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Changes of glucose levels precede dementia in African Americans with diabetes but not in Caucasians

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Abstract

INTRODUCTION—Changes in glucose levels may represent a powerful metabolic indicator for dementia in African Americans with diabetes. It is unclear whether these changes also occur in Caucasians.

METHODS—A secondary data analysis using electronic medical records from 5228 African Americans and Caucasians 65 years and older. Mixed effects models with repeated serum glucose measurements were used to compare changes in glucose levels between African Americans and Caucasian patients with and without incident dementia.

RESULTS—African Americans and Caucasians with diabetes had significantly different changes in glucose levels by dementia status ($p<0.0001$). African Americans experienced a significant decline in glucose levels before the dementia diagnosis (estimated glucose decline 1.3421 mg/dL

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per year, p<0.0001) than those who did not develop dementia. Caucasians with and without dementia showed stable glucose levels over time (p=0.3071).

DISCUSSION—Significant changes in glucose levels precede dementia in African American patients with diabetes but not in Caucasians.

Keywords

dementia; Alzheimer's disease; longitudinal risk factors; diabetes; glucose levels; African Americans; Caucasians; electronic medical records; early detection

1. Introduction

Type 2 diabetes is increasing in the United States particularly for African Americans [1, 2]. African Americans also have higher rates of diabetes complications and poorer glycemic control than Caucasians [3–5]. The reasons for these discrepancies are unclear. It has been suggested that a combination of socio-economic, clinical, health care and self-management factors may explain the greater severity in African Americans [5–8]. Metabolic differences, involving insulin resistance, have also been reported between African Americans and Caucasians [9, 10]. Type 2 diabetes, particularly in midlife, has been reported as a risk factor for cognitive decline [11–13] and for dementia but again the association appears to be stronger in African Americans, where dementia rates are also higher, as compared to Caucasians [3, 13–16].

The possible pathophysiological pathways explaining the relationship between diabetes and dementia remain uncertain. Insulin resistance associated with variations in cerebral glucose uptake has been implicated [17]. A previous study by Crane and colleagues suggested that the effect may be mediated through elevated blood glucose levels among individuals with or without diabetes [18]. There have been few reports on change or variability of glucose levels in the lengthy pre-dementia period. In a previous paper we reported that high glucose levels in African Americans with diabetes were followed by a significant decline in these levels before dementia diagnoses [19]. However, in participants without diabetes there was no difference in the changes of glucose levels between participants who developed incident dementia and those without dementia. These changes, we hypothesized, may represent a powerful pre-symptomatic metabolic indicator for dementia in people with diabetes. In order to determine whether a similar glucose trajectory can be seen in Caucasian patients with diabetes and to compare glucose trajectories prior to dementia diagnosis between African Americans and Caucasians, we analyzed data from a large cohort of both African Americans and Caucasians with diabetes attending a city-wide community health system using data from their electronic medical records. The purpose of this paper is to report on the results from this analysis.

2. Methods

2.1. Study Population

The study population was defined by patients who received care at Eskenazi Health Services (an urban health care system in Indianapolis, IN) from January 1, 1992 to December 31,

2014, had a diagnosis of diabetes, and were 65 years or older during that time frame (total number of patients: 10205). Data for these patients were obtained from electronic medical records (EMR) that include diagnoses, laboratory test results, and medication prescriptions. For each individual we retrieved serum glucose measures associated with outpatient visits, ICD-9 codes for diabetes, dementia, and common comorbidities (diabetes: 250.*; dementia: 290.*, 294.*, 331.*, 291.2, 310.0, 333.0, 797) and the use of diabetes medications classified as insulin only, oral antidiabetic medication only, or both insulin and oral medications. Height and weight measures were retrieved to calculate body mass index (BMI). In addition, ICD-9 codes from the EMR were used to define diabetes complications including hypoglycemia (hypoglycemia: 250.3, 250.8, 251.0, 251.1, 251.2, 270.3, 775.0, 775.6, 962.3). This analysis included individuals with a history of diabetes and who were either African American or Caucasian. Individuals belonging to other racial groups were excluded from the analyses (n=665). In addition, we excluded 484 patients with prevalent dementia and another nine patients with missing information on gender leaving 9074 eligible patients in the analysis.

2.2. Statistical Analyses

Our analysis focused on longitudinal change in glucose levels prior to dementia diagnosis and whether these changes differed between African American and Caucasian groups. Patients who had a diagnosis of dementia prior to their first glucose measures were excluded from the analysis. Since we were interested in the within-person changes in glucose levels prior to dementia diagnosis, only patients with at least two glucose measures before reaching study endpoints were included in this analysis. In order to minimize potential influences from outlier observations, we excluded glucose measures below the first percentile or above the 99^{th} percentile in the overall patient population.

To examine changes in glucose levels prior to dementia diagnosis, we aligned the timing of glucose measurements to an index time point defined as the date of the first diagnosis of dementia using ICD-9 codes for patients with dementia diagnosis or as date of death for those deceased without dementia or date of last clinic encounter in the EMR for surviving patients without dementia. Repeated serum glucose measures prior to index times were included as the dependent variable in this analysis. In all of our statistical models, index time was coded as time zero. For example, a participant with glucose measured at 1999 and a diagnosis of dementia in 2007 would have this measurement time coded as −8, indicating that this glucose measure was obtained 8 years prior to dementia diagnosis. Since we were interested in within-person changes in glucose levels, only patients with at least two glucose measures before index time were included in this analysis.

Demographic characteristics and comorbidities were compared using chi-square tests for categorical variables and analysis of variance (ANOVA) for continuous variables by both dementia status and racial group. Linear mixed effects models with unstructured variance covariance structure were used to explore three-way interactions among time, dementia status and race while adjusting for demographic variables including age, gender, BMI, and various medical conditions. A significant three-way interaction would indicate racial differences in changes of glucose levels between patients with dementia and those without.

Following a significant three-way interaction among time, dementia status and race, we used mixed effects models with repeated glucose measures in African Americans and Caucasians separately to further examine glucose change over time in each of the two racial groups.

Additional analyses were conducted to determine the robustness of our model results and to detect the subgroups that may account for the observed differences. We repeated the mixed effects models in several subsets of the study sample: by excluding individuals with cerebrovascular disease, those who were not taking antidiabetic medications, those with cerebrovascular disease and not taking anti-diabetic medications, and those with hypoglycemia. The statistical software SAS version 9.4 was used for the analyses.

3. Results

Out of the 9074 eligible patients for the analysis, we excluded 739 subjects who had no glucose measure or only one glucose measure, and 3107 patients for missing covariates (mostly BMI). A total of 5228 individuals with diabetes and at least two glucose measures were included in this analysis. There were 913 participants diagnosed with dementia during the course of the study. The median length of time from the first glucose measure to index time for African Americans was 13.8 years (interquartile range: 9.3, 17.8) and 12.2 years (interquartile range: 8.5, 16.5) for Caucasians. The average number of glucose measures per person was 2.2 per year and there was no difference between the two racial groups ($p=0.3628$). The number of glucose measures per person per year did not differ by dementia status within African Americans or Caucasians.

Demographic characteristics and comorbidities by dementia status within each racial group are presented in Table 1. In both African Americans and Caucasians, participants with dementia were significantly older, had lower BMI, and lower percentages of COPD, arthritis, cancer, hyperlipidemia, and renal disease, but higher percentages of depression and stroke.

In Table 2, we present results of the mixed effects model examining changes in glucose over time including a significant three-way interaction among time, dementia status, and race while adjusting for baseline age, gender, and BMI indicating significant differences in glucose change by dementia status in the two racial groups. While Caucasian participants with dementia showed similar and stable glucose levels over time compared to Caucasian participants without dementia (estimated glucose decline of 0.2729 mg/dL per year, $p=0.3071$), African American participants with dementia had a significant decline in glucose levels prior to dementia diagnosis compared to African American participants without dementia (estimated glucose decline 1.3421 mg/dL per year, $p<0.0001$). Estimated glucose trajectories from the mixed effects model in Table 2 are illustrated in Figure 1 for African Americans with dementia, African Americans without dementia, Caucasians with dementia and Caucasians without dementia. African American participants with incident dementia had significantly higher glucose levels at least two years before their dementia diagnosis than those without dementia ($p=0.0202$). In Caucasians, there were no significant changes in glucose levels in both participants with dementia and those without dementia ($p=0.3071$).

Results from adjusting for additional comorbid conditions were similar (see eTable 1 in Supplement).

In order to determine whether there were racial differences in diabetes severity and whether the difference in severity accounted for the differences in glucose trajectories, we compared the rates of diabetes complications among participants with and without dementia by race (Table 3). African Americans had higher total numbers of diabetic complications and also higher rates of having at least one complication than Caucasians. Using the total number of diabetic complications as a measure of diabetes severity, we added the number of complications and the interaction between the number of complications and time to the mixed model in Table 2 (eTable 2). Patients with more complications showed significantly greater decline in glucose levels over time. However, the difference in glucose trajectories between Caucasians and African Americans were similar to those reported in Table 2 even after adjusting for the number of diabetic complications.

To determine whether the racial difference in glucose change over time reported in Table 2 was related to cerebrovascular disease or poor glucose control, we conducted additional sensitivity analyses in certain subsets of the participant sample (Supplemental document). The same three-way interaction mixed effects model was used by excluding participants with cerebrovascular disease (eTable 3). We re-ran the model using participants who were on anti-diabetes medications (eTable 4) and another model by excluding participants with cerebrovascular disease and including only those on antidiabetic medications (eTable 5). We also fitted the mixed effects models by excluding participants with hypoglycemia (eTable 6). Racial differences in glucose change over time between participants with dementia and without remained in all the models in the sensitivity analyses suggesting that the observed racial differences were not explained by differences in cerebrovascular disease, anti-diabetic medication use or hypoglycemia. Comparisons of characteristics between patients included in the analyses and those excluded due to the lack of repeated glucose measures or missing covariates are also included (see eTable 7). Patients included in our analysis sample were more likely to be African American, female, younger, and had higher rates on a number of medical conditions than those excluded from our analysis.

A subset of 3176 patients also had repeated hemoglobin A1C measures. As hemoglobin A1c reflects a more integrated measure of blood sugar control than a single time point measure of blood glucose we also fitted mixed effects models with repeated hemoglobin A1C as the dependent variable to examine the three-way interaction among race, dementia group and time while adjusting for baseline age, gender and BMI in this subset. A significant three way interaction on hemoglobin A1C was seen with similar trajectories to those for glucose levels (see eTable 8).

4. Discussion

In this analysis of repeated glucose levels obtained up to 22 years before the diagnosis of dementia from a large cohort of patients with diabetes attending the Eskenazi health system clinics, we found a significant difference in changes in glucose levels by dementia status between African Americans and Caucasians. African Americans with diabetes who

developed dementia had significantly higher glucose levels than those who did not develop dementia and they also experienced a significant decline in their glucose levels in the years prior to the diagnosis of dementia compared to those who did not develop dementia. There was no significant difference in the change in glucose levels in the Caucasian population between participants who developed dementia and those who did not. The findings in the African American patients were similar to those we previously reported [19].

In our previous paper the difference in glucose trajectories between the dementia and non-dementia groups in African American participants weakened when those with cerebrovascular disease were excluded from the analysis, suggesting that the difference in glucose trajectories may be explained to a large extent by cerebrovascular disease. In this analysis, however, excluding participants with cerebrovascular disease made little difference to the results (supplement eTable 3). It has been reported that African Americans have not only higher rates of dementia than Caucasians but that the dementia was more likely to have a vascular component [14, 20, 21]. As a large percentage of dementia in elderly people is mixed in nature [22, 23] this vascular component may not have been identified in those with dementia diagnoses in this analysis particularly for African Americans. The African American participants also had higher rates of stroke than Caucasians but not significantly so ($p=0.1067$). Type 2 diabetes in African Americans without dementia has been associated with evidence of both brain macrovascular and microvascular disease including measures of cortical atrophy and white matter lesions [1] supporting our previous hypothesis that the pre-dementia decline in glucose levels may be a result of an early effect on brain metabolic homeostatic mechanisms during the dementing process [19].

In contrast there was no significant difference in the change in glucose levels in the Caucasian population between participants who developed dementia and those who did not. There are a number of possibilities to explain the African American/Caucasian differences in the association between glucose levels and incident dementia. It has been reported that diabetes is associated with higher rates of chronic complications in African Americans than in Caucasians and that glycemic control is also poorer among African Americans [3–5]. In our study the African American participants were more likely to have recorded hypoglycemia. They also had higher rates of retinopathy and nephropathy but not of vascular disease. Adjusting for diabetic complications however did not change the differences in glucose trajectories for either group (Supplement eTable 1). ICD-9 diagnoses of hypoglycemia were significantly more frequent in African Americans than in Caucasians and were significantly associated with the development of dementia in both groups. However when patients with diagnoses of hypoglycemia were excluded from the model the significant decline in glucose levels remained for the African Americans with dementia, albeit somewhat attenuated (see supplement eTable 6) indicating that rates of recorded hypoglycemia may explain some but not all of the differences between the groups.

Differences in diabetic treatment have been proposed as one explanation for the disparities in diabetes severity and glycemic control between African Americans and Caucasians [4]. In our study African American patients were more likely to be treated with insulin than Caucasians perhaps as a response to the higher glucose levels in African Americans. But adjusting for diabetic medication did not change the difference in glucose trajectories

between the two racial groups (see supplement eTables 4 and 5). Changes in the treatment of diabetes have occurred over the study period, particularly with the use of metformin which has been associated with better cognitive function [24, 25]. We intend to explore the possible implications of these therapy changes in a more detailed analysis of medication use.

Discrepancies in socio-economic, health care and self-management factors have also been proposed to explain the increased severity of diabetes in African Americans [5–8]. Unfortunately the records did not allow us to explore fully these factors. As in a previous paper which used this EMR system, we did include enrollment in Medicaid as a possible surrogate for socioeconomic status [26]. Although there was a higher percentage of African American on Medicaid than Caucasians, there was no difference between dementia groups. The Medicaid variable was not significant in any of the mixed effect models for repeated glucose or hemoglobin A1c. It should be noted that all the individuals were attendees at an urban safety net health care system.

Other possibilities have been suggested that may explain the differences in diabetic severity between African Americans and Caucasians including different pathophysiological mechanisms of insulin resistance and differences in insulin sensitivity [9, 27]. However these are beyond the scope of this analysis. One intriguing hypothesis which could explain the association between insulin resistance and pre-clinical brain regions controlling metabolism in dementia involves its effect on regional cerebral glucose uptake [17, 28]. It is worthy to note, however, that BMI levels (which are associated with insulin resistance) were relatively similar across ethnic groups in our cohorts.

In prior studies, high glucose levels in participants with diabetes have been associated with cognitive decline in middle-aged African Americans but not in Whites [3]. Crane et al. however reported that high glucose levels were associated with an increased risk for dementia among not only people with diabetes but also without, in a predominantly white population [18]. Our analysis focused on individuals with diabetes compared to less than 10% with diabetes in the Crane study. Our cohort also had a larger number of recorded co-morbidities than did the Crane cohort. The difference in results in regard to Caucasians may also be attributable to the differences in statistical methods used between the studies. Our studies examined how the change in glucose levels over time differed between participants who developed dementia and those who did not, while the Crane study did not explore the within-subject change in glucose levels. In our analysis glucose levels were recorded for an up to 22 year period before the diagnosis of dementia while the Crane study focused on glucose levels five years prior to dementia diagnosis.

In summary our results support the findings of our previous analysis that high glucose levels occurring many years before diagnosis in African Americans with diabetes are associated with an increased risk for dementia. As in our previous study, we also found that glucose levels decline as the participants progress to dementia, perhaps as a result of early disruption of the brain metabolic control mechanisms and representing therefore a pre-symptomatic metabolic indicator for future dementia in these patients. Caucasian participants with diabetes did not however show this relationship between glucose levels and dementia. The reason for this disparity is not clear at this time perhaps reflecting differences in glycemic

control as indicated by higher rates of hypoglycemia in African Americans with diabetes. Our findings certainly reinforce previous reports that clinicians need to be particularly vigilant in ensuring control of glucose levels in African American patients with diabetes. Further explorations of these racial differences may also lead to a greater understanding of the possible neuropathological and metabolic links between diabetes and dementia.

4.1 Strengths

The present study has a number of strengths, including the large number of participants and the lengthy follow up period. The use of EMR allowed access to repeated laboratory measures associated with outpatient visits. Although many research studies have measured blood glucose as part of a biomarker panel, few have had the resources to support the collection of repeated biomarker measures.

4.2 Limitations

This analysis was confined only to individuals with diabetes with repeated glucose measurements which was approximately 57.6% of the total sample. Our analysis sample included patients with a higher burden of comorbidities than those excluded because of missing comorbidities. An analysis conducted on a community based sample to confirm these results would be worthwhile. It was not possible from our database to distinguish between fasting and non-fasting glucose levels. Reports from previous studies have suggested that midlife rather than late life diabetes is a risk factor for dementia and that longer duration is associated with greater risk. Unfortunately our EMR system was unable to capture midlife data for all participants. The records did not allow us to explore fully some factors such as treatment compliance or socioeconomic issues which have also been identified factors which may explain variations in diabetic severity. It should be noted that all the individuals were attendees at an urban safety net health care system. One additional limitation lies in the use of clinical records rather than direct examination particularly for diagnoses such as dementia where dementia subtypes may not be clearly identified.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- There are racial differences in the relationship between glucose levels and dementia
- High glucose levels precede dementia in diabetic African Americans, not in Caucasians
- A significant decline in these levels occur in African Americans, not in Caucasians
- African American diabetics have higher rates of hypoglycemia
- The differences may reflect poorer levels of glycemic control in African Americans

Research in Context

Systematic Review

The author's review of the literature included PUBMED. Diabetes increases risk for dementia particularly in African Americans. High glucose levels have been identified as a possible mediating factor. There were few reports in the literature on change or variability in glucose levels in the pre-dementia period. The relevant citations are included in the manuscript.

Interpretation

The results confirm our previous findings of high glucose levels followed by decline occurring years prior to dementia in African Americans with diabetes but did not in Caucasians.

Future Directions

Our findings implicate possible mechanisms linking diabetes with dementia which should be explored further. 1) The association between diabetes and cerebral micro and macro vascular disease, which may be more common in African Americans. Cerebrovascular disease may affect brain regions associated with metabolic control. 2) The association may be stronger in African Americans because of differences in glycemic control or insulin sensitivity affecting regional cerebral glucose metabolism.

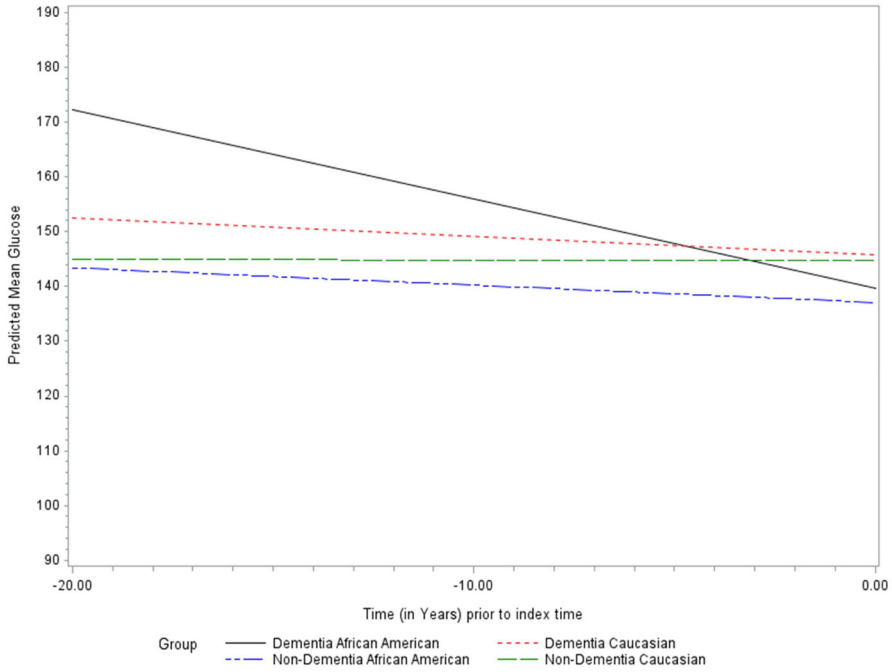

Figure 1.

Predicted mean glucose levels over time from mixed linear effects models for diabetes individuals with and without dementia diagnosis by race adjusting for baseline age, gender, and body mass index.

Table 1

Demographic characteristics of individuals by dementia status and race (all individuals with history of diabetes).

	Caucasian (n=2403)			African American (n=2825)			Combined (n=5228)		
Characteristics	**No Dementia (n=2021)**	**Dementia (n=382)**	**p-value**	**No Dementia (n=2294)**	**Dementia (n=531)**	**p-value**	**Caucasian (n=2403)**	**African American (n=2825)**	**p-value**
Age at baseline, mean (sd)	62.3(7)	64.6(7.6)	<.0001	61.8(7.3)	64.5(8.2)	<.0001	62.7(7.1)	62.3(7.6)	0.0583
Female, n (%)	1333 (66.0%)	262 (68.6%)	0.3186	1612 (70.2%)	383 (72.1%)	0.3970	1595 (66.4%)	1995(70.6%)	0.0010
On Medicaid, n (%)	1088(53.8%)	214(56%)	0.4316	1352(58.9%)	304(57.3%)	0.4772	1302(54.2%)	1656(58.6%)	0.0013
BMI, mean (sd)	32.8(6.8)	31.4(6.6)	0.0002	32.3(6.9)	31.6(6.6)	0.0336	32.6(6.8)	32.2(6.8)	0.0390
Coronary artery disease, n (%)	1098(54.3%)	223(58.4%)	0.1448	1075(46.9%)	229(43.1%)	0.1197	1321(55%)	1304(46.2%)	<.0001
Congestive heart failure, n (%)	955(47.3%)	184(48.2%)	0.7429	1008(43.9%)	212(39.9%)	0.0923	1139(47.4%)	1220(43.2%)	0.0023
Chronic obstructive pulmonary, n (%)	521(25.8%)	76(19.9%)	0.0147	397(17.3%)	58(10.9%)	0.0003	597(24.8%)	455(16.1%)	<.0001
Hypertension, n (%)	1927(95.3%)	355(92.9%)	0.0476	2251(98.1%)	524(98.7%)	0.3811	2282(95%)	2775(98.2%)	<.0001
Arthritis, n (%)	952(47.1%)	158(41.4%)	0.0389	1221(53.2%)	253(47.6%)	0.0204	1110(46.2%)	1474(52.2%)	<.0001
Cancer, n (%)	1429(70.7%)	238(62.3%)	0.0011	1561(68%)	304(57.3%)	<.0001	1667(69.4%)	1865(66%)	0.0098
Depression, n (%)	1001(49.5%)	240(62.8%)	<.0001	793(34.6%)	234(44.1%)	<.0001	1241(51.6%)	1027(36.4%)	<.0001
Hyperlipidemia, n (%)	1459(72.2%)	245(64.1%)	0.0015	1566(68.3%)	309(58.2%)	<.0001	1704(70.9%)	1875(66.4%)	0.0004
Liver disease, n (%)	184(9.1%)	30(7.9%)	0.4311	198(8.6%)	36(6.8%)	0.1630	214(8.9%)	234(8.3%)	0.4230
Renal Disease, n (%)	439(21.7%)	52(13.6%)	0.0003	657(28.6%)	101(19%)	<.0001	491(20.4%)	758(26.8%)	<.0001
Stroke, n (%)	226(11.2%)	67(17.5%)	0.0005	282(12.3%)	105(19.8%)	<.0001	293(12.2%)	387(13.7%)	0.1067
Diabetes Medications			0.0479			0.0004			<.0001
Insulin only, n (%)	149 (7.4%)	42 (11.0%)		246(10.7%)	69 (13.0%)		191 (8.0%)	315(11.2%)	
Oral only, n (%)	712 (35.2%)	121 (31.7%)		829 (36.1%)	158 (29.8%)		833(34.7%)	987(34.9%)	
Both Insulin and Oral, n (%)	611 (30.2%)	125 (32.7%)		708 (30.9%)	206 (38.8%)		736(30.6%)	914(32.4%)	
Not on any medications, n (%)	549 (27.2%)	94 (24.6%)		511 (22.3%)	98 (18.5%)		643(26.8%)	609(21.6%)	
Age at endpoint, mean (sd)	75(6.1)	75(6.8)	0.9938	75.6(6.3)	76(7.1)	0.1971	75.7(6.5)	75(6.2)	0.0001
Length of follow-up, median (interquartile range)	12.7 (8.7, 16.9)	10.3 (7.0, 13.7)	<.0001	14.2 (9.9, 18.3)	11.6 (8.0, 15.7)	<.0001	12.2 (8.5, 16.5)	13.8 (9.3, 17.8)	<.0001

	Caucasian (n=2403)			African American (n=2825)			Combined (n=5228)		
Characteristics	**No Dementia (n=2021)**	**Dementia (n=382)**	**p-value**	**No Dementia (n=2294)**	**Dementia (n=531)**	**p-value**	**Caucasian (n=2403)**	**African American (n=2825)**	**p-value**
Mean glucose measures per person per year (sd)	2.2(2.7)	2.3(2.6)	0.7540	2.2(3)	2.1(2.5)	0.6579	2.2(2.9)	2.3(2.6)	0.3628
Baseline Glucose, mean (sd)	145.7(67.2)	147.7(70.6)	0.5926	141.5(70.1)	155.7(76.5)	<.0001	146(67.7)	144.1(71.5)	0.3411
Average Glucose *, mean (sd)	144.1(36.4)	145.4(41.2)	0.5299	139.3(34.9)	150.4(40.5)	<.0001	144.3(37.2)	141.4(36.3)	0.0035

* mean glucose level per person during the follow-up period.

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Table 2

Results from mixed effects model with repeated glucose levels over time as the dependent variable in individuals with diabetes (n=5228).

Effect	Estimate	Standard Error	Pr > |t|
Female	−4.0056	1.3136	0.0023
Age at baseline	0.07330	0.08521	0.3896
African American	−7.3265	1.4539	<.0001
BMI	0.2819	0.07059	<.0001
Group			
demented	2.0318	1.9339	0.2934
Non demented	Ref	.	.
Time	−0.02115	0.09923	0.8312
Time*Group*Race			<.0001
Time*demented*African American	−1.6324	0.2166	<.0001
Time* demented *Caucasian	−0.2729	0.2672	0.3071
Time * non demented *African American	−0.2903	0.1228	0.0181
Time * non demented *Caucasian	Ref	.	.

[#]estimated glucose slope difference between African American with dementia and African Americans without dementia is $\beta=-1.3421$ and $p<0.0001$

Table 3

Comparisons of the rates of diabetic complications in individuals with diabetes (n=5228).

	Caucasian (n=2403)			African American (n=2825)			Combined (n=5228)		
Complications	**No Dementia (n=2021)**	**Dementia (n=382)**	**p-value**	**No Dementia (n=2294)**	**Dementia (n=531)**	**p-value**	**Caucasian (n=2403)**	**African American (n=2825)**	**p-value**
Retinopathy, n (%)	552(27.3%)	93(24.3%)	0.2300	844(36.8%)	209(39.4%)	0.2701	645(26.8%)	1053(37.3%)	<.0001
Nephropathy, n (%)	468(23.2%)	72(18.8%)	0.0643	683(29.8%)	129(24.3%)	0.0119	540(22.5%)	812(28.7%)	<.0001
Neuropathy, n (%)	667(33%)	129(33.8%)	0.7705	810(35.3%)	155(29.2%)	0.0074	796(33.1%)	965(34.2%)	0.4305
Cerebrovascular disease, n (%)	268(13.3%)	74(19.4%)	0.0017	338(14.7%)	114(21.5%)	0.0001	342(14.2%)	452(16%)	0.0759
Cardiovascular disease, n (%)	676(33.4%)	127(33.2%)	0.9386	653(28.5%)	120(22.6%)	0.0063	803(33.4%)	773(27.4%)	<.0001
Peripheral vascular disease, n (%)	525(26%)	106(27.7%)	0.4706	522(22.8%)	116(21.8%)	0.6515	631(26.3%)	638(22.6%)	0.0020
Metabolic disease, n (%)	0(0%)	1(0.3%)	0.0214	5(0.2%)	0(0%)	0.2816	1(0%)	5(0.2%)	0.1496
Hypoglycemia, n (%)	175(8.7%)	47(12.3%)	0.0241	303(13.2%)	109(20.5%)	<.0001	222(9.2%)	412(14.6%)	<.0001
Number of complications, mean (SD)	1.6(1.3)	1.6(1.4)	0.8467	1.7(1.4)	1.6(1.3)	0.1561	1.6(1.6)	1.7(1.4)	0.0079
Any complication, n (%)	1532(75.8%)	275(72%)	0.1134	1777(77.5%)	418(78.7%)	0.5308	1807(75.2%)	2195(77.7%)	0.0334