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Original Contribution

Sex Differences in the Association of Diabetes With Cardiovascular Disease Outcomes Among African-American and White Participants in the Atherosclerosis Risk in Communities Study

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A sex × diabetes interaction in cardiovascular disease (CVD) has been established among white persons; however, it is unknown whether this interaction occurs among African Americans. We hypothesized that there was a multiplicative sex × diabetes interaction for CVD among African Americans participating in the Atherosclerosis Risk in Communities Study (1987–2013). Race-specific Cox models were run in three stages: Stage 1 examined baseline diabetes status; stage 2 examined baseline diabetes status with the competing risk of non-CVD death; and stage 3 examined time-varying diabetes status with a competing risk of non-CVD death. There were 1,073 incident CVD events among 3,767 African Americans and 2,475 among 10,291 white persons. Among African Americans, in stage 1 analysis, the hazard ratio for women with diabetes was 2.3 (95% confidence interval (CI): 2.0, 2.7) compared with women without diabetes after adjustment for age, and the corresponding hazard ratio for men was 1.8 (95% CI: 1.5, 2.1) (*P* for interaction = 0.014). After full adjustment, the diabetes hazard ratio was attenuated to 2.0 (95% CI: 1.8, 2.3) among women and remained 1.8 (95% CI: 1.5, 2.1) for men (*P* for interaction = 0.058). A synergistic influence on CVD risk between being a black woman and having diabetes was consistent across stage 2 and stage 3 analyses, with marginally significant interaction, mirroring sex differences seen in whites.

African Americans; cardiovascular disease; diabetes; health disparities

Abbreviations: ARIC, Atherosclerosis Risk in Communities Study; CVD, cardiovascular disease.

Editor's note: *An invited commentary on this article appears on page 411, and the authors' response appears on page 415.*

An estimated 9.3% of the United States population has diabetes mellitus, primarily type 2 diabetes, and the prevalence is expected to continue increasing (1). Diabetes is an established risk factor for cardiovascular disease (CVD), and CVD is the leading cause of morbidity and mortality among people with diabetes (2). Further, diabetes—particularly chronic diabetes as opposed to recently diagnosed—is considered a coronary heart disease risk equivalent and used as a tool for prescribing statin treatment (3, 4). Women in the general population are at a lower absolute risk of a CVD event compared with men of similar age, although this advantage is reduced with age (5, 6). For women with diabetes, the CVD risk advantage is largely lost compared with similarly aged men with diabetes, although this absolute risk equivalence becomes attenuated after adjustment for CVD risk factors (5, 6).

Sex differences in the association of diabetes with CVD outcomes have been studied comprehensively in white persons; however, further study is needed to examine sex differences among minority populations for whom the diabetes burden is particularly high (1). Specifically, the incidence and prevalence of diabetes is higher among African Americans, particularly African-American women, than among white persons (7, 8). A previous study has suggested that some of the excess risk of diabetes among African Americans is accounted for by modifiable risk factors, especially among African-American women compared with white women (8). However, little is known about whether there are sex differences in the association between diabetes and CVD among African Americans, as has been well-documented among whites (5, 6). As pointed out by a recent

review (5), there have been no studies testing the interaction of sex with diabetes in relation to CVD outcomes in African Americans. The sex × diabetes interaction established in white persons leads us to believe a similar interaction would be seen in African Americans, but this must be explicitly tested.

The Atherosclerosis Risk in Communities Study (ARIC) offers an opportunity to examine CVD outcomes among African-American men and women to determine whether sex and diabetes interact to affect CVD incidence. The CVD outcomes of interest included incident coronary heart disease, total stroke, peripheral artery disease, and heart failure. We hypothesized that there was a multiplicative sex × diabetes interaction for CVD incidence among African Americans in the ARIC Study. That is, we expected the joint risk of CVD for women with diabetes to be greater than expected risk based on a multiplicative risk model. For comparison, we verified whether the interaction was present for white participants in ARIC as well.

METHODS

Between 1987 and 1989, 15,792 participants aged 45–64 years were enrolled into the ARIC prospective cohort, using probability sampling, from Forsyth County, North Carolina (African-American and white participants); Jackson, Mississippi (only African-American); the northwestern suburbs of Minneapolis, Minnesota (mostly white); and Washington County, Maryland (mostly white) (9). Data from visit 1, during 1987–1989, were used as baseline, and CVD events and death from non-CVD causes were ascertained through 2013. Participants were censored administratively on December 31, 2013, or were censored due to death from a non-CVD related cause or loss-to-follow-up (approximately 17%) over the 24-year contact period. Participants were excluded if they were neither African-American nor white, were missing information on baseline diabetes status, or reported prevalent coronary heart disease, stroke, peripheral artery disease, or heart failure at baseline. After exclusions, 14,058 participants were included in analysis: 3,767 African-American (27%) and 10,291 white (73%).

Exposures of interest included sex and diabetes (defined as nonfasting glucose ≥200 mg/dL, fasting blood glucose ≥126 mg/dL), self-report of physician diagnosis of diabetes, or reporting taking medication for diabetes or high blood sugar. Diabetes status was assessed at visit 1 and the 4 subsequent visits, as well as via self-report at annual or semiannual follow-up calls that occurred following visit 4 and extended through visit 5, during 2011–2013. For analysis, a baseline diabetes status variable was used as well as a time-varying diabetes status variable. Baseline diabetes was determined using visit 1 (1987–1989), and diabetes status and time-varying diabetes status were assessed through 2013 using diabetes diagnoses at an ARIC visit or self-reported diabetes at an annual follow-up call. Person-time of diabetes exposure was calculated as the time from when ARIC became aware of a participant's diabetes diagnosis to a CVD event, non-CVD death, or administrative censoring (on December 31, 2013).

Other covariates, established risk factors for diabetes, and CVD were measured at visit 1 (baseline) and included body mass index, sport and leisure activity, alcohol drinking status, tobacco smoking status, level of education, hypertension, low-density lipoprotein cholesterol level, high-density lipoprotein cholesterol level, total cholesterol level, and kidney function. Body mass index was calculated from weight and height measurements. Drinking status, smoking status, and level of education were ascertained via questionnaire. Sport and leisure activity were measured using the Baecke questionnaire, and the sum of scores was used in analysis (10). Hypertension was defined as a systolic blood pressure of ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or report of taking hypertensive medication at visit 1. Low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, total cholesterol, and kidney function (measured via estimated glomerular filtration rate using serum creatinine) were ascertained from blood tests as part of the clinical exam at visit 1 (11).

Incident outcomes of interest included incident definite or probable myocardial infarction or fatal coronary heart disease, based on hospital or death record abstraction and adjudication using published criteria (12); coronary revascularization by *International Classification of Diseases* codes; stroke based on hospital record abstraction and adjudication (13); peripheral artery disease, defined as lower extremity revascularization by *International Classification of Diseases* codes or an ARIC examination with an ankle brachial index of less than 0.9 (14); and heart failure determined using hospital or underlying cause-of-death *International Classification of Diseases* codes (15). Hospitalizations and deaths were identified through annual and semiannual follow-up calls, local hospital surveillance, state vital statistics databases, and the National Death Index (16). For analysis, deaths were classified using *International Classification of Diseases* codes for the underlying cause of death as CVD-related or non-CVD-related (16).

Race-specific Poisson regression was used to calculate incidence rates of CVD stratified by diabetes status only and then stratified by diabetes status and sex. Race-specific Cox proportional hazards were used to assess the relationship between diabetes and CVD with potential interaction by sex. Hazard ratios for these models were calculated with women without diabetes as the referent. Regardless of the significance of the interaction term, results were also presented stratified by diabetes status and sex. Hazard ratios for these sex-specific models were calculated with nondiabetic participants as the reference group within sex and were the main focus of our discussion. Model 1 adjusted for age; model 2 additionally adjusted for body mass index, smoking status, physical activity, alcohol consumption, and education; and model 3 additionally adjusted for hypertension, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and estimated glomerular filtration rate.

All Cox proportional hazards models were run in three stages. Stage 1 assessed baseline diabetes status with the outcome of CVD, the conventional method of survival analysis. Stage 2 assessed baseline diabetes status with the outcome of CVD and included the competing risk of non-CVD death. This was done to account for participants who died without developing CVD. Due to the long follow-up period and older population being studied, traditional Cox proportional hazards regression likely overestimates the risk of CVD because of the strong competing risk of non-CVD related death (17). Stage 3 incorporated changes in diabetes status during follow up in a "time-varying diabetes" model, with the outcome being CVD through 2013, and included a competing risk of non-CVD death. Time-varying

diabetes status was used in order to account for the prevalence of diabetes more than doubling over the follow-up time in all race and sex categories. Finally, sensitivity analyses were conducted to assess Poisson and Cox models using coronary heart disease, including revascularization, as the outcome instead of CVD. The results from this analysis mirrored the results using CVD (see Web Table 1, available at https://academic.oup.com/aje).

RESULTS

As shown in Table 1, at baseline, African-American participants, on average, were younger than white participants, had higher body mass index, reported less sport and leisure activity, were less likely to be current drinkers, and had lower levels of education. African Americans were more likely to have hypertension, had higher estimated glomerular filtration rate measurements, and higher prevalence and incidence of diabetes.

Stage 1 of our analysis examined the association between baseline diabetes status and incident CVD from visit 1 (1987–1989) through 2013. As shown in Figure 1 and Table 2, among African Americans, both men and women with diabetes had an almost 2-fold greater incidence of CVD, compared with their counterparts without diabetes. Further, among African Americans with diabetes, the CVD incidence rate was very similar in women and men (Figure 1). Correspondingly the sex-specific diabetes hazard ratio for CVD in model 1 (Table 2) was greater among women (compared with nondiabetic women, hazard ratio = 2.3) than among men (compared with nondiabetic men, hazard ratio = 1.8) (P for interaction = 0.014). Similarly, for models 2 and 3, results followed our hypothesized pattern, with the hazard ratio for CVD with diabetes being higher in women than men. These associations were attenuated slightly over the three models with greater adjustment, but the P values for interaction remained <0.06. Overall, the sex-specific patterns of diabetes hazard ratios for CVD among African-American participants were very similar to patterns for white participants.

Stage 2 of the analysis (Table 3) assessed the association between baseline diabetes status and incident CVD with adjustment for the competing risk of death from a non-CVD related cause. In this sample, 22% of African-American women, 33% of African-American men, 20% of white women, and 29% of white men died from a non-CVD cause between baseline and 2013 without developing CVD. With competing-risk adjustment, the hazard ratio associated with diabetes remained higher among African-American women compared with African-American men. The P for interaction was only slightly larger after full adjustment (model 3) at 0.106 compared with analysis that did not account for competing risk of non-CVD death (stage 1, model 3: P for interaction = 0.058). In contrast, among white participants, the sex × diabetes interaction terms were no longer significant with adjustment for competing risk of non-CVD death (Table 3).

Stage 3 of the analysis assessed the association between time-varying diabetes status during follow-up and incident CVD and adjusted for the competing risk of death from a non-CVD related cause. In the time-varying analysis, the

Table 1. Baseline Characteristics Stratified by Race and Sex at Visit 1, Atherosclerosis Risk in Communities Study, United States, 1987–1989

Characteristic	African-American				White			
	Men (n = 1,462)		Women (n = 2,305)		Men (n = 4,747)		Women (n = 5,544)	
	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%	Mean (SD)	%
Age, years	53.6 (5.9)		53.1 (5.7)		54.5 (5.7)		53.8 (5.7)	
Body mass index[a]	27.5 (4.9)		30.6 (6.4)		27.4 (3.9)		26.4 (5.3)	
Sport and leisure activity score, units	4.3 (1.1)		4.2 (1.0)		5.1 (1.1)		4.9 (1.1)	
Current alcohol drinker		50.9		21.5		70.4		61.3
Current tobacco smoker		37.8		24.2		24.3		24.3
Basic education[b]		43.1		38.5		16.7		15.7
Hypertension[c]		52.8		52.1		25.2		23.7
Low-density lipoprotein cholesterol, mg/dL	137 (42)		137 (43)		139 (35)		135 (40)	
High-density lipoprotein cholesterol, mg/dL	51 (17)		58 (17)		43 (12)		58 (17)	
Total cholesterol, mg/dL	211 (44)		217 (46)		210 (38)		218 (42)	
Estimated glomerular filtration rate, mL/min/1.73m^2	108 (18)		114 (20)		98 (12)		101 (12)	
Baseline diabetes[d]		16.3		18.7		8.8		7.2
Diabetes[e]		36.2		41.1		26.9		22.0

Abbreviation: SD, standard deviation.

[a] Weight (kg)/height (m)^2.

[b] Based on self-report of some high school education or less at visit 1.

[c] Based on diastolic blood pressure ≥90 mm Hg, systolic blood pressure of ≥140 mm Hg, or use of medication for hypertension at visit 1.

[d] Defined as nonfasting blood glucose ≥200 mg/dL, fasting blood glucose ≥126 mg/dL, self- report of diabetes, or reporting taking medication for diabetes or high blood sugar at visit 1.

[e] Defined as nonfasting blood glucose ≥200 mg/dL, fasting blood glucose ≥126 mg/dL, self- report of diabetes, or reporting taking medication for diabetes or high blood sugar at any point during follow-up from visit 1 through 2013.

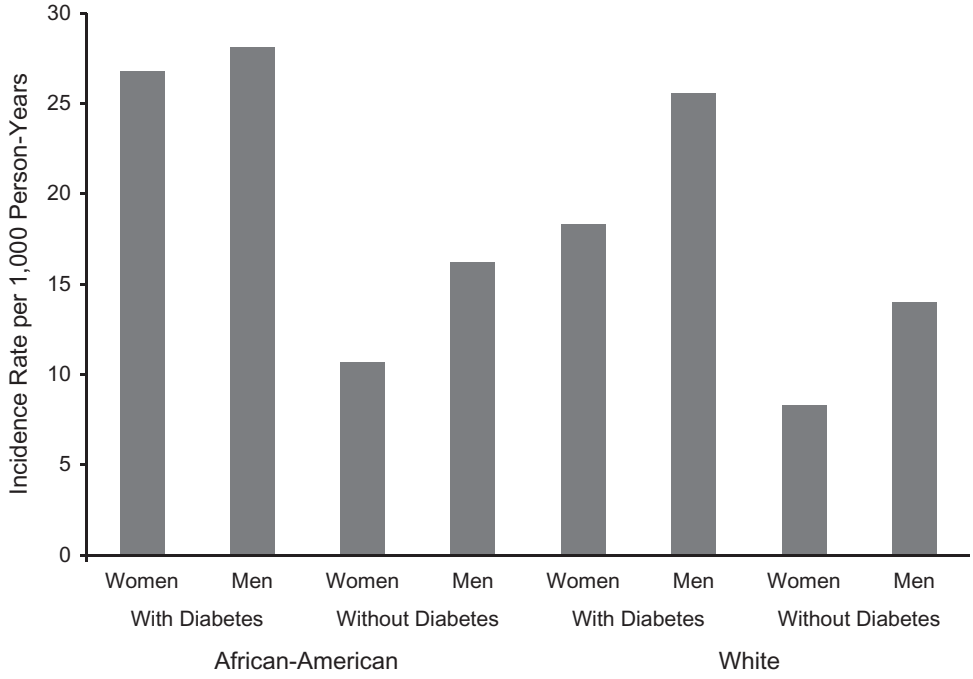

Figure 1. Unadjusted incidence rates (per 1,000 person-years) of cardiovascular disease outcomes according to baseline diabetes status and sex among African-American and white participants, Atherosclerosis Risk in Communities Study, United States, 1987–2013.

incidence rates of CVD for those with diabetes (Web Figure 1) were somewhat lower than for the baseline analysis (Figure 1). The diabetes hazard ratios for CVD in the stage 3 analysis (Table 4) were weaker than for stages 1 and 2 (Tables 2 and 3, respectively), but the *P* for interaction remained <0.06 among African Americans, indicating that African-American women had a higher hazard ratio for diabetes for CVD than did African-American men. As with stage 2 analysis, interactions were not statistically significant among white participants (Table 4).

DISCUSSION

In this prospective population-based study, we found that diabetes was a stronger risk factor for CVD among African-American women than among African-American men, replicating a sex × diabetes multiplicative interaction reported in previous studies of white persons (5, 6). Results were generally consistent across all three stages of analysis, though strongest when we used our stage 1 analysis of baseline diabetes, which most closely mirrored the approach used in previous cohort studies (4, 5). Diabetes is an established risk factor for CVD in African Americans (18), but to our knowledge this is the first study to formally test an interaction between sex and diabetes in African Americans. In fact, the absolute incidence of CVD was almost as high among African-American women with diabetes as among African-American men with diabetes. However, consistent with the literature, the absolute risk of CVD remained somewhat higher in diabetic men compared with women for both races even with statistically significant sex × diabetes interactions. These finding suggest that African-American women with diabetes are at elevated risk, compared with men with diabetes, of CVD and could have implications for screening and prevention strategies.

Our findings on modification by sex of the diabetes-CVD relationship were consistent, but somewhat weaker in magnitude, with those of previous studies using baseline diabetes status in whites. Previous studies have estimated an at least 2-fold greater relative risk of CVD among white women with (versus without) diabetes compared with white men with (versus without) diabetes (5, 6). We are uncertain why the diabetes × sex interaction for white participants was not as strong in ARIC as in previous studies. However, we also showed that more attention to competing risks and time-varying diabetes status affects the interaction. Our stage 2 adjustment for competing risk of non-CVD death weakened the associations between diabetes and CVD events for black and white participants. It has been documented previously that ignoring competing risks can bias hazard ratio estimates, and consideration of competing risks is important because diabetes increases risk of death from multiple causes (e.g., renal disease and cancer) (19). Moreover, the assignment of cause of death in diabetes is especially complicated given the wide range of underlying conditions associated with the disease that contribute to mortality (20, 21).

The addition of time-varying diabetes via our stage 3 analysis attenuated the associations compared with the previous non–time-varying analyses. We believe this is likely due to one or more of the following: 1) more self-reported diabetes being included in the time-varying analysis; 2) shorter follow-up time for CVD in recently-diagnosed diabetic ARIC participants than

Table 2. Hazard Ratios for Cardiovascular Disease Outcomes According to Baseline Diabetes Status and Sex in Separate Analyses for African-American and White Participants, Atherosclerosis Risk in Communities Study, United States, 1987–2013

Stratum	African-American					White				
	No Diabetes[a] (n = 3,011)		Diabetes[b] (n = 649)		Sex × Diabetes P for Interaction	No Diabetes[c] (n = 9,449)		Diabetes[d] (n = 818)		Sex × Diabetes P for Interaction
	HR	95% CI	HR	95% CI		HR	95% CI	HR	95% CI	
Model 1[e]					0.014					0.002
Women	1	Referent	2.3	2.0, 2.6		1	Referent	2.3	2.0, 2.6	
Men	1.7	1.5, 1.9	3.0	2.6, 3.5		1.7	1.6, 1.8	3.0	2.7, 3.4	
Women only	1	Referent	2.3	2.0, 2.7		1	Referent	2.3	2.0, 2.6	
Men only	1	Referent	1.8	1.5, 2.1		1	Referent	1.8	1.6, 2.0	
Model 2[f]					0.028					0.03
Women	1	Referent	2.3	2.0, 2.6		1	Referent	2.0	1.7, 2.2	
Men	1.6	1.4, 1.8	2.8	2.4, 3.3		1.6	1.5, 1.7	2.6	2.3, 3.0	
Women only	1	Referent	2.2	1.9, 2.6		1	Referent	2.0	1.7, 2.2	
Men only	1	Referent	1.9	1.6, 2.2		1	Referent	1.6	1.4, 1.8	
Model 3[g]					0.058					0.102
Women	1	Referent	2.1	1.8, 2.4		1	Referent	1.8	1.5, 2.0	
Men	1.6	1.4, 1.8	2.7	2.2, 3.2		1.5	1.4, 1.7	2.3	2.0, 2.7	
Women only	1	Referent	2.0	1.8, 2.3		1	Referent	1.8	1.5, 2.0	
Men only	1	Referent	1.8	1.5, 2.1		1	Referent	1.5	1.4, 1.7	

Abbreviations: CI, confidence interval; CVD, cardiovascular disease, HR, hazard ratio.

[a] Incident CVD: n = 778.

[b] Incident CVD: n = 295.

[c] Incident CVD: n = 2,165.

[d] Incident CVD: n = 310.

[e] Model 1 adjusted for age.

[f] Model 2 adjusted for age, body mass index, smoking status, physical activity, alcohol consumption, and education.

[g] Model 3 adjusted for age, body mass index, smoking status, physical activity, alcohol consumption, education, systolic blood pressure and hypertension medication, low-density lipoprotein cholesterol level, high-density lipoprotein cholesterol level, and estimated glomerular filtration rate.

for those with diabetes at baseline, which may indicate differing severity or control of diabetes; 3) the clinical definition of diabetes in the United States becoming more sensitive during the more than 25-year follow-up, thereby allowing detection of milder cases of diabetes, in which there might be a more favorable CVD risk profile; and 4) treatment for CVD risk factors improving between 1987 and 2013 for people with diabetes (19). These changes in diabetes morbidity and treatment may have reduced the degree of interaction seen between sex and diabetes status for CVD outcomes in the stage 3 analysis compared with the stage 1 analysis. Finally, as mentioned, there is evidence that excess risk of diabetes among African Americans is accounted for by modifiable risk factors, especially among African-American women. By adding adjustments and more advanced statistical methods, the completeness of risk-factor adjustment may have differed for black men compared with women. The more rapid attenuation of the diabetes-on-CVD association seen with adjustment among African-American men compared with women may have been evidence of this.

There are some limitations to this study. First, with respect to the time-varying analysis, some cases of diabetes ascertained via self-report at annual or semiannual follow-up calls may have been incorrectly reported. Conversely, some people reporting no diabetes in ARIC follow-up may have had undiagnosed diabetes. Furthermore, the date of diabetes diagnosis during follow-up was not collected, so diabetes status could only be updated at the time of a follow-up call or clinic visit. Literature suggests that the average time between type 2 diabetes onset and diagnosis is 4–7 years, and almost one-third of cases are undiagnosed without screening (22, 23). Given the considerable lag between onset and diagnosis in the general population, the additional time to ARIC identification of diabetes likely has a minimal effect on our findings; ARIC investigators questioned participants annually about their diabetes status and screened for diabetes at each exam.

A second limitation is that our time-varying diabetes analysis does not capture separately the effect of long-term diabetes compared with shorter-term diabetes. Those with longer-term diabetes may have worse cumulative effects of diabetes and CVD risk factors than those with short-term diabetes. At baseline, a relatively small proportion (13%) of the participants reported a previous history of diabetes and can be considered

Table 3. Hazard Ratios for Cardiovascular Disease Outcomes With a Competing Risk of Death According to Baseline Diabetes Status and Sex in Separate Analyses for African-American and White Participants, United States, Atherosclerosis Risk in Communities Study, 1987–2013

Stratum	African-American					White				
	No Diabetes[a] (n = 3,011)		Diabetes[b] (n = 649)		Sex × Diabetes P for Interaction	No Diabetes[c] (n = 9,449)		Diabetes[d] (n = 818)		Sex × Diabetes P for Interaction
	HR	95% CI	HR	95% CI		HR	95% CI	HR	95% CI	
Model 1[e]					0.019					0.314
Women	1	Referent	2.2	1.9, 2.7		1	Referent	1.9	1.6, 2.3	
Men	1.4	1.2, 1.6	2.2	1.7, 2.7		1.6	1.5, 1.7	2.7	2.3, 3.2	
Women only	1	Referent	2.2	1.8, 2.6		1	Referent	1.8	1.5, 2.2	
Men only	1	Referent	1.6	1.3, 2.0		1	Referent	1.7	1.5, 2.2	
Model 2[f]					0.039					0.05
Women	1	Referent	2.1	1.7, 2.5		1	Referent	1.5	1.3, 1.9	
Men	1.4	1.2, 1.6	2.1	1.6, 2.6		1.6	1.4, 1.7	2.3	1.9, 2.8	
Women only	1	Referent	2.0	1.7, 2.5		1	Referent	1.5	1.2, 1.9	
Men only	1	Referent	1.5	1.2, 1.9		1	Referent	1.5	1.3, 1.8	
Model 3[g]					0.106					0.996
Women	1	Referent	1.9	1.5, 2.3		1	Referent	1.4	1.1, 1.7	
Men	1.3	1.1, 1.5	1.9	1.5, 2.4		1.4	1.2, 1.5	1.9	1.6, 2.3	
Women only	1	Referent	1.9	1.5, 2.3		1	Referent	1.4	1.1, 1.7	
Men only	1	Referent	1.4	1.1, 1.8		1	Referent	1.4	1.2, 1.7	

Abbreviations: CI, confidence interval; CVD, cardiovascular disease, HR, hazard ratio.

[a] Incident CVD: n = 778.

[b] Incident CVD: n = 295.

[c] Incident CVD: n = 2,165.

[d] Incident CVD: n = 310.

[e] Model 1 adjusted for age.

[f] Model 2 adjusted for age, body mass index, smoking status, physical activity, alcohol consumption, and education.

[g] Model 3 adjusted for age, body mass index, smoking status, physical activity, alcohol consumption, education, systolic blood pressure and hypertension medication, low-density lipoprotein cholesterol level, high-density lipoprotein cholesterol level, and estimated glomerular filtration rate.

long-term cases. Further, the difference in average follow-up time between date of diabetes diagnosis and CVD outcome in those identified as cases at baseline was 10 years and for time-varying cases was 12 years. This indicates that the time to CVD did not differ greatly between participants who had prevalent diabetes and those with incident diabetes, so the impact of duration on the sex interaction may be small.

A third limitation was that, despite ARIC's large sample size and long follow-up, power to assess interaction between diabetes status and sex was limited with respect to African Americans, particularly because African-American men were most likely to be censored over the follow-up period. Using a competing-risk model helped account for differential censoring by sex. Adjustment for multiple confounders with the limited sample size may have also reduced power to detect an interaction. The P values for interaction in the full-adjustment models in stages 1, 2, and 3 of analysis were marginally significant among African American participants, at 0.058, 0.106, and 0.047, respectively, while P values for interaction for the reduced models were almost all less than 0.05. Certainly, it would be helpful if these analyses were replicated with a larger sample of African Americans.

Finally, the results may not be fully generalizable to other African-American populations. The African Americans in this sample were from 2 ARIC centers in southern US communities, where prevalence of CVD risk factors is likely higher than in many other African-American communities. Our models adjusted for CVD risk factors; however, there is a possibility of residual confounding. Because the sex × diabetes interaction in African Americans mirrored what has been reported in white persons, who typically have less prevalent CVD risk factors, it is unlikely that including a more diverse African-American sample would completely eliminate the interaction we observed.

As with white participants, among African Americans the hazard ratio for CVD in the presence of diabetes was higher for women than for men, and the absolute risk of CVD was similar for both women and men who had diabetes. Efforts to prevent diabetes and to control CVD risk factors are salient to both men and women but are particularly salient to women. Further

Table 4. Hazard Ratios for Cardiovascular Disease Outcomes With a Competing Risk of Death According to Time-Varying Diabetes Status and Sex in Separate Analyses for African-American and White Participants, United States, Atherosclerosis Risk in Communities Study, 1987–2013

Stratum	African-American					White				
	No Diabetes[a] (n = 2,290)		Diabetes[b] (n = 1,477)		Sex × Diabetes P for Interaction	No Diabetes[c] (n = 7,794)		Diabetes[d] (n = 2,497)		Sex × Diabetes P for Interaction
	HR	95% CI	HR	95% CI		HR	95% CI	HR	95% CI	
Model 1[e]					0.053					0.261
Women	1	Referent	1.6	1.4, 1.9		1	Referent	1.7	1.5, 1.8	
Men	1.3	1.1, 1.6	1.9	1.6, 2.3		1.6	1.5, 1.8	2.3	2.1, 2.6	
Women only	1	Referent	1.6	1.4, 1.9		1	Referent	1.7	1.5, 1.9	
Men only	1	Referent	1.4	1.1, 1.7		1	Referent	1.4	1.3, 1.6	
Model 2[f]					0.033					0.343
Women	1	Referent	1.5	1.3, 1.8		1	Referent	1.4	1.2, 1.6	
Men	1.3	1.1, 1.6	1.9	1.5, 2.3		1.6	1.4, 1.7	2.1	1.8, 2.4	
Women only	1	Referent	1.5	1.3, 1.8		1	Referent	1.4	1.2, 1.6	
Men only	1	Referent	1.3	1.1, 1.6		1	Referent	1.3	1.2, 1.5	
Model 3[g]					0.047					0.50
Women	1	Referent	1.4	1.2, 1.6		1	Referent	1.3	1.1, 1.5	
Men	1.3	1.0, 1.5	1.6	1.3, 2.0		1.4	1.2, 1.5	1.7	1.5, 2.0	
Women only	1	Referent	1.4	1.2, 1.6		1	Referent	1.3	1.1, 1.5	
Men only	1	Referent	1.2	1.0, 1.5		1	Referent	1.3	1.1, 1.4	

Abbreviations: CI, confidence interval; CVD, cardiovascular disease, HR, hazard ratio.

[a] Incident CVD: n = 584.

[b] Incident CVD: n = 520.

[c] Incident CVD: n = 1,688.

[d] Incident CVD: n = 794.

[e] Model 1 adjusted for age.

[f] Model 2 adjusted for age, body mass index, smoking status, physical activity, alcohol consumption, and education.

[g] Model 3 adjusted for age, body mass index, smoking status, physical activity, alcohol consumption, education, systolic blood pressure and hypertension medication, low-density lipoprotein cholesterol level, high-density lipoprotein cholesterol level, and estimated glomerular filtration rate.

research is needed to explore this interaction among African Americans using larger sample sizes, gathering more representative samples of blacks in the United States, and examining individual cardiovascular diseases separately. Health disparities in CVD according to race have been well established, but studies analyzing potential racial differences in fundamental CVD associations are still needed.

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