral Vascular Disease	1.68 (1.45–1.94)	2.41 (2.1–2.77)	3.08 (2.52–3.77)	<0.01
Lower Extremity Amputation	1.01 (0.85–1.2)	1.28 (1.08–1.52)	1.72 (1.34–2.21)	<0.01
Coronary Artery Disease	8.48 (7.88–9.13)	11.47 (10.66–12.33)	15.09 (13.61–16.74)	<0.01
Cerebrovascular Disease	5.41 (4.95–5.91)	9.83 (9.08–10.64)	17.79 (16.13–19.62)	<0.01
Congestive Heart Failure	6.83 (6.29–7.41)	12.64 (11.76–13.58)	24.24 (22.16–26.51)	<0.01
Mortality	19.61 (18.76–20.5)	42.69 (41.17–44.26)	105.20 (101.17–109.4)	<0.01

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Table 3

Sex and Race-Adjusted Incidence of Diabetes Complications in Older Adults with Longer Duration of Type 2 Diabetes (Events/1000 person-years). Kaiser Permanente Northern California. 2004–2010.

10+ Years Duration	Ages: 60–69	Ages: 70–79	Ages: 80+	P-Value
Acute Hyperglycemic Events	1.85 (1.44–2.37)	1.76 (1.36–2.27)	2.35 (1.68–3.27)	0.21
Acute Hypoglycemic Events	9.62 (8.7–10.64)	15.88 (14.56–17.32)	19.60 (17.48–21.98)	<0.01
End Stage Renal Disease	7.92 (7.08–8.84)	7.64 (6.83–8.54)	5.75 (4.8–6.88)	<0.01
Eye Disease	20.26 (18.41–22.30)	14.97 (13.45–16.66)	14.89 (12.69–17.47)	<0.01
Peripheral Vascular Disease	4.02 (3.47–4.67)	4.90 (4.25–5.64)	5.67 (4.67–6.88)	<0.01
Lower Extremity Amputation	3.94 (3.38–4.6)	4.26 (3.66–4.95)	3.92 (3.16–4.88)	0.97
Coronary Artery Disease	15.15 (13.89–16.51)	18.98 (17.5–20.59)	24.09 (21.55–26.92)	<0.01
Cerebrovascular Disease	8.51 (7.65–9.46)	14.62 (13.37–15.99)	18.90 (16.74–21.32)	<0.01
Congestive Heart Failure	13.83 (12.62–15.15)	23.86 (22.1–25.76)	33.10 (29.88–36.66)	<0.01
Mortality	33.21 (31.55–34.95)	65.87 (63.28–68.56)	132.90 (127.09– 138.98)	<0.01