Associations of Cardiometabolic Multimorbidity With All-Cause and Coronary Heart Disease Mortality Among Black Adults in the Jackson Heart Study

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Abstract

IMPORTANCE A combination of diabetes, coronary heart disease (CHD), and stroke has multiplicative all-cause mortality risk compared with any individual morbidity in White populations, but there is a lack of studies in Black populations in the US.

OBJECTIVE To examine the association of cardiometabolic multimorbidity (diabetes, stroke, and CHD) individually and collectively with all-cause and CHD mortality.

DESIGN, SETTING, AND PARTICIPANTS This cohort study included Black adults in the Jackson Heart Study followed over a median of 15 years. Baseline examinations were performed between 2000 and 2004, with follow-up on all-cause and CHD mortality through May 31, 2018. Participants were categorized into mutually exclusive groups at baseline: (1) free of cardiometabolic morbidity, (2) diabetes, (3) CHD, (4) stroke, (5) diabetes and stroke, (6) CHD and stroke, (7) diabetes and CHD, and (8) diabetes, stroke, and CHD. Data were analyzed from 2019 to 2021.

EXPOSURE Cardiometabolic disease alone or in combination.

MAIN OUTCOMES AND MEASURES The main outcomes were all-cause mortality and CHD mortality. Cox models estimated hazard ratios (HRs) with 95% CIs adjusted for sociodemographic and cardiovascular risk factors.

RESULTS Among 5064 participants (mean [SD] age, 55.4 [12.8] years; 3200 [63%] women) in the Jackson Heart Study, 897 (18%) had diabetes, 192 (4%) had CHD, and 104 (2%) had a history of stroke. Among participants with cardiometabolic morbidities, the crude all-cause mortality rates were lowest for diabetes alone (24.4 deaths per 1000 person-years) and highest for diabetes, CHD, and stroke combined (84.1 deaths per 1000 person-years). For people with only 1 cardiometabolic morbidity, risk for all-cause mortality was highest for people with stroke (HR, 1.74; 95% CI, 1.24-2.42), followed by CHD (HR, 1.59 [95% CI, 1.22-2.08]) and diabetes (HR, 1.50; 95% CI, 1.22-1.85), compared with no cardiometabolic morbidities. There were also increased risks of mortality with combinations of diabetes and stroke (HR, 1.71; 95% CI, 1.09-2.68), CHD and stroke (HR, 2.23; 95% CI, 1.35-3.69), and diabetes and CHD (HR, 2.28; 95% CI, 1.65-3.15). The combination of diabetes, stroke, and CHD was associated with the highest all-cause mortality (HR, 3.68; 95% CI, 1.96-6.93). Findings were similar for CHD mortality, but with a larger magnitude of association (eg, diabetes, stroke, and CHD: HR, 13.52; 95% CI, 3.38-54.12).

CONCLUSIONS AND RELEVANCE In this cohort study, an increasing number of cardiometabolic multimorbidities was associated with a multiplicative increase in risk of all-cause mortality among Black adults, with a greater magnitude of association for CHD mortality.

Key Points

Question Is there an association of increasing number of cardiometabolic comorbidities (diabetes, stroke, and coronary heart disease [CHD]) with all-cause mortality and CHD mortality in a population of US Black adults?

Findings In this cohort study of 5064 Black adults followed-up for 15 years, participants with cardiometabolic morbidities individually and collectively showed statistically significant multiplicative increased risks of all-cause and CHD mortality.

Meaning These findings suggest that a higher number of cardiometabolic comorbidities was associated with multiplicative increased risks of all-cause mortality and CHD mortality; thus, primordial and primary prevention of cardiometabolic morbidities are critical to reduce disparities in mortality.

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Introduction

In the United States, inequities exist in life expectancy across racial and ethnic groups, with Black populations noted to have the shortest life expectancy at birth.\(^1\) Diabetes, stroke, and coronary heart disease (CHD) are 3 of the top 7 contributors to the differential life expectancy between non-Hispanic Black (hereafter, *Black*) and non-Hispanic White (hereafter, *White*) populations.\(^2\) Structural inequities lead to a higher prevalence of many cardiometabolic diseases in Black populations.\(^3-5\) For instance, the total diabetes prevalence is 17.4% in Black populations, compared with 13.6% in White populations.\(^6\) Although age-adjusted stroke death rates declined by 7% or more among all racial and ethnic groups between 2008 and 2018, rates remained higher in Black populations (52.3 deaths per 100,000 population; change since 2008, −12.7%) compared with White populations (35.9 deaths per 100,000 population; change since 2008, −11.4%).\(^7\) While Black and White populations have similar prevalence of CHD,\(^5,8,9\) Black populations have higher rates of mortality from stroke, CHD, and diabetes compared with White populations.\(^8\) The all-cause mortality rates for a history of diabetes, stroke, or myocardial infarction are approximately 16 per 1000 person-years for each condition among White populations, while a combination of these conditions is associated with a multiplicative mortality risk (32.0 per 1000 person-years with diabetes and myocardial infarction, 32.5 per 1000 person-years with diabetes and stroke, 32.8 per 1000 person-years with stroke and myocardial infarction, and 59.5 per 1000 person-years with diabetes, stroke, and myocardial infarction).\(^10\) Given the known higher rates of mortality from CHD, stroke, and diabetes among Black populations compared with White populations,\(^8\) it is paramount to examine the association of a combination of these cardiometabolic conditions with mortality among Black populations. Thus, we examined the association of diabetes, stroke, and CHD singularly and in combination with all-cause and CHD mortality among Black adults in the Jackson Heart Study (JHS). We hypothesized a multiplicative increase in mortality with greater combinations of morbidities.

Methods

This cohort study was approved by the institutional review boards of all participating institutions, and written informed consent was obtained from all participants. This report followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Study Participants

The JHS is a prospective cohort study of 5306 Black adults (self-classified), aged 21 to 94 years from the tricounty area of metropolitan Jackson, Mississippi. Baseline examinations were performed between 2000 and 2004, with 2 subsequent follow-up examinations conducted in 2005 to 2008 and 2009 to 2013. The design of the study has been described elsewhere.\(^11\)

In this prospective secondary analysis to examine the association of a combination of these cardiometabolic conditions with mortality among Black adults, 242 participants were excluded for missing data on exposures, outcomes, or primary covariates (age, sex, education, occupation, smoking, physical activity, alcohol intake, and waist circumference). After these exclusions, 5064 participants were included in the primary analysis. Additionally, 502 participants were excluded in an additional model including systolic blood pressure, estimated glomerular filtration rate (eGFR), low-density lipoprotein (LDL) cholesterol, and hemoglobin A\(_{1c}\) (HbA\(_{1c}\)), for a final sample of 4562 participants in secondary models (eFigure in the Supplement).

Ascertainment of Baseline Diabetes, CHD, or Stroke

Diabetes was defined as HbA\(_{1c}\) of 6.5% or greater (to convert to proportion of total hemoglobin, multiply by 0.01), fasting blood glucose of 126 mg/dL or greater (to convert to millimoles per liter, multiply by 0.0555), using diabetes medications, or a self-reported physician diagnosis.\(^12\) Fasting glucose was measured on a Vitros 950 or 250, Ortho-Clinical Diagnostics analyzer using standard
procedures that met the College of American Pathologists accreditation requirement. A high-performance liquid chromatography system (Tosoh Corporation) was used to measure HbA1c concentrations. History of CHD was defined as evidence of a previous myocardial infarction by electrocardiogram (ECG) based on Minnesota Code criteria (codes 1.1 and 1.2 plus 4.1-4.2, or 5.1-5.2) or history of physician-diagnosed myocardial infarction, percutaneous coronary intervention, or coronary bypass surgery. The definition of stroke was based on the history of stroke (by personal history, stroke signs, and symptoms ascertained by standardized questionnaires), transient ischemic attack, or carotid endarterectomy and/or angioplasty. Details of these procedures have been described previously.

Outcomes
The 2 outcomes of interest were all-cause mortality and CHD mortality. Methods for ascertaining all-cause mortality in the JHS have been described previously. Briefly, deaths were ascertained through a combination of active and passive surveillance. Annual follow-up included interviews with participants and next of kin to ascertain health events, such as cardiac events, hospitalizations, or death, through questionnaires completed by physicians and medical examiners or coroners and reviewed by the medical record abstraction unit to generate diagnosis information. Mortality was also assessed through death certificates requested from the Mississippi State Department of Health and National Death Index searches. Diagnoses were reviewed and adjudicated by trained medical personnel. The full protocol for CHD mortality is included in the eMethods in the Supplement. The International Classification of Diseases, Ninth Revision (ICD-9) and International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) codes used for CHD mortality are shown in eTable 1 in the Supplement.

Covariates
The covariates included demographics (age, sex), occupation (management or professional vs not), level of education (=bachelor's degree vs <bachelor's degree attained), smoking status (current smoking vs not smoking), alcohol use (in the past 12 months vs no alcohol), and current prescription medication use. Waist circumference was calculated using the mean of 2 measurements around the umbilicus. Physical activity was categorized according to the American Heart Association 2020 cardiovascular health guidelines as poor, intermediate, or ideal health, as described previously. Fasting serum LDL cholesterol level was assayed using standard techniques and calculated by the Friedewald equation. eGFR was derived using the Chronic Kidney Disease Epidemiology Collaboration equation. Serum aldosterone was measured by radioimmunoassay (Siemens) and the intra-assay coefficients of variation were 8.7% for low concentrations and 6.2% for high concentrations.

Statistical Analysis
Baseline characteristics of participants are presented by baseline cardiometabolic multimorbidity status using the χ² test for categorical variables, analysis of variance for parametric continuous variables, and Kruskal-Wallis test for nonparametric continuous variables. Baseline characteristics are also shown by all-cause mortality (eTable 2 in the Supplement) and CHD mortality (eTable 3 in the Supplement) over follow-up using the χ² test for categorical variables, 2-sample t test for normally distributed continuous variables, and Wilcoxon 2-sample nonparametric test for nonnormally distributed continuous variables. Time to all-cause mortality was defined based on the adjudicated date. We censored data for participants at the time of study participation drop out or the end of study follow-up (May 31, 2018). We created cardiometabolic multimorbidity groups by categorizing participants in 8 mutually exclusive groups (participants without a history of diabetes, CHD, or stroke [reference group]; only diabetes; only stroke; only CHD; diabetes and stroke; diabetes and CHD; stroke and CHD; and diabetes, stroke, and CHD). Cox proportional hazards models were used to examine the associations of cardiometabolic multimorbidity with death. Based on prior analyses,
covariates were selected a priori, and multivariable modeling was performed with sequential adjustment as follows: model 1 adjusted for age, sex, education, current occupation status, smoking, physical activity, alcohol use, and waist circumference; model 2: model 1 plus systolic blood pressure, eGFR, LDL, and HbA1c.

Additional adjustments were performed for aldosterone and aldosterone plus use of angiotensin converting enzyme–inhibitor, angiotensin-receptor blocker, mineralocorticoid receptor antagonist, statins, and aspirin (eTable 4 and eTable 5 in the Supplement). The proportional hazards assumption was assessed using Schoenfeld residuals, and no significant violations were noted. Direct adjusted survival curves (adjusted for model 2) were plotted by cardiometabolic multimorbidity groups. Statistical significance was defined as 2-sided \( \alpha < .05 \) in the main analysis. Analyses were performed using SAS statistical software version 9.4 (SAS Institute). Data were analyzed from 2019 to 2021.

Results

Among 5064 participants (mean [SD] age, 55.4 [12.8] years; 3200 [63%] women) 897 (18%) had diabetes, 192 (4%) had CHD, and 104 (2%) had a history of stroke (Table 1). Individuals with vs without diabetes, stroke, and CHD were older, more likely to be men, and less educated and had a higher prevalence of cardiovascular risk factors (eg, higher waist circumference, systolic blood pressure, glucose, HbA1c, and hypertension prevalence) except for lower diastolic blood pressure (Table 1). Similar findings were shown for individuals who had all-cause mortality (eTable 2 in the Supplement) or CHD mortality (eTable 3 in the Supplement) over the course of follow-up. Additionally, participants with mortality over the follow-up periods had a higher prevalence of baseline diabetes, stroke, and CHD.

Over a median (IQR) follow-up period of 15.3 (14.3-16.1) years, there were 1068 all-cause deaths and 111 CHD deaths. Table 2, Figure 1A, and Figure 2A show the association of cardiometabolic multimorbidity with all-cause mortality. The crude mortality rate among participants without a history of diabetes, CHD, or stroke (reference group) was 9.65 (95% CI, 8.85-10.52) deaths per 1000 person-years. The crude mortality rates were 24.4 (95% CI, 21.78-27.34) deaths per 1000 person-years in participants with a history of diabetes, 32.95 (95% CI, 24.52-44.28) deaths per 1000 person-years in participants with a history of stroke, 29.07 (95% CI:23.11-36.56) deaths per 1000 person-years in participants with CHD, 40.18 (95% CI, 28.25-57.13) deaths per 1000 person-years in participants with diabetes and stroke, 48.02 (95% CI:29.85-77.25) deaths per 1000 person-years in participants with CHD and stroke, 48.62 (95% CI, 38.46-61.45) deaths per 1000 person-years in participants with diabetes and CHD, and 84.06 (95% CI, 54.80-128.92) deaths per 1000 person-years in participants with a history of diabetes, stroke, and CHD.

In the fully adjusted model, risk for all-cause mortality were significantly increased for participants with diabetes, (HR, 1.50; 95% CI, 1.22-1.85), stroke (HR, 1.74; 95% CI, 1.24-2.42), or CHD (HR, 1.59; 95% CI,1.22-2.08) alone. Risk was also increase in participants with diabetes and stroke (HR, 1.71; 95% CI, 1.09-2.68), CHD and stroke (HR, 2.23; 95% CI, 1.35-3.69), or diabetes and CHD (HR, 2.28; 95% CI, 1.65-3.15). The combination of diabetes, stroke, and CHD was associated with the greatest risk of all-cause mortality (HR, 3.68; 95% CI, 1.96-6.93).

Table 3, Figure 1B, and Figure 2B show the association of cardiometabolic multimorbidity with CHD mortality. In the fully adjusted model, there was no significant increased risk for CHD mortality for participants with diabetes (HR, 1.95; 95% CI, 0.96-3.97) or stroke (HR, 1.31; 95% CI, 0.31-5.59) alone, but there was increased risk for participants with CHD alone (HR, 3.51; 95% CI, 1.56-7.90). For participants with combined comorbidities, there was increased risk of CHD mortality for those with diabetes and stroke (HR, 5.57; 95% CI, 1.97-15.73), CHD and stroke (HR, 10.97; 95% CI, 4.12-29.22), diabetes and CHD (HR, 13.47; 95% CI, 6.54-27.74), or diabetes, stroke, and CHD (HR, 13.52; 95% CI, 3.38-54.12). Similar findings were noted after adjustment for aldosterone and use of medications.
Table 1. Baseline Characteristics of Participants Classified by Baseline Cardiometabolic Multimorbidity

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Participants, No. (%)</th>
<th>Overall (N = 5064)</th>
<th>No diabetes, stroke, or CHD (n = 3629)</th>
<th>Diabetes (n = 897)</th>
<th>Stroke (n = 104)</th>
<th>CHD (n = 192)</th>
<th>Diabetes and stroke (n = 60)</th>
<th>CHD and stroke (n = 31)</th>
<th>Diabetes and CHD (n = 125)</th>
<th>Diabetes, stroke, and CHD (n = 26)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>55.4 (12.8)</td>
<td>53.1 (12.9)</td>
<td>59.6 (10.8)</td>
<td>63.6 (10.9)</td>
<td>61.1 (11.4)</td>
<td>63.7 (100)</td>
<td>65.1 (9.0)</td>
<td>64.9 (8.5)</td>
<td>66.4 (8.5)</td>
<td>&lt;.001</td>
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<tr>
<td>Sex</td>
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<tr>
<td>Men</td>
<td>1864 (37)</td>
<td>1338 (37)</td>
<td>288 (32)</td>
<td>43 (41)</td>
<td>92 (48)</td>
<td>24 (40)</td>
<td>13 (42)</td>
<td>53 (42)</td>
<td>13 (50)</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>3200 (63)</td>
<td>2291 (63)</td>
<td>609 (68)</td>
<td>61 (59)</td>
<td>100 (52)</td>
<td>36 (60)</td>
<td>18 (58)</td>
<td>72 (58)</td>
<td>13 (50)</td>
<td>&lt;.001</td>
<td></td>
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<tr>
<td>&lt; High school education</td>
<td>1018 (20)</td>
<td>565 (16)</td>
<td>244 (27)</td>
<td>42 (40)</td>
<td>67 (35)</td>
<td>24 (40)</td>
<td>15 (48)</td>
<td>45 (36)</td>
<td>16 (62)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Occupation, working full time</td>
<td>1812 (36)</td>
<td>1378 (38)</td>
<td>287 (32)</td>
<td>25 (24)</td>
<td>56 (29)</td>
<td>20 (33)</td>
<td>9 (29)</td>
<td>34 (27)</td>
<td>3 (12)</td>
<td>&lt;.001</td>
<td></td>
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<tr>
<td>Current smoking</td>
<td>665 (13)</td>
<td>470 (13)</td>
<td>94 (10)</td>
<td>22 (21)</td>
<td>44 (23)</td>
<td>6 (10)</td>
<td>7 (23)</td>
<td>19 (15)</td>
<td>3 (12)</td>
<td>&lt;.001</td>
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<tr>
<td>AHA Poor Physical Activityb</td>
<td>2482 (49)</td>
<td>1649 (45)</td>
<td>511 (57)</td>
<td>64 (62)</td>
<td>106 (55)</td>
<td>32 (53)</td>
<td>22 (71)</td>
<td>79 (63)</td>
<td>19 (73)</td>
<td>&lt;.001</td>
<td></td>
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<tr>
<td>Alcohol consumption</td>
<td>2327 (46)</td>
<td>1824 (50)</td>
<td>311 (35)</td>
<td>37 (36)</td>
<td>86 (45)</td>
<td>12 (20)</td>
<td>6 (19)</td>
<td>45 (36)</td>
<td>6 (23)</td>
<td>&lt;.001</td>
<td></td>
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<tr>
<td>BMI, mean (SD)</td>
<td>31.8 (7.2)</td>
<td>31.1 (7.1)</td>
<td>34.2 (7.2)</td>
<td>30.2 (5.8)</td>
<td>30.6 (7.4)</td>
<td>34.4 (7)</td>
<td>31.0 (7.3)</td>
<td>33.9 (7.0)</td>
<td>32.4 (6.4)</td>
<td>&lt;.001</td>
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<tr>
<td>Waist circumference, mean (SD), cm</td>
<td>100.8 (16.1)</td>
<td>98.5 (15.7)</td>
<td>108.6 (15.6)</td>
<td>100.1 (12.8)</td>
<td>98.9 (16)</td>
<td>109.6 (16.2)</td>
<td>102.4 (16)</td>
<td>107.7 (13.9)</td>
<td>106.2 (11.9)</td>
<td>&lt;.001</td>
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<tr>
<td>Blood pressure, mean (SD), mm Hg</td>
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<tr>
<td>Systolic</td>
<td>127.5 (16.8)</td>
<td>125.9 (16.3)</td>
<td>131.6 (16.6)</td>
<td>130.2 (18)</td>
<td>133.6 (19.8)</td>
<td>136.4 (18.8)</td>
<td>132.7 (17.7)</td>
<td>131.8 (17.5)</td>
<td>130.6 (18.5)</td>
<td>&lt;.001</td>
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<tr>
<td>Diastolic</td>
<td>75.8 (8.8)</td>
<td>76.3 (8.6)</td>
<td>74.7 (8.5)</td>
<td>74.9 (9.6)</td>
<td>76.4 (9.9)</td>
<td>73 (8.8)</td>
<td>76.0 (11.0)</td>
<td>72.4 (9.7)</td>
<td>69.5 (10.3)</td>
<td>&lt;.001</td>
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<tr>
<td>Hypertensionc</td>
<td>2864 (57)</td>
<td>1707 (47)</td>
<td>1157 (62)</td>
<td>106 (55)</td>
<td>101 (55)</td>
<td>101 (55)</td>
<td>101 (55)</td>
<td>101 (55)</td>
<td>101 (55)</td>
<td>&lt;.001</td>
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<tr>
<td>LDL cholesterol, mean (SD), mg/dL, (n = 4495)</td>
<td>126.6 (36.5)</td>
<td>127.7 (36.3)</td>
<td>124 (37)</td>
<td>122.5 (36)</td>
<td>124.5 (37)</td>
<td>124.5 (37.4)</td>
<td>124.6 (30.2)</td>
<td>123.4 (36.4)</td>
<td>129.6 (36.6)</td>
<td>&lt;.001</td>
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<tr>
<td>eGFR, mean (SD), mL/min per 1.73 m²</td>
<td>85.9 (18.5)</td>
<td>87.3 (16.4)</td>
<td>84.7 (21.9)</td>
<td>78.3 (18.3)</td>
<td>80.9 (24)</td>
<td>76.8 (20.6)</td>
<td>74.0 (22.4)</td>
<td>77.7 (24)</td>
<td>70.1 (32.5)</td>
<td>&lt;.001</td>
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<td>Laboratory measures, median (IQR)</td>
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<tr>
<td>Aldosterone, ng/dL</td>
<td>4.4 (2.6-7.2)</td>
<td>4.3 (2.5-6.9)</td>
<td>4.6 (2.9-8.1)</td>
<td>3.9 (2.5-7.2)</td>
<td>4.4 (2.3-7)</td>
<td>4.6 (2.2-9.4)</td>
<td>3.9 (2.4-9.0)</td>
<td>5.0 (3.3-7.9)</td>
<td>6.9 (4.1-10.0)</td>
<td>&lt;.001</td>
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<tr>
<td>Fasting plasma glucose, mg/dL, (n = 4545)</td>
<td>91 (85-99)</td>
<td>89 (84-95)</td>
<td>122 (103-160)</td>
<td>92.5 (88-97)</td>
<td>91 (86-98)</td>
<td>124 (106-162)</td>
<td>95 (91-100)</td>
<td>124 (101-158)</td>
<td>189 (136-244)</td>
<td>&lt;.001</td>
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<tr>
<td>HbA1c, %, (n = 4801)</td>
<td>5.7 (5.3-6.2)</td>
<td>5.5 (5.2-5.8)</td>
<td>7.2 (6.6-8.4)</td>
<td>5.7 (5.3-6.0)</td>
<td>5.6 (5.3-5.9)</td>
<td>6.9 (6.5-7.8)</td>
<td>5.8 (5.5-6.1)</td>
<td>7.3 (6.6-8.3)</td>
<td>7.9 (6.6-9.2)</td>
<td>&lt;.001</td>
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<tr>
<td>Medication use</td>
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<tr>
<td>ACEI</td>
<td>968 (19)</td>
<td>434 (12)</td>
<td>339 (38)</td>
<td>24 (23)</td>
<td>53 (28)</td>
<td>30 (50)</td>
<td>14 (45)</td>
<td>60 (48)</td>
<td>14 (54)</td>
<td>&lt;.001</td>
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<tr>
<td>ARB</td>
<td>413 (8)</td>
<td>213 (6)</td>
<td>131 (15)</td>
<td>15 (14)</td>
<td>16 (8)</td>
<td>9 (15)</td>
<td>3 (10)</td>
<td>24 (19)</td>
<td>2 (8)</td>
<td>&lt;.001</td>
<td></td>
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<tr>
<td>MRA</td>
<td>64 (1)</td>
<td>51 (1)</td>
<td>13 (1)</td>
<td>1 (1)</td>
<td>6 (3)</td>
<td>2 (3)</td>
<td>0 (0)</td>
<td>6 (5)</td>
<td>1 (4)</td>
<td>&lt;.001</td>
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<tr>
<td>Statins</td>
<td>574 (11)</td>
<td>222 (6)</td>
<td>196 (22)</td>
<td>14 (13)</td>
<td>51 (27)</td>
<td>20 (33)</td>
<td>12 (39)</td>
<td>47 (38)</td>
<td>12 (46)</td>
<td>&lt;.001</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ACEI, angiotensin converting enzyme inhibitor; AHA, American Heart Association; ARB, angiotensin receptor blocker; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; LDL, low-density lipoprotein; MRA, mineralocorticoid receptor antagonist.

* P values were calculated using χ² for categorical variables, analysis of variance for parametric continuous variables, and Kruskal-Wallis test for nonparametric continuous variables.

b Poor physical activity was defined by AHA 2020 guidelines. Physical activity was considered poor if participant achieved 0 minutes/week moderate intensity or vigorous intensity physical activity.

c Hypertension was defined as systolic blood pressure of 140 mm Hg or greater, diastolic blood pressure of 90 mm Hg or greater, or use of antihypertensive therapy.
affecting the renin-angiotensin-aldosterone system and statins (eTable 4 and eTable 5 in the Supplement).

**Discussion**

In this prospective cohort study of Black adults, the risks of all-cause and CHD mortality were significantly increased with increasing numbers of cardiometabolic conditions (diabetes, stroke, and CHD), with the highest risk among participants with diabetes, stroke, and CHD. For participants with a combination of diabetes, stroke, and CHD, the unadjusted risk of all-cause mortality was increased approximately 10-fold and risk of CHD mortality was increased approximately 43-fold. With adjustment for established mortality risk factors, including systolic blood pressure, eGFR, LDL cholesterol, and HbA1c, risk of all-cause mortality was increased approximately 4-fold and risk of CHD mortality was increased approximately 3-fold. Participants with diabetes, stroke, and CHD had high-risk profiles for all-cause and CHD mortality.

**Table 2. Association of Cardiometabolic Multimorbidity With All-Cause Mortality Among Black Adults in the Jackson Heart Study**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Full cohort</th>
<th>No diabetes, stroke or CHD</th>
<th>Diabetes</th>
<th>Stroke</th>
<th>CHD</th>
<th>Diabetes and stroke</th>
<th>CHD and stroke</th>
<th>Diabetes and CHD</th>
<th>Diabetes, stroke, and CHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>No./total No.</td>
<td>1068/5064</td>
<td>515/3629</td>
<td>297/897</td>
<td>44/104</td>
<td>73/192</td>
<td>31/60</td>
<td>17/31</td>
<td>70/125</td>
<td>21/26</td>
</tr>
<tr>
<td>Crude incidence rate, No. per 1000 person-years (95% CI)</td>
<td>14.79 (13.93-15.70)</td>
<td>9.65 (8.85-0.52)</td>
<td>24.40 (21.78-27.34)</td>
<td>32.95 (24.52-44.28)</td>
<td>29.07 (23.11-36.56)</td>
<td>40.18 (28.25-57.13)</td>
<td>48.02 (29.85-77.25)</td>
<td>48.62 (38.46-61.45)</td>
<td>84.06 (54.80-128.92)</td>
</tr>
<tr>
<td>Model, HR (95% CI)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>NA</td>
<td>1 [Reference]</td>
<td>2.58 (2.24-2.98)</td>
<td>3.53 (2.59-4.80)</td>
<td>3.1 (2.42-3.96)</td>
<td>4.32 (3.01-6.21)</td>
<td>5.08 (3.14-8.24)</td>
<td>5.37 (4.18-7.13)</td>
<td>10.14 (6.55-15.70)</td>
</tr>
<tr>
<td>1</td>
<td>NA</td>
<td>1 [Reference]</td>
<td>1.78 (1.54-2.07)</td>
<td>1.61 (1.17-2.20)</td>
<td>1.76 (1.38-2.26)</td>
<td>2.09 (1.45-3.02)</td>
<td>2.54 (1.56-4.14)</td>
<td>2.7 (2.10-3.47)</td>
<td>4.60 (2.96-7.15)</td>
</tr>
<tr>
<td>2</td>
<td>NA</td>
<td>1 [Reference]</td>
<td>1.50 (1.22-1.85)</td>
<td>1.74 (1.24-2.42)</td>
<td>1.59 (1.22-2.08)</td>
<td>1.71 (1.09-2.68)</td>
<td>2.23 (1.35-3.69)</td>
<td>2.28 (1.65-3.15)</td>
<td>3.68 (1.96-6.93)</td>
</tr>
</tbody>
</table>

Abbreviations: CHD, coronary heart disease; HR, hazard ratio; NA, not applicable.

* Model 0 was unadjusted. Model 1 adjusted for age, sex, education, occupation, smoking, physical activity, alcohol intake, and waist circumference. Model 2 adjusted for model 1 plus systolic blood pressure, estimated glomerular filtration rate, low-density lipoprotein cholesterol, and hemoglobin A1c. Analysis included 4562 participants in model 2 due to missing data on low-density lipoprotein cholesterol level for 4695 participants and on hemoglobin A1c for 4968 participants.

Figure 1. Adjusted Survival Curves for All-Cause and Coronary Heart Disease (CHD) Mortality by Cardiometabolic Multimorbidity in Black Adults

The survival curves were adjusted for age, sex, education, occupation, smoking, physical activity, alcohol intake, waist circumference, systolic blood pressure, estimated glomerular filtration rate, low-density lipoprotein, and hemoglobin A1c.
mortality was increased approximately 14-fold. Thus, a combination of cardiometabolic conditions was associated with significantly increased risk of all-cause mortality and CHD mortality among Black adults, even after adjusting for established cardiovascular risk factors.

Comparing Black adults in the JHS to the predominantly White cohorts in the Emerging Risk Factors Collaboration (ERFC), the crude mortality rate in the referent group free of cardiometabolic morbidities was higher in the JHS, at 9.6 deaths per 1000 person-years, compared with 6.8 deaths per 1000 person-years in the ERFC, while crude mortality rates were higher for each cardiometabolic morbidity (24.4 deaths per 1000 person-years for diabetes, 32.9 deaths per 1000 person-years for stroke, and 3.51 deaths per 1000 person-years for CHD).

**Figure 2. Forest Plots of the Association of Cardiometabolic Multimorbidity With All-Cause and Coronary Heart Disease (CHD) Mortality in Black Adults**

**Table 3. Association of Cardiometabolic Multimorbidity With CHD Mortality in the Jackson Heart Study**

<table>
<thead>
<tr>
<th>Participants</th>
<th>Full cohort</th>
<th>No diabetes, stroke or CHD</th>
<th>Diabetes</th>
<th>Stroke</th>
<th>CHD</th>
<th>Diabetes and stroke</th>
<th>CHD and stroke</th>
<th>Diabetes and CHD</th>
<th>Diabetes, stroke, CHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality, No./total No.</td>
<td>111/5064</td>
<td>30/3629</td>
<td>29/897</td>
<td>2/104</td>
<td>9/192</td>
<td>5/60</td>
<td>6/1</td>
<td>24/125</td>
<td>6/26</td>
</tr>
<tr>
<td>Crude incidence rate, No. per 1000 person-years (95% CI)</td>
<td>1.54 (1.28-1.85)</td>
<td>0.56 (0.39-0.80)</td>
<td>2.38 (1.66-3.43)</td>
<td>1.50 (0.37-5.99)</td>
<td>3.58 (1.86-6.89)</td>
<td>6.48 (2.70-15.57)</td>
<td>16.95 (7.61-37.73)</td>
<td>16.67 (11.17-24.87)</td>
<td>24.02 (10.79-53.46)</td>
</tr>
<tr>
<td>Model, HR (95% CI)*</td>
<td>0</td>
<td>NA</td>
<td>1 [Reference]</td>
<td>4.24 (2.55-7.07)</td>
<td>2.65 (0.63-11.10)</td>
<td>6.39 (3.03-13.46)</td>
<td>11.50 (4.46-29.64)</td>
<td>30.4 (12.65-73.05)</td>
<td>29.77 (17.39-50.96)</td>
</tr>
<tr>
<td>1</td>
<td>NA</td>
<td>1 [Reference]</td>
<td>2.63 (1.16-4.44)</td>
<td>1.00 (0.33-3.27)</td>
<td>3.63 (1.71-7.69)</td>
<td>4.67 (1.79-12.14)</td>
<td>14.23 (5.84-34.56)</td>
<td>13.81 (7.98-23.91)</td>
<td>17.51 (7.17-42.74)</td>
</tr>
<tr>
<td>2</td>
<td>NA</td>
<td>1 [Reference]</td>
<td>1.95 (0.96-3.97)</td>
<td>1.31 (0.31-5.59)</td>
<td>3.51 (1.56-7.90)</td>
<td>5.57 (1.97-15.73)</td>
<td>10.97 (4.12-29.22)</td>
<td>13.47 (6.54-27.74)</td>
<td>13.52 (3.38-54.12)</td>
</tr>
</tbody>
</table>

Abbreviations: CHD, coronary heart disease; HR, hazard ratio; NA, not applicable.

* Model 0 was unadjusted. Model 1 adjusted for age, sex, education, occupation, smoking, physical activity, alcohol intake, and waist circumference. Model 2 adjusted for model 1 plus systolic blood pressure, estimated glomerular filtration rate, low-density lipoprotein cholesterol, and hemoglobin A1c. Analyses included 4562 participants due to missing data on low-density lipoprotein (4695 participants) and hemoglobin A1c (4968 participants).
stroke, and 29 deaths per 1000 person-years for CHD in the JHS vs approximately 16 deaths per
1000 person-years for each condition in the ERFC). In the JHS, crude mortality rates were 40.2
deaths per 1000 person-years for participants with diabetes and stroke, 48 deaths per 1000 person-
years for participants with CHD and stroke, and 48.6 deaths per 1000 person-years for participants
with diabetes and CHD, compared with approximately 32 deaths per 1000 person-years for each
combination in ERFC. Participants with all 3 conditions in the JHS had a crude mortality rate of 84.1
deaths per 1000 person-years compared with approximately 60 deaths per 1000 person-years in
the ERFC. In summary, the Black participants in the JHS had higher crude mortality rates per
individual and combined cardiometabolic morbidity, but the multiplicative increase in risk was similar
due to overall higher risk of mortality among Black participants free of cardiometabolic morbidities
in the JHS. Both the JHS and ERFC included middle-aged participants (mean ages at baseline of 55
years in the JHS vs 52 years in the ERFC). The ERFC included more men than the JHS (57% vs 37%).
The higher crude mortality rates among Black adults is concordant with higher rates of mortality
among Black adults with CHD, stroke, or diabetes.8

**CHD, Diabetes, and Stroke Mortality**

The prevalence of diabetes is increasing, with 14.7% of the US population with diagnosed or
undiagnosed diabetes and higher rates in racial and ethnic minority groups, including Black
populations.19 Individuals with diabetes are at higher risk of cardiovascular and all-cause mortality
than those without diabetes.20 Racial disparities in mortality have been documented, with a 2-fold
higher all-cause mortality in Black compared with White populations,21 although CVD and mortality
rates are lower for Black individuals with equal access to care.22 For instance, among US veterans
with diabetes, Black veterans had a 49% lower prevalence of CVD and a 13% lower incidence of
mortality over 18 months than White veterans,23 which is consistent with data from other insured
populations.22-24 This demonstrates the importance of glycemic and cardiovascular disease risk
factor control, which are known to be less controlled among Black populations.25,26

CVD affects Black populations at an earlier age than White populations, and Black individuals
with CHD have lower long-term survival than White individuals with CHD and higher rates of fatal
CHD (2.2-fold higher for men; 1.6-fold higher for women), which may be mediated by a higher
prevalence of risk factors.27-29 Since the mid-20th century, stroke mortality has decreased by 80%,
but the racial disparity between Black and White adults remains, with 4- to 5-fold higher mortality
among Black compared with White populations.8 The underlying cause of the higher stroke mortality
is not completely known but may be attributable to higher stroke incidence and mortality after
stroke events.8

**Interventions**

The multiplicative increased risk of all-cause and CHD mortality seen in this US Black population is a
call to action to prevent the development of cardiometabolic disease and advance the treatment of
care of those with known cardiometabolic morbidities.4 Over 30 years since the Heckler report,30
and 20 years since the Unequal Treatment report,31 we are still grappling as a society and medical
community with how best to address racial and ethnic disparities in chronic disease and life
expectancy. Much of the discussion on prevention revolves around individual lifestyle change, but
appreciating that individual lifestyle change occurs in the environment and context of a person’s
living situation and is impacted by the social determinants of health (SDOH) is critical to addressing
inequities.32-34 Thus, intervening upstream in the sociopolitical and economic context, including
structural racism and discrimination, accessible quality education and health care, socioeconomic
status, and healthier built environments, could help to improve midstream determinants like
nonmedical health-related social needs (eg, social and community context, social risk, and lived
personal experience), which, through impacting psychological and environmental stressors, as well
as biological and psychological sequelae, would help to improve CVD prevention and outcomes.33
Recent evidence suggests that addressing the SDOH may reduce Black vs White disparities in CVD
risk factors by as much as 50%. Thus, emerging interventions that address SDOH in addition to traditional CVD prevention are critical to cardiovascular equity.

One pillar of equity-based interventions is to address multiple levels of the socioecological model, including through community-engaged and community-based participatory research centered on equity to advance cardiometabolic health equity. More ideal levels of American Heart Association’s Life’s Simple 7 are associated with lower risk of diabetes, heart disease, and stroke. Unfortunately, community-based participatory research to improve all components of Life’s Simple 7 in US Black populations are lacking. The 24-week Black Impact Study focused on health education, physical activity, and addressing social needs to improve Life’s Simple 7 in Black men and showed a significant impact in improving cardiovascular health metrics. The FAITH! trial used an innovative app-based platform to advance Life’s Simple 7. Innovative solutions, such as expansion of equity-based efforts (eg, Black Impact and FAITH!), are urgently needed to advance cardiometabolic health equity. Policy approaches to eradicate structural inequities in historically marginalized communities would catalyze further gains toward eliminating health disparities, as evidenced by the Moving to Opportunity study, in which women using housing vouchers to move to a low-poverty census track had lower rates of class II and III obesity and HbA1c levels more than 10 years later.

Strengths of our study include a large, community-based, socioeconomically diverse, contemporaneous Black cohort with more than 15 years of follow-up to assess mortality. We used validated questionnaires to assess risk factors and a comprehensive documentation of diabetes over time, including fasting glucose, HbA1c, medication use, and self-reported physician diabetes diagnosis. We performed a comprehensive ascertainment of deaths.

Limitations
This study has some potential limitations. First, the participants in the JHS are from 1 geographic area in the southeastern United States recruited from 4 recruitment pools (Atherosclerosis Risk in Communities participants, random selection, family members, and volunteers). Hence JHS participants may not be representative of all Black adults in the US, limiting generalizability. Second, the cardiometabolic morbidities were established at baseline with no adjustment for acquired morbidities over the course of the study. Third, baseline differences existed across the cardiometabolic multimorbidity groups, which we adjusted for in the models, but residual confounding may still exist. Fourth, statistical associations were interpreted without correction for multiple comparisons, as typical multiple comparison corrections assume tests are independent and are too conservative for correlated hypotheses, as have been performed. Fifth, while adjustments were made for socioeconomic status (ie, education and current occupation status) and lifestyle behaviors (ie, smoking and physical activity), we did not comprehensively examine potential mediators and confounders, including SDOH, psychosocial stressors, and lifestyle behaviors. Therefore, some caution is warranted in the interpretation of our study results.

Conclusions
This cohort study reveals a novel association of an increasing number of cardiometabolic multimorbidities with a multiplicative increase in all-cause and CHD mortality risk among Black adults in the US, with a greater magnitude of association for CHD mortality. Given the increasing prevalence of obesity and type 2 diabetes in the US, along with recent increases in cardiovascular mortality, it is imperative to accelerate the development and implementation of preventive interventions to decrease cardiometabolic disease and advance treatment and care among those with cardiometabolic conditions.
ARTICLE INFORMATION
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Obtained funding: Joseph.

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Supervision: Joseph, Wu, Golden.

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REFERENCES


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eTable 4. Association of Cardiometabolic Multimorbidity With All-Cause Mortality Among Black Adults in the Jackson Heart Study
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