# Mortality Implications of Prediabetes and Diabetes in Older Adults

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## OBJECTIVE

**Diabetes in older age is heterogeneous, and the treatment approach varies by patient characteristics. We characterized the short-term all-cause and cardiovascular mortality risk associated with hyperglycemia in older age.**

## RESEARCH DESIGN AND METHODS

**We included 5,791 older adults in the Atherosclerosis Risk in Communities Study who attended visit 5 (2011–2013; ages 66–90). We compared prediabetes ($HbA_{1c}$ 5.7% to <6.5%), newly diagnosed diabetes ($HbA_{1c}$ ≥6.5%, prior diagnosis <1 year, or taking antihyperglycemic medications <1 year), short-duration diabetes (duration ≥1 year but <10 years [median]), and long-standing diabetes (duration ≥10 years). Outcomes were all-cause and cardiovascular mortality (median follow-up of 5.6 years).**

## RESULTS

**Participants were 58% female, and 24% had prevalent cardiovascular disease. All-cause mortality rates, per 1,000 person-years, were 21.2 (95% CI 18.7, 24.1) among those without diabetes, 23.7 (95% CI 20.8, 27.1) for those with prediabetes, 33.8 (95% CI 25.2, 45.5) among those with recently diagnosed diabetes, 29.6 (95% CI 25.0, 35.1) for those with diabetes of short duration, and 48.6 (95% CI 42.4, 55.7) for those with long-standing diabetes. Cardiovascular mortality rates, per 1,000 person-years, were 5.8 (95% CI 4.6, 7.4) among those without diabetes, 6.6 (95% CI 5.2, 8.5) for those with prediabetes, 11.5 (95% CI 7.0, 19.1) among those with recently diagnosed diabetes, 8.2 (95% CI 5.9, 11.3) for those with diabetes of short duration, and 17.3 (95% CI 13.8, 21.7) for those with long-standing diabetes. After adjustment for other cardiovascular risk factors, prediabetes and newly diagnosed diabetes were not significantly associated with a higher risk of all-cause mortality (hazard ratio [HR] 1.03 [95% CI 0.85, 1.23] and HR 1.31 [95% CI 0.94, 1.82], respectively) or cardiovascular mortality (HR 1.00 [95% CI 0.70, 1.43] and HR 1.35 [95% CI 0.74, 2.49], respectively). Excess mortality risk was primarily concentrated among those with long-standing diabetes (all-cause: HR 1.71 [95% CI 1.40, 2.10]; cardiovascular: HR 1.72 [95% CI 1.18, 2.51]).**

## CONCLUSIONS

**In older adults, long-standing diabetes has a substantial and independent effect on short-term mortality. Older individuals with prediabetes remained at low mortality risk over a median 5.6 years of follow-up.**


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Diabetes and prediabetes are established risk factors for cardiovascular events and mortality in middle-aged adults (1–3). Risks of microvascular and macrovascular complications in adults with diabetes increase with longer duration of disease (4), consistent with the accumulation of physiologic dysfunction associated with chronic hyperglycemia (5,6). Most of our knowledge of diabetes as a cardiovascular risk factor is derived from studies in middle-aged adults. Older adults comprise a clinically heterogeneous group (7–9), and the strength of the association between risk factors and clinical outcomes may differ in older age compared with middle age (10).

Recommendations for screening and diagnosis of diabetes in older adults are largely based on data from middle-aged populations. Guidelines from the American Diabetes Association recommend screening for prediabetes or diabetes at least every 3 years among all adults older than 45 and yearly screenings for individuals with prediabetes (11). Nonetheless, information on mortality risk in prediabetes and newly diagnosed diabetes in older age is lacking.

Emerging evidence suggests that diabetes, especially in older age, is heterogeneous (12). For example, we previously showed in a cross-sectional analysis of data from the National Health and Nutrition Examination Survey that older adults with diabetes diagnosed in later life appeared to have a comparable burden of macrovascular disease but a lower burden of microvascular outcomes compared with older adults with longstanding diabetes diagnosed in middle age (13). Evidence from the Swedish National Diabetes Registry further supports the hypothesis that the implications of hyperglycemia may differ in middle age compared with older age, as those diagnosed with diabetes at younger ages experienced a relatively higher mortality risk (14). However, the prognostic implications of hyperglycemia, especially prediabetes and undiagnosed diabetes, in older adults remains incompletely characterized and has been identified as by the American Diabetes Association as a pressing knowledge gap (15,16).

The objective of this study was to assess the prospective association of prediabetes, newly diagnosed diabetes, and longer-duration diabetes with short-term (~6 year) all-cause and cardiovascular mortality among older black and white participants in the prospective Atherosclerosis Risk in Communities (ARIC) Study.

## RESEARCH DESIGN AND METHODS

### Study Population

Our analyses included older adults, aged 66–90, who attended visit 5 (2011–2013) of the ARIC Study, fasted at least 8 h, and provided complete demographic, physical examination, and laboratory information. We excluded participants who self-reported race other than black or white or who were missing data on covariates (Supplementary Fig. 1). Of the 6,538 individuals who attended visit 5, our final analytic population included 5,791 participants. Details for the design and data collection in ARIC have been published previously (17). The ARIC protocols were approved by institutional review boards at each study site, and all participants provided written informed consent.

### Assessment of Diabetes Status at Baseline and Definitions

Diabetes status was defined based on the American Diabetes Association diagnostic criteria (11): prediabetes was defined as an $HbA_{1c}$ of 5.7–6.4% (39–46 mmol/mol) in adults without a history of diabetes, and newly diagnosed diabetes was defined as an $HbA_{1c} \geq 6.5\%$ (48 mmol/mol), prior physician diagnosis of diabetes, or antihyperglycemic medication use within the past year. We further categorized participants with diabetes with at least 1-year duration based on duration (above and below 10 years, the median duration among those with diabetes of at least 1-year duration at baseline in our study population). We used the time of the first report of diabetes (physician diagnosis or antihyperglycemic medication use) at a prior visit or during the semiannual telephone follow-up. Individuals with diabetes defined solely based on an elevated $HbA_{1c}$ at visit 5 were assigned a duration of 0 years ($n = 89$). In sensitivity analyses, we subdivided newly diagnosed diabetes into *1*) undiagnosed diabetes, defined as an $HbA_{1c} \geq 6.5\%$ (48 mmol/mol) among those without a diagnosis of diabetes or antihyperglycemic medication use within the past year, and *2*) diabetes of duration <1 year, defined as a diagnosis or antihyperglycemic medication use within the past year. We also conducted analyses with diabetes defined based on American Diabetes Association reference ranges for fasting blood glucose (prediabetes: 100–125 mg/dL; diabetes: ≥126 mg/dL, prior physician diagnosis, or antihyperglycemic medication use) (11). Finally, we considered a more sensitive definition of glycemic status based on an abnormality in $HbA_{1c}$ or fasting blood glucose, thus creating a more stringent normoglycemic reference group with normal $HbA_{1c}$ and normal fasting blood glucose. $HbA_{1c}$ was measured in EDTA whole blood using the Tosoh G7 Automated HPLC Analyzer (Tosoh Bioscience, San Francisco, CA). Glucose was measured in serum using the hexokinase method with the Beckman Coulter Olympus AU400e analyzer.

### Assessment of Cardiovascular Disease Status at Baseline and Definitions

Prevalent cardiovascular disease (CVD) was defined as a composite of prevalent coronary heart disease (CHD), heart failure (HF), or stroke at visit 5. Prevalent CHD was defined as an adjudicated definite or probable myocardial infarction, cardiac procedure, or serial electrocardiogram changes indicative of a myocardial infarction before visit 5. Prevalent HF was defined as any adjudicated HF event after 2005, any first position International Classification of Diseases, 9th revision code of 428.x before 2005, any physician report of HF, at least two reports of self-reported HF or use of HF medication, or any single self-reported HF with subsequent N-terminal prohormone brain natriuretic peptide (NT-proBNP) >125 pg/mL at ARIC visits 4 or 5. Prevalent stroke was defined as any adjudicated stroke event before visit 5 or self-reported baseline history of stroke at ARIC visit 1 (1987–1989).

### Covariate Assessment and Definitions

All covariates were measured at visit 5, with the exception of education attainment, which was assessed at visit 1 (1987–1989). We categorized education attainment as less than high school, high school or equivalent, or college equivalent or higher. BMI was calculated from measured height and weight and categorized as <25 kg/m$^2$, 25 to <30 kg/m$^2$, or ≥30 kg/m$^2$. Blood pressure

**Table 1—Baseline characteristics of participants according to diabetes status, the ARIC Study, visit 5 (2011–2013)**

| | No diabetes | Prediabetes | Newly diagnosed diabetes† | Short duration diabetes‡ | Long-standing diabetes§ |
|---|---|---|---|---|---|
| | ($n$ = 2,100) | ($n$ = 1,737) | ($n$ = 251) | ($n$ = 851) | ($n$ = 852) |
| Age, years | 75.4 (5.0) | 75.7 (5.2) | 75.7 (5.3) | 75.2 (5.0) | 75.9 (5.2) |
| Male | 42.1 | 39.8 | 47.8 | 41.5 | 43.7 |
| Race-center | | | | | |
| Minneapolis-whites | 36.4 | 31.5 | 32.3 | 23.0 | 20.7 |
| Jackson-blacks | 12.2 | 20.8 | 30.3 | 24.8 | 32.4 |
| Washington-whites | 26.4 | 22.1 | 20.7 | 34.2 | 27.0 |
| Forsyth-blacks | 0.7 | 2.1 | 1.6 | 1.5 | 2.9 |
| Forsyth-whites | 24.2 | 23.5 | 15.1 | 16.5 | 17.0 |
| Education attainment | | | | | |
| Less than high school | 9.1 | 13.1 | 20.7 | 18.4 | 21.4 |
| High school/GED | 55.7 | 57.3 | 60.2 | 58.5 | 54.7 |
| College graduate | 35.2 | 29.6 | 19.1 | 23.0 | 23.9 |
| Current smoker | | | | | |
| No | 91.6 | 90.9 | 90.8 | 91.4 | 90.7 |
| Yes | 5.2 | 6.2 | 8.8 | 5.3 | 5.0 |
| Unknown | 3.2 | 2.9 | 0.4 | 3.3 | 4.2 |
| BMI category, kg/m$^2$ | | | | | |
| <25 | 37.1 | 25.7 | 17.5 | 14.7 | 14.0 |
| 25–<30 | 39.6 | 41.5 | 39.4 | 37.1 | 36.9 |
| ≥30 | 23.3 | 32.8 | 43.0 | 48.2 | 49.2 |
| Family history of diabetes | 18.3 | 21.8 | 23.5 | 31.5 | 40.4 |
| $HbA_{1c}$, % | 5.4 (0.2) | 5.9 (0.2) | 6.3 (0.7) | 6.3 (0.9) | 7.0 (1.3) |
| Fasting blood glucose, mg/dL | 101.2 (11.3) | 107.2 (12.5) | 121.7 (22.3) | 127.1 (32.8) | 139.4 (44.9) |
| hs-CRP, mg/L | 1.7 (0.8–3.6) | 2.0 (1.0–4.4) | 2.7 (1.2–5.2) | 2.3 (1.1–4.8) | 2.3 (1.1–4.8) |
| Blood pressure, mmHg | | | | | |
| Systolic | 130.0 (18.0) | 130.2 (17.5) | 130.9 (18.1) | 129.4 (19.0) | 132.3 (19.6) |
| Diastolic | 66.8 (10.6) | 67.0 (10.5) | 66.2 (10.6) | 65.7 (11.0) | 64.3 (10.8) |
| Total cholesterol, mg/dL | 189.8 (41.4) | 184.7 (40.7) | 176.8 (38.4) | 168.1 (37.7) | 167.2 (44.8) |
| HDL-cholesterol, mg/dL | 55.7 (15.0) | 52.6 (13.0) | 48.4 (13.0) | 48.1 (12.3) | 47.5 (11.9) |
| eGFR, mL/min/1.73 m$^2$ | 67.6 (16.7) | 66.5 (18.0) | 65.6 (17.9) | 64.5 (18.3) | 59.4 (20.3) |
| Stage 3+ CKD | 30.3 | 35.7 | 37.1 | 42.1 | 51.3 |
| Prevalent CVD | 16.7 | 22.4 | 27.5 | 29.5 | 36.4 |
| Number of medications* | 8.4 (5.0) | 8.6 (4.6) | 9.2 (5.0) | 10.2 (4.9) | 11.1 (5.1) |
| Medication use | | | | | |
| Hypertension | 62.9 | 72.9 | 82.1 | 89.5 | 91.8 |
| Cholesterol-lowering | 41.9 | 57.3 | 61.0 | 70.2 | 72.8 |
| Diabetes | | | | | |
| Oral(s) only | — | — | 16.3 | 36.8 | 50.4 |
| Insulin only | — | — | 0.4 | 1.7 | 12.9 |
| Insulin and oral | — | — | 0.4 | 1.4 | 13.7 |
| Unknown | — | — | 0.0 | 0.3 | 0.6 |

Continuous variables are reported as the mean (SD) or median (interquartile range). Categorical variables are reported as percentages. CKD, chronic kidney disease. *4.3% missing. †Diabetes diagnosed at ARIC visit 5 or within 1 year of the visit 5 examination. ‡Median diabetes duration <10 years among those with diabetes duration ≥1 year. §Median diabetes duration ≥10 years among those with diabetes duration ≥1 year.

was measured in triplicate using an Omron HEM 907-XL. The average of the second and third measurements was used as the participant blood pressure. Total cholesterol and HDL-cholesterol were measured in plasma. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration creatinine-cystatin C equation (18). Stage 3+ chronic kidney disease was defined as an eGFR <60 mL/min/1.73 m$^2$. hs-CRP was assessed using the antibody-based assay using the Beckman Coulter Olympus analyzer. Participants were asked to bring all medications to their visit to determine the type and number of medications taken.

### Outcomes

Vital status of all ARIC participants was ascertained via semiannual telephone follow-up, state records, and linkage to the National Death Index. We defined cardiovascular death as an adjudicated fatal CHD, HF, or hemorrhagic or ischemic stroke, or ICD-10 codes from death certificates for cardiovascular causes (390–398, 401–404, 410–427, 430–438, 440–448, 451–459, I00-I78). At the time of analysis, follow-up was complete through 31 December 2017.

### Statistical Analyses

We compared baseline characteristics using ANOVA for continuous variables

and Pearson $\chi^2$ testing for categorical covariates. We calculated rates of all-cause and cardiovascular mortality (per 1,000 person-years of follow-up) overall and by diabetes status and compared them using ratios and differences. Cumulative mortality was calculated using the Kaplan-Meier approach. We used Cox regression models, with the Efron method to account for any ties in survival times (19), to estimate hazard ratios and their corresponding 95% CIs for the association of diabetes status with all-cause mortality. For analyses of cardiovascular mortality, deaths due to other causes were modeled as competing outcomes using the Fine and Gray approach (20). Measures of association were age-, sex-, and race-center–adjusted (model 1), with additional adjustment for education attainment, family history of diabetes (model 2), current smoking, BMI, systolic blood pressure, antihypertensive medication use, eGFR modeled using a linear spline with a knot at 60 mL/min/1.73 $m^2$, total cholesterol, HDL-cholesterol, cholesterol medication use, and log-transformed hs-CRP (model 3). Among those with diabetes at visit 5 based on $HbA_{1c}$ $\geq$6.5%, prior physician diagnosis, or antihyperglycemic medication use ($n$ = 1,324), the association of diabetes duration with all-cause and cardiovascular mortality outcomes was modeled continuously with restricted cubic splines with five knots at the 5th, 25th, 50th, 75th, and 95th percentiles. The reference group were participants without diabetes. All $P$ values were based on two-sided tests, and $P < 0.05$ was considered statistically significant. Interactions with sex, race, and prevalent CVD status at baseline were assessed using the $F$ test of the interaction terms in age-, sex-, and race-center–adjusted regression models. Because low $HbA_{1c}$ in adults without diabetes has been linked to elevated mortality risk (21,22), we conducted sensitivity analyses excluding participants without diagnosed diabetes and with an $HbA_{1c}$ <5% (31 mmol/mol; $n$ = 118). All analyses were conducted using Stata 15.0 software (StataCorp, College Station, TX).

## RESULTS

ARIC participants attending visit 5 were between 66 and 90 years old (mean, 75.5 years), 22% were black, 58% female, and 24% had prevalent CVD. Those with diabetes were more likely to be black, have uncontrolled hypertension, lower eGFR, and have prevalent CVD compared with those who were normoglycemic. Those with long-standing diabetes (≥10 years) were more likely to report insulin use compared with those with diabetes of shorter duration. On average, those with diabetes were taking more medications (approximately one additional medication among those with newly diagnosed diabetes, two among those with diabetes of short duration, and three among those with long-standing diabetes), compared with those without diabetes (Table 1). Compared with those with undiagnosed diabetes, ~26% of those with diabetes diagnosed within the past year reported antihyperglycemic medication use and were using an average of one more medication compared with those who were normoglycemic or with undiagnosed diabetes (Supplementary Table 1). Those with undiagnosed diabetes had a higher average $HbA_{1c}$ and higher total cholesterol compared with those with diabetes diagnosed in the past year (Supplementary Table 1).

Over a median of 5.6 years of follow-up, 849 deaths were observed, 254 of which were attributable to cardiovascular causes. Mortality rates were highest among participants with long-standing diabetes (Table 2). Crude and adjusted mortality rates among those with prediabetes were not statistically different from those without diabetes (Tables 2–4). After adjustment for traditional cardiovascular risk factors, diabetes and other cardiovascular risk factors, such as low eGFR, but not prediabetes, remained associated with all-cause and cardiovascular mortality (model 3) (Tables 3 and 4). When diabetes duration was modeled continuously, mortality risk increased with longer duration of disease (Supplementary Figs. 2 and 3).

These findings were generally robust to alternative definitions of diabetes status based on fasting blood glucose, either in isolation or in combination with $HbA_{1c}$ (Supplementary Table 2). However, in a more sensitive definition of hyperglycemia based on fasting blood glucose alone or in combination with

**Table 2—Incidence rates (95% CI) and 5-year cumulative incidence of all-cause and cardiovascular mortality associated with diabetes status**

| | Events | Incidence rate (per 1,000 person-years) | Incidence rate ratio | Incidence rate difference (per 1,000 person-years) | 5-year cumulative incidence, % |
|---|---|---|---|---|---|
| All-cause mortality | | | | | |
| Overall | 849 | 27.6 (25.8, 29.5) | | | 12.6 |
| No diabetes | 241 | 21.2 (18.7, 24.1) | 1 (Reference) | 0 (Reference) | 10.0 |
| Prediabetes | 222 | 23.7 (20.8, 27.1) | 1.1 (0.9, 1.3) | 2.5 (−1.6, 6.6) | 10.7 |
| Newly diagnosed diabetes | 44 | 33.8 (25.2, 45.5) | 1.6 (1.1, 2.2) | 12.6 (2.3, 23.0) | 15.5 |
| Short-duration diabetes | 134 | 29.6 (25.0, 35.1) | 1.4 (1.1, 1.7) | 8.4 (2.7, 14.1) | 13.0 |
| Long-duration diabetes | 208 | 48.6 (42.4, 55.7) | 2.3 (1.9, 2.8) | 27.4 (20.2, 34.5) | 21.5 |
| Cardiovascular mortality | | | | | |
| Overall | 254 | 8.2 (7.3, 9.3) | | | 3.9 |
| No diabetes | 66 | 5.8 (4.6, 7.4) | 1 (Reference) | 0 (Reference) | 2.7 |
| Prediabetes | 62 | 6.6 (5.2, 8.5) | 1.1 (0.8, 1.6) | 0.8 (−1.4, 3.0) | 3.3 |
| Newly diagnosed diabetes | 15 | 11.5 (7.0, 19.1) | 2.0 (1.1, 3.5) | 5.7 (−0.3, 11.7) | 6.3 |
| Short-duration diabetes | 37 | 8.2 (5.9, 11.3) | 1.4 (0.9, 2.1) | 2.4 (−0.6, 5.4) | 3.4 |
| Long-duration diabetes | 74 | 17.3 (13.8, 21.7) | 3.0 (2.1, 4.2) | 11.5 (7.3, 15.7) | 7.9 |

**Table 3—Hazard ratios (95% CI) for all-cause mortality associated with diabetes status and other cardiovascular risk factors at baseline**

| | Model 1 | Model 2 | Model 3 |
|---|---|---|---|
| Diabetes status | | | |
| No diabetes | 1 (Reference) | 1 (Reference) | 1 (Reference) |
| Prediabetes | 1.07 (0.89, 1.28) | 1.06 (0.88, 1.27) | 1.01 (0.84, 1.22) |
| Newly diagnosed diabetes | 1.48 (1.07, 2.05) | 1.41 (1.02, 1.96) | 1.31 (0.94, 1.82) |
| Short-duration diabetes | 1.43 (1.16, 1.77) | 1.39 (1.12, 1.73) | 1.26 (1.01, 1.57) |
| Long-standing diabetes | 2.17 (1.79, 2.62) | 2.09 (1.73, 2.54) | 1.71 (1.40, 2.10) |
| Age, per 5 years | 1.74 (1.63, 1.85) | 1.72 (1.61, 1.83) | 1.55 (1.45, 1.66) |
| Male | 1.44 (1.26, 1.65) | 1.47 (1.28, 1.68) | 1.44 (1.24, 1.68) |
| Race-center | | | |
| Minneapolis-whites | 1 (Reference) | 1 (Reference) | 1 (Reference) |
| Jackson-blacks | 1.26 (1.04, 1.53) | 1.17 (0.96, 1.44) | 1.17 (0.95, 1.39) |
| Washington-whites | 1.00 (0.83, 1.20) | 0.93 (0.77, 1.12) | 0.94 (0.79, 1.14) |
| Forsyth-blacks | 0.51 (0.24, 1.09) | 0.51 (0.24, 1.07) | 0.47 (0.22, 1.01) |
| Forsyth-whites | 0.95 (0.78, 1.16) | 0.95 (0.78, 1.15) | 0.84 (0.68, 1.03) |
| Family history of diabetes | — | 1.03 (0.88, 1.20) | 1.04 (0.89, 1.22) |
| Education attainment | | | |
| Less than high school | — | 1.47 (1.19, 1.82) | 1.32 (1.08, 1.63) |
| High school/GED | — | 1.19 (1.00, 1.40) | 1.20 (1.01, 1.42) |
| College graduate | — | 1 (Reference) | 1 (Reference) |
| Current smoking | — | — | 1.34 (1.17, 1.54) |
| Total cholesterol, per 100 mg/dL | — | — | 1.44 (0.92, 2.27) |
| HDL-cholesterol, per 100 mg/dL | — | — | 0.53 (0.31, 0.90) |
| Cholesterol-lowering medication use | | | 0.81 (0.69, 0.96) |
| Systolic blood pressure, per 10 mmHg | — | — | 1.00 (0.97, 1.04) |
| Hypertension medication use | — | — | 0.79 (0.65, 0.95) |
| eGFR, per 10 mL/min/1.73 $m^2$ | | | |
| $<$60 mL/min/1.73 $m^2$ | — | — | 0.77 (0.72, 0.82) |
| $>$60 mL/min/1.73 $m^2$ | — | — | 0.92 (0.85, 1.00) |
| hs-CRP, $\log_2$ mg/L | — | — | 1.13 (1.08, 1.18) |
| Prevalent CVD | — | — | 1.69 (1.45, 1.97) |

Model 1: age, sex, and race-center. Model 2: model 1 plus education attainment and family history of diabetes. Model 3: model 2 plus current smoking systolic blood pressure, total cholesterol, HDL-cholesterol, cholesterol-lowering medication use, log-transformed hs-CRP, eGFR with spline knot at 60 mL/min/1.73 $m^2$, hypertension medication use, and prevalent CVD.

$HbA_{1c}$, short-duration diabetes was not significantly associated with elevated mortality risk (Supplementary Tables 2 and 3). No statistically significant interactions were observed with sex, race, or baseline CVD status (all $P_{interaction} > 0.05$).

## CONCLUSIONS

Among older adults in our cohort with prediabetes, risks of all-cause and cardiovascular mortality were similar to adults with normoglycemia after accounting for cardiovascular risk factors. Excess short-term (median follow-up: 5.6 years) risk of mortality associated with hyperglycemia in older age was highest in those with long-standing diabetes. Our results are in contrast to studies in middle-aged adults that have demonstrated robust associations of prediabetes and undiagnosed diabetes with mortality (23–26).

Evidence for the health risks associated with hyperglycemia in older adults, particularly prediabetes, is limited. Most intervention trials in type 2 diabetes populations have excluded older adults (27). Observational studies have documented a higher absolute risk of complications in older adults with diabetes (9,28–30). However, older adults with diabetes comprise clinically distinct groups: those with long-standing diabetes (i.e., diagnosed in middle age) as well as those with recent-onset diabetes (9). Our findings suggest that when considering hyperglycemic status in older age, only adults with long-standing diabetes have a significantly elevated short-term risk for mortality independent of other cardiovascular risk factors. Our results are consistent with findings from the Diabetes and Aging Study and Framingham Heart Study, which observed higher risks of complications and mortality among those with longer duration of disease (4,31), and the Swedish National Diabetes Registry, which observed excess mortality risk associated with diabetes among those diagnosed at younger but not older ages (14). Diabetes duration has previously been associated with higher risk of end-organ complications, including retinopathy and kidney disease (32,33), highlighting the cumulative effects of hyperglycemia on microvascular dysfunction that may underlie the excess mortality risk observed among those with long-standing diabetes.

Our results support current guidelines from the American Diabetes Association that recommend focusing on lifestyle modification rather than initiation of pharmacologic intervention in older adults with prediabetes (34). The risks of adverse effects of glucose-lowering medications—particularly hypoglycemia—and polypharmacy are heightened in older adults (3,35,36). In this community-based cohort, participants with diagnosed diabetes, on average, were taking more total medications compared with those with prediabetes or normoglycemia. The lack of significant elevations in all-cause or cardiovascular mortality risk among older adults with prediabetes supports focusing on lifestyle modification and management of other cardiovascular risk factors for diabetes prevention in this age group. This is in contrast to recommendations in middle-aged adults for initiation of pharmacologic therapy for diabetes prevention with medications such as metformin (34). Prior work in the Diabetes Prevention Program supports the efficacy of intensive lifestyle modification, consisting of physical activity and weight loss, in older adults (37). Furthermore, those with newly diagnosed diabetes based on more sensitive screening definitions did not appear to be at an elevated short-term mortality risk, suggesting that intensive glycemic screening and use of highly sensitive diagnostic criteria, particularly for prediabetes, may not be efficient in older adults. Less aggressive treatment, including delaying pharmacologic therapy, may be appropriate for older patients with prediabetes or new-onset diabetes, especially those with shorter life expectancies.

Participants with diabetes diagnosed within the past year appeared to be

**Table 4—Subhazard ratios (95% CI) for cardiovascular mortality associated with diabetes status and other cardiovascular risk factors at baseline**

| | Model 1 | Model 2 | Model 3 |
|---|---|---|---|
| Diabetes status | | | |
| No diabetes | 1 (Reference) | 1 (Reference) | 1 (Reference) |
| Prediabetes | 1.06 (0.75, 1.51) | 1.05 (0.74, 1.50) | 1.00 (0.70, 1.43) |
| Newly diagnosed diabetes | 1.63 (0.91, 2.91) | 1.54 (0.85, 2.80) | 1.35 (0.74, 2.49) |
| Short-duration diabetes | 1.32 (0.88, 1.99) | 1.30 (0.85, 1.97) | 1.09 (0.72, 1.66) |
| Long-standing diabetes | 2.39 (1.68, 3.39) | 2.31 (1.60, 3.33) | 1.72 (1.18, 2.51) |
| Age, per 5 years | 1.76 (1.56, 1.99) | 1.73 (1.53, 1.95) | 1.49 (1.30, 1.70) |
| Male | 1.54 (1.20, 1.97) | 1.54 (1.20, 1.98) | 1.39 (1.05, 1.85) |
| Race-center | | | |
| Minneapolis-whites | 1 (Reference) | 1 (Reference) | 1 (Reference) |
| Jackson-blacks | 1.86 (1.31, 2.63) | 1.62 (1.12, 2.32) | 1.51 (1.03, 2.20) |
| Washington-whites | 1.10 (0.87, 1.54) | 1.00 (0.70, 1.43) | 0.99 (0.70, 1.42) |
| Forsyth-blacks | 0.28 (0.04, 2.03) | 0.26 (0.04, 1.54) | 0.26 (0.03, 1.93) |
| Forsyth-whites | 0.84 (0.57, 1.24) | 0.82 (0.56, 1.22) | 0.74 (0.49, 1.11) |
| Family history of diabetes | — | 1.00 (0.76, 1.33) | 1.02 (0.76, 1.36) |
| Education attainment | | | |
| Less than high school | — | 1.56 (1.06, 2.28) | 1.29 (0.87, 1.90) |
| High school/GED | — | 1.06 (0.78, 1.46) | 1.05 (0.76, 1.46) |
| College graduate | — | 1 (Reference) | 1 (Reference) |
| Current smoking | — | — | 1.16 (0.87, 1.54) |
| Total cholesterol, per 100 mg/dL | — | — | 1.16 (0.44, 3.04) |
| HDL-cholesterol, per 100 mg/dL | — | — | 0.83 (0.28, 2.44) |
| Cholesterol-lowering medication use | — | — | 0.77 (0.56, 1.04) |
| Systolic blood pressure, per 10 mmHg | — | — | 1.01 (0.94, 1.08) |
| Hypertension medication use | — | — | 0.81 (0.55, 1.19) |
| eGFR, per 10 mL/min/1.73 $m^2$ | | | |
| $<$60 mL/min/1.73 $m^2$ | — | — | 0.76 (0.68, 0.86) |
| $>$60 mL/min/1.73 $m^2$ | — | — | 0.91 (0.76, 1.07) |
| hs-CRP, $\log_2$ mg/L | — | — | 1.12 (1.04 1.21) |
| Prevalent CVD | — | — | 2.94 (2.23, 3.87) |

Model 1: age, sex, and race-center. Model 2: model 1 plus education attainment and family history of diabetes. Model 3: model 2 plus current smoking, systolic blood pressure, hypertension medication use, total cholesterol, HDL-cholesterol, cholesterol-lowering medication use, log-transformed hs-CRP, eGFR with spline knot at 60 mL/min/1.73 $m^2$, and prevalent CVD.

at a higher mortality risk compared with those with undiagnosed diabetes detected at the visit. There may be several possible explanations for this finding. First, it is possible that this is a result of "detection bias"; that is, those participants with other health conditions may have been more likely to receive laboratory screening, including blood glucose or $HbA_{1c}$ testing, leading to a diagnosis of diabetes. While speculative, another major difference between the undiagnosed and newly diagnosed diabetes groups was that more than one-quarter of those with newly diagnosed diabetes were initiated on a hyperglycemic medication (primarily oral antihyperglycemics). Whether this pharmacologic intervention is associated with increased mortality in this group is uncertain.

Our study has some limitations. First, the median follow-up of 5.6 years and number of recorded deaths limited our power to evaluate subgroup effects, especially for cardiovascular mortality. However, this time frame is clinically relevant for older populations. Second, despite adjustment for rigorously measured risk factors, including kidney function, there remains the possibility of residual confounding. Third, we did not have information on follow-up $HbA_{1c}$ or glucose measurements, limiting our ability to account for the time-varying nature of glycemic status. Finally, we are unable to account for any medication initiation or changes among participants after their study visit. Given the small sample size of those with newly diagnosed diabetes, we were unable to further stratify and compare those who initiated pharmacologic intervention with those who did not.

Strengths of the study include the large, community-based sample of older black and white adults with active follow-up for all-cause and cardiovascular mortality. The availability of measurements for both $HbA_{1c}$ and fasting blood glucose allowed us to assess the robustness of our findings to different definitions of prediabetes and diabetes status.

Diabetes in older adults is heterogeneous. Our results suggest that glycemic status alone is not effective at identifying older adults at highest risk of all-cause or cardiovascular mortality. Diabetes was associated with excess mortality, with the risk increasing with longer duration of disease. However, prediabetes was not independently associated with elevated cardiovascular or all-cause mortality over a median ~6-year window. Our results confirm that diabetes duration is important to consider in the care of older adults with diabetes and support focusing on lifestyle factors and cardiovascular risk management (such as smoking cessation or cholesterol control) to prevent diabetes and reduce mortality in older adults with prediabetes.

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