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Diabetes and fracture risk in older U.S. adults[1]

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Abstract

OBJECTIVE—We examined the diabetes-fracture relationship by race/ethnicity, including the link between pre-diabetes and fracture.

RESEARCH DESIGN AND METHODS—We used Medicare- and mortality-linked data for respondents age 65 years and older from the third National Health and Nutrition Examination Survey (NHANES III) and NHANES 1999–2004 for three race/ethnic groups: non-Hispanic whites (NHW), non-Hispanic blacks (NHB), and Mexican Americans (MA). Diabetes was defined as diagnosed diabetes (self-reported) and diabetes status: diagnosed and undiagnosed diabetes (positive diagnosis or hemoglobin A_{1c} (A1C) ≥ 6.5%); pre-diabetes (no diagnosis and A1C between 5.7%–6.4%); and no diabetes (no diagnosis and A1C < 5.7%). Non-skull fractures (n=750) were defined using published algorithms. Hazards ratios (HRs) were calculated using Cox proportional hazards models.

RESULTS—The diabetes-fracture relationship differed significantly by race/ethnicity ($p_{interaction}$ <0.05). Compared to those without diagnosed diabetes, the HRs for those with diagnosed diabetes were 2.37 (95% CI 1.49–3.75), 1.87 (95% CI 1.02–3.40), and 1.22 (95% CI 0.93–1.61) for MA, NHB, and NHW, respectively, after adjusting for significant confounders. HRs for diagnosed and undiagnosed diabetes were similar to those for diagnosed diabetes alone. Pre-diabetes was not significantly related to fracture risk, however. Compared to those without diabetes, adjusted HRs for those with pre-diabetes were 1.42 (95% CI 0.72–2.81), and 1.20 (95% CI 0.96–1.51) for MA and NHW, respectively. There were insufficient fracture cases to examine detailed diabetes status in NHB.

CONCLUSIONS—The diabetes-fracture relationship was stronger in MA and NHB. Pre-diabetes was not significantly associated with higher fracture risk, however.

[1]The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

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Keywords

Diabetes; hemoglobin A1c; fracture; NHANES

1. Introduction

Diabetes has been linked to an increased risk of fracture [1–14], but many aspects of this relationship remain unclear. For example, few previous studies have examined the diabetes-fracture relationship in race/ethnic groups other than Caucasians [4, 6, 7], despite the higher prevalence of diabetes in many nonwhite groups [15]. There are also conflicting data regarding the relationship between pre-diabetes and fracture risk, as it has been associated with a significantly lower risk in some [9, 11], but not all [5, 6, 12, 16] studies published to date.

We used linked Medicare and mortality data for respondents age 65 years and older from the third National Health and Nutrition Examination Survey (NHANES III) and NHANES 1999–2004 to address these data gaps. We examined differences in the diabetes-fracture relationship by race/ethnicity for three groups: non-Hispanic whites (NHW), non-Hispanic blacks (NHB), and Mexican Americans (MA). We also assessed the relationship between pre-diabetes and fracture risk after using data on diagnosed diabetes and whole blood hemoglobin A_{1c} (A1C) to classify respondents as having diabetes, pre-diabetes, or no diabetes. Finally, we examined the relationship by diagnosed diabetes without regard to A1C values.

2. Research Design and Methods

2.1 Sample

The baseline data for this study came from NHANES III (1988–1994) and NHANES 1999–2004, which were conducted by the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention, to assess the health and nutritional status of a large representative sample of the non-institutionalized, civilian population of the U.S. All procedures in each NHANES were approved by the NCHS Ethics Review Board, and written informed consent was obtained from all subjects [17, 18]. In each NHANES, data were collected via household interviews and direct standardized physical examinations conducted in specially equipped mobile examination centers [17, 18].

NHANES III and NHANES 1999–2004 were designed to provide reliable estimates for three race/ethnic groups: NHW, NHB, and MA. Race and ethnicity were self-reported in both surveys.

Both surveys were linked with mortality files created by NCHS and with Medicare enrollment and claims records in order to have a longitudinal follow-up of the survey participants. Vital status of study participants through 2007 was determined from the restricted access versions of the NHANES III and NHANES 1999–2004 Linked Mortality Files [19].

Medicare enrollment and utilization data were available for NHANES respondents who agreed to provide personal identification [19]. Medicare claims data were provided from respondents who participated in fee-for-service care only from 1991 through 2007 for NHANES III and for 1999–2007 for NHANES 1999–2004. A list of the Medicare files used in the present study is provided in Supplementary Appendix 1.

The analytic sample in this study was restricted to respondents ages 65 years and older at the time of their NHANES interview at baseline because Medicare provides comprehensive health care for roughly 98% of the US population in this age range. Table A in Supplementary Appendix 2 shows the number of persons excluded from the analytic sample and reason for exclusion for each survey. After excluding a total of 2274 individuals, 2978 (57%) of the original 5252 eligible interviewed individuals from NHANES III were included in the final analytic sample. After excluding a total of 2295 individuals, 2054 (47%) of the original 4349 eligible interviewed individuals from NHANES 1999–2004 were included in the final analytic sample. Approximately 18% of the eligible interviewed sample from both surveys was excluded because they did not receive physical examinations; this nonresponse was addressed by inclusion of nonresponse adjustments in the creation of sample weights for the examined sample. Roughly 13% of the eligible sample was excluded due to prior fracture at baseline. A relatively large number of respondents in NHANES 1999–2004 also were excluded because they were either ineligible for Medicare linkage[2] (10% excluded) or were enrolled in an HMO at baseline (12% excluded). Descriptive characteristics and risk factors were compared between the analytic sample and excluded respondents to assess possible nonresponse bias. The excluded respondents were older, more likely to be women, had higher body mass index (BMI), and self-rated their health as fair or poor than respondents who were included. There were no differences in self-reported diabetes diagnosis between included and excluded respondents, however.

2.2 Fracture case identification

Respondents with fractures at skeletal sites other than the skull were identified using an approach based on previously published methods [20–22]. Skull fractures were not included since they are unlikely to be due to osteoporosis [23]. Cases were defined using relevant International Classification of Disease (ICD), Healthcare Common Procedure Coding System (HCPCS) or Current Procedural Terminology (CPT) codes for the years 1991–2007 [24, 25]. Respondents with codes indicating care of previous fracture or other bone diseases, neoplasm or hip arthroplasty for arthritis were excluded from the analyses. Details regarding the definition of cases from Medicare records, including the specific codes, are provided in Supplementary Appendix 1 or have been published previously [26]. Cause of death information from the NHANES Linked Mortality Files was also used to identify hip fracture cases. Specifically, decedents with an ICD-9 code 820 or ICD-10 code S72.0–S72.2 listed anywhere on the death certificate were defined as hip fracture cases.

[2]See Table A in Supplement 2 for ineligibility criteria.

2.3 Variables

2.3.1 Diabetes status—Diabetes status was based on self-reported physician's diagnosis of diabetes and on A1C levels in the main analyses in the present study. A1C was measured at the University of Missouri-Columbia in both surveys using high-performance liquid chromatography performed on instruments certified by the National Glycohemoglobin Standardization Program [27, 28]. A1C results were standardized to the reference method used for the Diabetes Control and Complications Trial [29]. Fasting plasma glucose (FPG) was used to define diabetes for a sensitivity analysis in non-Hispanic whites only because it was only available for a subsample whose blood was drawn in the morning, and there were insufficient fracture cases in this subsample to permit analyses in the other race/ethnic groups. Plasma glucose was measured at the University of Missouri-Columbia in both surveys using the enzyme hexokinase [27, 28].

Two definitions of diabetes status were used when examining fracture risk. Diagnosed diabetes (yes v. no) was based on the self-reported questionnaire item only. Women who reported diagnosis of diabetes during pregnancy only were not considered to have diagnosed diabetes. The more detailed definition of diabetes status used in the main analyses combined self-reported diagnosis and A1C values as follows: a) diabetes (diagnosed and undiagnosed): self-reported diagnosis or A1C ≥ 6.5%; b) prediabetes: no self-reported diagnosis and A1C between 5.7%–6.4%; c) no diabetes: no self-reported diagnosis and A1C < 5.7%. The detailed definition used in the sensitivity analysis based on FPG used the following criteria: a) diabetes: self-reported diagnosis or FPG ≥ 126 mg/dL; b) prediabetes: no self-reported diagnosis and FPG between 100–125 mg/dL; c) no diabetes: no self-reported diagnosis and FPG < 100 mg/dL. The sensitivity analyses were limited to NHW whose blood was drawn in the morning after fasting between 8–24 hours.

Some additional diabetes-related variables were explored to assess their role in the observed race/ethnic differences in the diabetes-fracture relationship. Undiagnosed diabetes was defined as having A1C ≥ 6.5% but no self-reported diabetes. Lower glycemic level was defined for those with a diabetes diagnosis as having A1C < 7.0% [30, 31]. Other variables related to diabetes status were obtained by interview and included self-reported age at diagnosis, duration of diabetes, and diabetes treatment. Duration of diabetes was calculated by subtracting age at diagnosis from age at baseline. Diabetes treatment was based on questionnaire items regarding current diabetes medication use. Responses were categories as insulin only, oral medications only, insulin plus oral medication, and neither insulin or oral medication.

2.3.2 Confounding or exclusion variables—Only variables that were measured comparably in the two surveys were used. Variables that were measured during the physical examination included body weight and height, which were used to calculate body mass index (BMI, equal to body weight (kilograms) divided by height (meters squared). Variables obtained by interview at baseline included age, self-reported race-ethnicity, self-reported hip, wrist or spine fracture, self-reported lower extremity amputations, smoking status (ever vs never), self-reported physical activity level compared to others of the same age and sex (same, higher, lower), self-rated health status (excellent/very good/good versus fair/poor),

maternal history of hip fracture, hospital stays in the past year (none versus ≥ 1), chronic conditions (self-reported diagnosis of heart attack, congestive heart failure, stroke, emphysema, or cancer), doctor visits in the past year (none, 1–3, ≥4), time since last doctor visit (< 1 year versus ≥ 1 year or never), education (< 12 years, 12 years, > 12 years), alcohol use (consume ≥ 3 drinks versus < 3 drinks per drinking occasion), current glucocorticoid use, and poverty income ratio. Poverty income ratio is based on the number of family members and the annual family income and is calculated using poverty thresholds from the US Census Bureau.

2.4 Statistical Analysis

All analyses were performed using SAS 9.3 (SAS Institute, Cary NC) and SUDAAN software (Research Triangle Institute, Research Triangle Park, NC) for analysis of data from complex sample surveys. Descriptive characteristics and risk factors at baseline were compared between fracture cases and non-cases using linear and log linear regression or chi-square analyses. Cox proportional hazards models were used to model time to event and to calculate estimates of the hazards ratio (HR) for fracture by diabetes status. For fracture cases, length of follow-up was calculated as the time from date of examination to date of diagnosis or procedure for the fractures identified by Medicare records or date of death for hip fractures identified by death certificates but not by Medicare records. For non-fracture cases, follow-up time was calculated as time from baseline exam to date of death for decedents, date of entry into managed care for those who enrolled in a Medicare managed care program after their baseline examination, or end of follow-up (December 31, 2007) for all other respondents.

To assess the validity of pooling results for NHANES III and NHANES 1999–2004, a survey-by-diabetes interaction term was included in Cox models applied to the pooled sample from the two surveys. This interaction was not significant for either diagnosed diabetes ($p=0.69$) or detailed diabetes status ($p=0.26$), which indicates that the relationship between diabetes and fracture risk did not differ in the two surveys.

Secondary analyses were performed to assess the effect of adjusting the sample weights for nonresponse due to incomplete linkage or non-matches with Medicare data. Specifically, PROC WTADJUST was used to calculate sample weights that were adjusted for nonresponse in the Medicare linkage and results were compared with those obtained when the publicly-released sample weights that had not been adjusted for this nonresponse were used. Results were similar for both sets of sample weights, so only those based on the publicly-released sample weights are presented.

3. Results

A total of 750 non-skull fracture cases were identified in the analytic sample used in the present study. The distribution of fracture cases by skeletal site is shown in Table B in Supplementary Appendix 2. The four most common fractures were hip fracture (n=298), radius (n=122), tibia and fibula (n=67), and humerus (n=57). Baseline characteristics of non-skull fracture cases versus non-cases are compared in Table 1. Fracture cases were older, had lower BMI, more likely to be white, and female than non-cases. They were more likely

to report similar physical activity levels as others of the same age and sex, but less likely to smoke and to report at least one hospital stay in the past year. None of the other baseline variables differed significantly by fracture status at baseline. Mean follow-up time was 6.7 years (range 0.01—19.1 years) and mean age at fracture was 80.3 years.

The prevalence of diagnosed diabetes was 15% (n=897). The vast majority of these individuals were likely to have type 2 diabetes: only 27, or approximately 3%, of individuals with diagnosed diabetes met criteria consistent with type 1 diabetes (e.g., (e.g., reported a diabetes diagnosis before age 40 years and who currently used insulin only). Study results did not differ when these 27 individuals were excluded from the analytic sample, so they were retained. Nonetheless, study results essentially pertain to Type 2 diabetes.

Differences in the relationship between diabetes and fracture risk by age, sex, and race/ethnicity were tested by including interaction terms in a single Cox model. The age-by-diabetes and sex-by- diabetes interaction terms were not significant, but race/ethnicity-by-diabetes interaction term was significant ($p<0.05$), so all subsequent analyses were performed separately by race/ethnicity.

Hazard ratios for any non-skull fracture by diabetes status and race/ethnicity are shown in Table 2 before and after adjusting for the significant risk factors identified in Table 1. NHB or MA with diagnosed diabetes were significantly more likely to experience a non-skull fracture than NHB or MA without a diabetes diagnosis before and after adjusting for several other significant fracture risk factors. Risk was approximately 1.9 times higher in NHB and 2.3–2.4 times higher in MA. Non-skull fracture risk in NHW did not differ significantly by diabetes diagnosis status, however.

Hip fracture risk in NHW also did not differ significantly by diabetes diagnosis status (HR adjusted for age, sex, and survey =1.35, 95% CI 0.82, 2.22; n=222 hip fractures). There were insufficient hip fracture cases to permit analysis in NHB or MA.

HRs for non-skull fractures by detailed diabetes status are also shown in Table 2 for NHW and MA; there were insufficient non-skull fracture cases in NHB to permit this analysis. MA with diagnosed diabetes or elevated A1C were 2.2–2.7 times more likely to fracture than those without diabetes before and after adjusting for significant confounders. Risk in MA with pre-diabetes did not differ from risk in MA without diabetes, however. Among NHW, risk did not differ by detailed diabetes status.

The sensitivity analyses to compare HRs for non-skull fracture by detailed diabetes status using A1C or FPG criteria in NHW from the morning fasting subsample (n= 1305; 223 fractures) revealed similar results. Compared to NHW without diabetes, the HR for NHW with diabetes was 1.21 (95% CI 0.79–1.85) when based on AIC and 1.20 (95% CI 0.94–1.88) when based on FPG. Results for NHW with pre-diabetes were 1.02 (95% CI 0.77–1.34) and 1.10 (95% CI 0.82–1.33) based on A1C and FPG, respectively.

To explore possible reasons for race/ethnic differences in fracture risk by diabetes, the risk factors that had differed significantly by fracture status, as well as the proportion with incident non-skull fractures, were compared by diabetes status separately by race/ethnicity

(Table 3). Differences in these relationships between race/ethnic groups were tested by including race-by-risk factor interaction terms in log linear models (Table 3). None of the interaction terms for the risk factors were statistically significant, which indicates that the relationship between diabetes and these risk factors did not differ by race/ethnicity. However, there was a significant interaction between race and diabetes for incident non-skull fracture. When compared to those without diabetes, fewer NHW with diabetes had incident non-skull fractures, while the converse was true for NHB and MA. This finding is consistent with the lower HRs for fracture risk by diabetes status observed in NHW than in NHB or MA.

Selected characteristics of those with diabetes were also compared by race/ethnicity (Table 3). Characteristics in those with diabetes that differed significantly between race/ethnic groups included age at diabetes diagnosis (NHW > NHB and MA), duration of diabetes (NHB > NHW), and the proportion with undiagnosed diabetes (NHB > NHW and MA). Finally, type of diabetes treatment differed by race/ethnicity. Compared to NHW, NHB with diabetes were more likely to use insulin, whereas MA were more likely to use oral medication.

4. Discussion

The association between fracture risk and diabetes differed significantly by race/ethnicity. Among NHB and MA, risk was 1.9–2.4 times higher in those with diabetes than in those without diabetes even after adjusting for several confounders. In contrast, risk in NHW with diabetes was only 1.2 times higher than among those without diabetes, and was not statistically significant. Other studies in whites have reported a similar modest increase in all-fracture risk. The risk estimate was significant in several [2, 6, 7, 9, 10, 16], but not all [5, 8], of these studies.

Few studies have examined the diabetes-fracture risk relationship in a multi-race/ethnic cohort. Our results are consistent with those from the Women's Health Initiative Observational Study [7], where the risk of any fracture was somewhat higher in NHB women with diabetes (HR=1.33) than in NHW women (HR=1.18). However, no interaction between diabetes and fracture risk by race (white versus black) was observed in the Health ABC cohort [6]. Differences in the age range of the participants or methods to define diabetes and fracture outcomes could potentially account for these different results. To our knowledge, only one previous study has examined fracture risk by diabetes in MA [4]. Hip fracture risk was significantly higher in MA with diabetes than in MA without diabetes, but data for non-Hispanics were not available for comparison.

The reasons for a stronger relationship between diabetes and fracture in NHB and MA than in NHW are not clear. One possible explanation for this phenomenon is the higher absolute fracture risk in whites compared to blacks or Hispanics [32], which could act to attenuate the magnitude of relative effect estimates of fracture risk when comparing persons with a risk factor to persons without it. In the present study, the proportion of incident non-skull fractures was significantly higher among NHW without diabetes than in NHW with diabetes, which is consistent with this possibility. There were also some differences in

selected characteristics in those with diabetes that were consistent with higher fracture risk in NHB. For example, the proportion with undiagnosed diabetes, defined as A1C ≥ 6.5% in those without diagnosed diabetes, was significantly higher in NHB than in NHW. NHB with diabetes also differed significantly from NHW with diabetes on two other characteristics linked with increased fracture risk: longer diabetes duration [13, 14], and use of insulin [2, 8, 10, 16].

Other studies have found race/ethnic differences in the relationship between diabetes and non-skeletal risk factors or health outcomes. For example, NHB and some South Asian groups appear to be at risk of developing diabetes at a lower BMI than whites [33], and NHB may be at risk of developing retinopathy at a lower A1C level than whites [34]. NHB and MA with diabetes also appear to have higher risk of mortality, end-stage renal disease, diabetes-related amputations, and retinopathy than NHW [34, 35, 36–38]. The mechanisms underlying these race/ethnic differences are not clear, but could include physiological, socioeconomic, and health care access factors [36, 37]. In the present study, all study respondents were Medicare participants, which may have reduced the impact of race/ethnic differences in diabetes control due to health care access [31]. The lack of a significant race/ethnic difference in the proportion of diabetic persons with lower glycemic levels in the present study is consistent with this possibility.

The relationship between pre-diabetes and fracture risk has not been examined by race/ethnicity previously to our knowledge. In the present study, HRs for fracture in NHW or MA with pre-diabetes, although above 1.00, were not statistically significant. Previous studies of impaired glucose tolerance or impaired fasting glucose have found either a reduced fracture risk [5, 9, 11] or no significant increase in risk [6, 12, 16]. Differences in the approaches used to define pre-diabetes may partially explain these variation in results, since use of different indicators to define pre-diabetes may identify a somewhat different group of individuals with the condition [39].

Study limitations include the potential impact of time trends in diabetes prevalence, complications, and treatment during the study period [30, 40]. However, the survey-by-diabetes interaction term was not significant, which indicates that the relationship between diabetes and fracture was similar in those assessed in 1988–1994 versus 1999–2004. Another limitation was the inability to use FPG to define detailed categories of diabetes in all race/ethnic groups. Results of the sensitivity analyses performed in NHW revealed a similar diabetes-fracture relationship for both indicators. However, it is unclear whether the relationship would be similar in NHB or MA, since the relationship between A1C and FPG appears to differ by race/ethnicity [39]. Finally, we were unable to assess whether results differed by type of diabetes, due to the very limited number (n=27) of individuals who met criteria consistent with type 1 diabetes (.e.g, reported a diabetes diagnosis before age 40 years and who currently used insulin only). An analysis of more recent NHANES data using slightly different criteria also found a very low prevalence of Type 1 diabetes in persons ages 60 years and older [41].

Other limitations include the inability to include some important intermediate variables that were not measured comparably in the two surveys, such as falls and bone mineral density, as

well as the limited number of fracture cases in MA and NHB. Fracture cases were identified using administrative records and were not verified by x-ray. However, Ray et al [20] reported positive predictive value and estimated sensitivity of 94% and 91%, respectively, for the combination of the fracture types examined in the present study other than spine fracture, which suggests the identified cases most likely suffered a fracture. Furthermore, misclassification of cases as non-cases would likely tend to attenuate the relative risk estimates observed between fracture risk and diabetes.

Results from the present study also apply only to the segment of the population ages 65 years and older that was not institutionalized at baseline and participated in Medicare fee-for-service programs because medical records for respondents who received care from managed care programs or in Veterans Administration facilities were not available. Exclusions for missing data or loss to follow-up were also made. The respondents who were excluded from the analytic sample were more likely to have some characteristics that are associated with greater fracture risk (older, female, and poorer health) than respondents who were included. Nonresponse to the baseline interview and examination is partially addressed by inclusion of nonresponse adjustments to the baseline sample weights, and additional adjustment to the weights to account for nonresponse to the Medicare linkage were evaluated in the present study to further address nonresponse. Nonetheless, although based on a cohort that was derived from nationally representative samples of the civilian, non-institutionalized population at baseline, results from the present study cannot be generalized to the entire adult population over age 65 years.

In summary, the relationship between diagnosed diabetes and fracture was stronger in NHB and MA than in NHW. However pre-diabetes was not linked with a significant increase in fracture risk in NHW or MA, the two groups for which this relationship could be examined. Given the higher prevalence of diabetes in nonwhite groups in the U.S. [15], more work is needed to better understand the basis of the race/ethnic difference in the diabetes-fracture relationship.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

No conflicts of interest relevant to this article were reported. ACL, MSE and SHS developed the study concept and analysis strategy. ACL conducted statistical analyses and wrote the manuscript. ACL, MSE and SHS participated in editing and revising the draft manuscript.

References

1. Janghorbani M, Van Dam RM, Willett WC, Hu FB. Systematic review of Type 1 and Type 2 diabetes mellitus and risk of fracture. American Journal of Epidemiology. 2007; 166:495–505. [PubMed: 17575306]
2. Schwartz AV, Sellmeyer DE, Ensrud KE, Cauley JA, Tabor HK, Schreiner PJ, Jamal SA, Black DM, Cummings SR. Older women with diabetes have an increased risk of fracture: a prospective study. J Clin Endocrinol Metab. 2001; 86:32–8. [PubMed: 11231974]

3. Ivers RQ, Cumming RG, Mitchell P, Peduto AJ. Diabetes and risk of fracture: The Blue Mountains Eye Study. Diabetes Care. 2001; 24:1198–203. [PubMed: 11423502]

4. Ottenbacher KJ, Ostir GV, Peek MK, Goodwin JS, Markides KS. Diabetes mellitus as a risk factor for hip fracture in mexican american older adults. J Gerontol A Biol Sci Med Sci. 2002; 57:M648–53. [PubMed: 12242318]

5. de Liefde II, van der Klift M, de Laet CE, van Daele PL, Hofman A, Pols HA. Bone mineral density and fracture risk in type-2 diabetes mellitus: the Rotterdam Study. Osteoporos Int. 2005; 16:1713–20. [PubMed: 15940395]

6. Strotmeyer ES, Cauley JA, Schwartz AV, Nevitt MC, Resnick HE, Bauer DC, Tylavsky FA, de Rekeneire N, Harris TB, Newman AB. Nontraumatic fracture risk with diabetes mellitus and impaired fasting glucose in older white and black adults: the health, aging, and body composition study. Arch Intern Med. 2005; 165:1612–7. [PubMed: 16043679]

7. Bonds DE, Larson JC, Schwartz AV, Strotmeyer ES, Robbins J, Rodriguez BL, Johnson KC, Margolis KL. Risk of fracture in women with type 2 diabetes: the Women's Health Initiative Observational Study. J Clin Endocrinol Metab. 2006; 91:3404–10. [PubMed: 16804043]

8. Ahmed LA, Joakimsen RM, Berntsen GK, Fonnebo V, Schirmer H. Diabetes mellitus and the risk of non-vertebral fractures: the Tromso study. Osteoporos Int. 2006; 17:495–500. [PubMed: 16283065]

9. Holmberg AH, Nilsson PM, Nilsson JA, Akesson K. The association between hyperglycemia and fracture risk in middle age. A prospective, population-based study of 22,444 men and 10,902 women. J Clin Endocrinol Metab. 2008; 93:815–22. [PubMed: 18073298]

10. Melton LJ 3rd, Leibson CL, Achenbach SJ, Therneau TM, Khosla S. Fracture risk in type 2 diabetes: update of a population-based study. J Bone Miner Res. 2008; 23:1334–42. [PubMed: 18348689]

11. Gagnon C, Magliano DJ, Ebeling PR, Dunstan DW, Zimmet PZ, Shaw JE, Daly RM. Association between hyperglycaemia and fracture risk in non-diabetic middle-aged and older Australians: a national, population-based prospective study (AusDiab). Osteoporos Int. 2010; 21:2067–74. [PubMed: 20306023]

12. Strotmeyer ES, Kamineni A, Cauley JA, Robbins JA, Fried LF, Siscovick DS, Harris TB, Newman AB. Potential explanatory factors for higher incident hip fracture risk in older diabetic adults. Curr Gerontol Geriatr Res. 2011; 2011:979270. [PubMed: 21837239]

13. Hothersall EJ, Livingstone SJ, Looker HC, Ahmed SF, Cleland S, Leese GP, Lindsay RS, McKnight J, Pearson D, Philip S, Wild SH, Colhoun HM. Contemporary risk of hip fracture in type 1 and type 2 diabetes: a national registry study from Scotland. J Bone Miner Res. 2014; 29:1054–60. [PubMed: 24155126]

14. Vestergaard P. Discrepancies in bone mineral density and fracture risk in patients with type 1 and type 2 diabetes--a meta-analysis. Osteoporos Int. 2007; 18:427–44. [PubMed: 17068657]

15. Centers for Disease Control and Prevention. Department of Health and Human Services. National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States 2014. Atlanta GA: Centers for Disease Control and Prevention; 2014.

16. Napoli N, Strotmeyer E, Ensrud K, Sellmeyer D, Bauer D, Hoffman A, Dam T-T, Barrett-Connor E, Palermo L, Orwoll E, Cummings S, Black D, Schwartz A. Fracture risk in diabetic elderly men: the MrOS study. Diabetologia. 2014:1–9.

17. Centers for Disease Control and Prevention National Center for Health Statistics. Department of Health and Human Services. Plan and Operation of the Third National Health and Nutrition Examination Survey, 1988–94. Hyattsville MD: Centers for Disease Control and Prevention, National Center for Health Statistics; 1994. p. 1-407.Series 1: Programs and collection procedures

18. Zipf, GCM.; Porter, KS.; Ostchega, Y.; Lewis, BG.; Dostal, J. National Health and Nutrition Examination Survey: Plan and Operations 1999–2010. Hyattsville MD: National Center for Health Statistics; 2013.

19. Centers for Disease Control and Prevention National Center for Health Statistics. NCHS Data Linkage Activities. Hyattsville MD: Centers for Disease Control and Prevention, National Center for Health Statistics; 2012.

20. Ray WA, Griffin MR, Fought RL, Adams ML. Identification of fractures from computerized Medicare files. Journal of Clinical Epidemiology. 1992; 45:703–714. [PubMed: 1619449]
21. Taylor AJ, Gary LC, Arora T, Becker DJ, Curtis JR, Kilgore ML, Morrisey MA, Saag KG, Matthews R, Yun H, Smith W, Delzell E. Clinical and demographic factors associated with fractures among older Americans. Osteoporosis International. 2011; 22:1263–1274. [PubMed: 20559818]
22. Curtis JR, Mudano AS, Solomon DH, Xi J, Melton E, Saag KG. Identification and validation of vertebral compression fractures using administrative claims data. Medical Care. 2009; 47:69–72. [PubMed: 19106733]
23. Warriner AH, Patkar NM, Curtis JR, Delzell E, Gary L, Kilgore M, Saag K. Which fractures are most attributable to osteoporosis? J Clin Epidemiol. 2011; 64:46–53. [PubMed: 21130353]
24. American Medical Association. CPT (Current Procedural Terminology) Assistant Archives 1990–2009. Chicago IL: American Medical Association; 2010.
25. National Center for Health Statistics. Conversion Table of New ICD-9-CM Codes. National Center for Health Statistics; 2010. http://www.cdc.gov/nchs/data/icd/ICD-9-CM_FY14_CNVTBL_Final.pdf
26. Looker AC. Serum 25-hydroxyvitamin D and risk of major osteoporotic fractures in older U.S. adults. J Bone Miner Res. 2013; 28:997–1006. [PubMed: 23184640]
27. Gunter, EWLB.; Kokickowski, SM. Centers for Disease Control NCHS. Laboratory methods used for the third National Health and Nutrition Examination Survey (NHANES III), 1988–1994. Centers for Disease Control, National Center for Health Statistics; 1996. http://www.cdc.gov/nchs/data/nhanes/nhanes3/cdrom/nchs/manuals/labman.pdf
28. National Center for Health Statistics. National Health and Nutrition Examination Survey Laboratory Methods 1999–2004. Hyattsville MD: Centers for Disease Control and Prevention National Center for Health Statistics; 2000.
29. Steffes M, Cleary P, Goldstein D, Little R, Wiedmeyer HM, Rohlfing C, England J, Bucksa J, Nowicki M. Hemoglobin A1c measurements over nearly two decades: sustaining comparable values throughout the Diabetes Control and Complications Trial and the Epidemiology of Diabetes Interventions and Complications study. Clin Chem. 2005; 51:753–8. [PubMed: 15684277]
30. Selvin E, Parrinello CM, Sacks DB, Coresh J. Trends in prevalence and control of diabetes in the United States, 1988–1994 and 1999–2010. Annals of Internal Medicine. 2014; 160:517–525. [PubMed: 24733192]
31. McWilliams JM, Meara E, Zaslavsky AM, Ayanian JZ. Differences in control of cardiovascular disease and diabetes by race, ethnicity, and education: U.S. trends from 1999 to 2006 and effects of medicare coverage. Ann Intern Med. 2009; 150:505–15. [PubMed: 19380852]
32. Dawson-Hughes B, Tosteson ANA, Melton LJ III, Baim S, Favus MJ, Khosla S, Lindsay RL. Implications of absolute fracture risk assessment for osteoporosis practice guidelines in the USA. Osteoporosis International. 2008; 19:449–458. [PubMed: 18292975]
33. Ntuk UE, Gill JMR, Mackay DF, Sattar N, Pell JP. Ethnic-specific obesity cuoffs for dabetes risk: cross-sectional study of 490,288 UK Biobank participants. Diabetes Care. 2014
34. Tsugawa Y, Mukamal KJ, Davis RB, Taylor WC, Wee CC. Should the hemoglobin A1c diagnostic cutoff differ between blacks and whites? A cross-sectional study. Ann Intern Med. 2012; 157:153–9. [PubMed: 22868832]
35. Harris MI, Klein R, Cowie CC, Rowland M, Byrd-Holt DD. Is the risk of diabetic retinopathy greater in non-Hispanic blacks and Mexican Americans than in non-Hispanic whites with type 2 diabetes?: A U.S. population study. Diabetes Care. 1998; 21:1230–1235. [PubMed: 9702425]
36. Hunt KJ, Gonzalez ME, Lopez R, Haffner SM, Stern MP, Gonzalez-Villalpando C. Diabetes is more lethal in Mexicans and Mexican-Americans compared to Non-Hispanic whites. Ann Epidemiol. 2011; 21:899–906. [PubMed: 21840730]
37. Lanting LC, Joung IMA, Mackenbach JP, Lamberts SWJ, Bootsma AH. Ethnic differences in mortality, end-stage complications, and quality of care among diabetic patients: A review. Diabetes Care. 2005; 28:2280–2288. [PubMed: 16123507]

38. Lavery LA, van Houtum WH, Ashry HR, Armstrong DG, Pugh JA. Diabetes-related lower-extremity amputations disproportionately affect Blacks and Mexican Americans. South Med J. 1999; 92:593–9. [PubMed: 10372853]

39. James C, Bullard KM, Rolka DB, Geiss LS, Williams DE, Cowie CC, Albright A, Gregg EW. Implications of alternative definitions of prediabetes for prevalence in U.S. adults Diabetes Care. 2011; 34:387–91. [PubMed: 21270196]

40. Gregg EW, Li Y, Wang J, Burrows NR, Ali MK, Rolka D, Williams DE, Geiss L. Changes in diabetes-related complications in the United States, 1990–2010. N Engl J Med. 2014; 370:1514–23. [PubMed: 24738668]

41. Menke A, Orchard TJ, Imperatore G, Bullard KM, Mayer-Davis E, Cowie CC. The prevalence of type 1 diabetes in the United States. Epidemiology. 2013; 24:773–4. [PubMed: 23903880]

Appendix 1 and 2 Supplementary Data

Supplementary data to this article can be found online.

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Table 1

Baseline risk factors by fracture status
Pooled NHANES III and NHANES 1999–2004 cohort age 65 years and older

	Any non-skull fracture						
	Yes			No			
	n	Mean or percent	SE	n	Mean or percent	SE	
Age (years)	728	74.8	0.26	4304	73.3	0.16	*
Body mass index (kg/m^2)	704	26.3	0.07	4192	27.4	0.11	*
Poverty Income Ratio	647	2.6	0.10	3874	2.8	0.07	
Age group							
65–79	451	73.1	1.65	3131	80.8	0.92	*
80+	277	26.9	1.65	1173	19.2	0.92	
Sex							
Men	258	28.5	1.92	2325	47.5	0.97	*
Women	470	71.5	1.92	1979	52.5	0.97	
Race/ethnicity							
Non-Hispanic white	548	91.3	1.00	2580	84.0	1.23	*
Non-Hispanic black	70	4.3	0.59	784	8.3	0.71	
Mexican American	95	1.9	0.40	791	2.5	0.47	
Other	15	2.5	0.73	149	5.2	0.82	
Physical activity compared to others of same age and sex							
More	321	44.8	2.26	1904	48.6	0.99	*
Less	96	11.1	1.34	659	13.8	0.61	
Same	285	44.2	2.36	1625	37.6	0.95	
Ever smoked							
Yes	322	45.1	2.64	2264	52.8	1.05	*
No	406	54.9	2.64	2036	47.2	1.05	
Self-rated health status							
Excellent/v. good/good	476	69.4	2.60	2848	72.3	0.90	
Fair/poor	251	30.6	2.60	1451	27.7	0.90	
Hospital stays in past year							

	Any non-skull fracture						
	Yes			No			
	n	Mean or percent	SE	n	Mean or percent	SE	
None	472	64.5	2.55	2302	50.2	1.78	*
One or more	254	35.5	2.55	1991	49.8	1.78	
Doctor visits in past year							
None	70	11.0	1.28	442	8.60	0.56	
1–3	285	41.1	2.53	1621	39.7	0.99	
>=4	368	47.9	2.72	2213	51.8	1.08	
Time since last doctor visit							
< 1 year	484	88.5	1.74	3077	90.9	0.60	
>= 1 year or never	57	11.5	1.74	368	9.1	0.60	
Chronic conditions[†]							
Yes	280	40.0	2.55	1667	39.9	1.07	
No	448	60.0	2.55	2637	60.1	1.07	
Maternal history hip fracture							
Yes	62	10.6	1.68	352	10.6	0.65	
No	637	89.4	1.68	3759	89.5	0.65	
Poverty status[‡]							
Poor	124	12.2	1.57	770	12.0	0.94	
Nonpoor	521	87.8	1.57	3096	88.0	0.94	
Years of education completed							
< 12	296	30.1	2.25	1810	29.0	1.46	
12	249	42.9	2.57	1414	38.6	1.27	
> 12	176	27.0	2.30	1058	32.4	1.20	
Consume 3+ alcohol drinks per occasion							
Yes	41	6.1	1.3	303	6.6	0.62	
No	621	93.9	1.3	3467	93.4	0.62	
Use glucocorticoids							
Yes	60	8.2	1.17	297	7.8	0.51	
No	658	91.9	1.17	3897	92.2	0.51	

SE=standard error

* $p < 0.05$ comparing within fracture status

† Self-reported diagnosis of heart attack, congestive heart failure, stroke, emphysema, or cancer.

‡ Poor = poverty income ratio < 1.00; nonpoor = poverty income ratio ≥1.00

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Table 2

Adjusted hazards ratios (HR) for non-skull fractures by diabetes and race/ethnicity
Pooled NHANES III and NHANES 1999–2004 cohort age 65 years and older

Diabetes		Base model*			Full model†		
Classification	n fractures	HR	LL	UL	HR	LL	UL
Diagnosed Diabetes							
Non-Hispanic white	517						
Yes	57	1.17	0.89	1.52	1.22	0.93	1.61
No	460	1.00	1.00	1.00	1.00	1.00	1.00
p value		0.25			0.18		
Non-Hispanic black	66						
Yes	18	1.86	1.05	3.30	1.87	1.02	3.40
No	48	1.00	1.00	1.00	1.00	1.00	1.00
p value		0.03			0.04		
Mexican American	79						
Yes	35	2.29	1.41	3.73	2.37	1.49	3.75
No	44	1.00	1.00	1.00	1.00	1.00	1.00
p value		0.001			0.0003		
Diabetes status‡							
Non-Hispanic white	517						
Diabetes	73	1.12	0.89	1.42	1.20	0.94	1.53
Pre-diabetes	154	1.17	0.93	1.47	1.20	0.96	1.51
No diabetes	290	1.00	1.00	1.00	1.00	1.00	1.00
p value		0.22			0.06		
Mexican American	79						
Diabetes	38	2.22	1.35	3.64	2.70	1.70	4.31
Pre-diabetes	20	1.14	0.55	2.36	1.42	0.72	2.81
No diabetes	21	1.00	1.00	1.00	1.00	1.00	1.00
p value		0.006			0.0003		

HR=hazards ratio; LL=lower limit of 95% confidence interval; UL=upper limit of 95% confidence interval

*Adjusted for age, sex and survey

† Adjusted for age, sex, survey, BMI, self-rated physical activity compared to others, hospital visits in past year, and smoking

‡ Diabetes=self-reported diagnosed diabetes OR A1C >=6.5%; Pre-diabetes=No self-reported diagnosed diabetes AND A1C 5.7–6.4%; No diabetes=No self-reported diagnosed diabetes AND A1C < 5.7%

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Table 3

Selected characteristics by race/ethnicity and diabetes status
Pooled NHANES III and NHANES 1999–2004 cohort age 65 years and older

	Non-Hispanic white		Non-Hispanic black		Mexican American		Race x characteristic interaction	Race main effect
Characteristic	**Mean or percent***	**SE**	**Mean or percent***	**SE**	**Mean or percent***	**SE**	**p value**	**p value**
By diabetes status:								
Sample size (n)								
Diagnosed diabetes	398	--	178	--	226	--	--	--
No diabetes	2554	--	631	--	601	--		
Incident non-skull fracture (%)								--
Diagnosed diabetes	13.6	1.87	10.7	2.49	16.1	3.13	0.03	
No diabetes	16.5	0.88	7.7	0.98	8.0	1.58		
Age at baseline (years)								
Diagnosed diabetes	73.3	0.32	73.1	0.52	71.5	0.50	0.65	--
No diabetes	73.7	0.18	73.0	0.35	72.1	0.30		
BMI (kg/m^2)								
Diagnosed diabetes	29.5	0.41	30.9	0.54	28.4	0.50	0.63	--
No diabetes	26.8	0.12	28.1	0.26	27.4	0.26		
Female (%)								
Diagnosed diabetes	55.3	2.91	63.5	3.77	56.5	4.00	0.21	--
No diabetes	54.9	0.89	56.7	2.03	48.3	2.29		
Ever smoked (%)								
Diagnosed diabetes	56.7	3.19	45.0	4.70	43.7	3.45	0.13	--
No diabetes	52.0	1.19	45.9	2.01	54.2	2.68		
Fair/poor health (%)								
Diagnosed diabetes	41.9	2.96	60.4	3.95	67.2	3.36	0.20	--
No diabetes	22.3	1.02	40.7	2.30	40.0	2.81		
Less physical activity than others of same age and sex (%)								
Diagnosed diabetes	21.9	2.21	28.8	4.13	26.7	2.99	0.93	--
No diabetes	10.1	0.69	17.4	1.79	16.2	1.49		

Characteristic	Non-Hispanic white		Non-Hispanic black		Mexican American		Race x characteristic interaction	Race main effect
	Mean or percent*	SE	Mean or percent*	SE	Mean or percent*	SE	p value	p value
One or more hospital stays in past year (%)								
Diagnosed diabetes	55.5	3.26	47.1	4.54	58.2	4.83	0.57	--
No diabetes	45.1	2.12	44.6	3.09	53.9	5.00		
Persons with diabetes only*:								
A1C (%)	7.3	0.12	7.4	0.15	7.6	0.17	--	0.37
Age at diabetes diagnosis (years)	59.6[a,b]	0.84	56.7[a]	1.18	56.9[b]	0.85	--	0.03
Duration of diagnosed diabetes (years)	13.7[a]	0.76	16.3[a]	1.13	14.6	0.86	--	0.05
Undiagnosed diabetes† (%)	25.4[a,b]	2.75	37.6[a,c]	3.93	18.2[b,c]	2.96	--	0.001
Lower glycemic level‡ (%)	49.3	3.05	49.6	4.15	57.0	3.71	--	0.22
Type of treatment (%)							--	
Insulin only	22.7[a,b]	2.39	38.3[a]	3.47	13.5[b]	3.29		0.001
Oral medication only	50.4	3.07	36.4	3.77	60.5	4.45		
Insulin and oral medication	6.6	1.48	8.1§	2.74§	8.2§	1.85§		
Neither insulin or oral medication	20.3	2.49	17.9	3.35	17.9	3.35		

SE=standard error

--Not applicable

*Means or percents sharing common letter superscripts differ significantly, $p<0.05$

†A1C ≥ 6.5% in those without diagnosed diabetes

‡Diagnosed diabetes with A1C < 7.0%

§may be statistically unreliable, percent/standard error > 30%.