Original Investigation

Stroke Incidence and Mortality Trends in US Communities, 1987 to 2011

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IMPORTANCE Prior studies have shown decreases in stroke mortality over time, but data on validated stroke incidence and long-term trends by race are limited.

OBJECTIVE To study trends in stroke incidence and subsequent mortality among black and white adults in the Atherosclerosis Risk in Communities (ARIC) cohort from 1987 to 2011.

DESIGN, SETTING, AND PARTICIPANTS Prospective cohort study of 14 357 participants (282 097 person-years) free of stroke at baseline was facilitated in 4 different US communities. Participants were recruited for the purpose of studying all stroke hospitalizations and deaths and for collection of baseline information on cardiovascular risk factors (via interviews and physical examinations) in 1987-1989. Participants were followed up (via examinations, annual phone interviews, active surveillance of discharges from local hospitals, and linkage with the National Death Index) through December 31, 2011. The study physician reviewers adjudicated all possible strokes and classified them as definite or probable ischemic or hemorrhagic events.

MAIN OUTCOMES AND MEASURES Trends in rates of first-ever stroke per 10 years of calendar time were estimated using Poisson regression incidence rate ratios (IRRs), with subsequent mortality analyzed using Cox proportional hazards regression models and hazard ratios (HRs) overall and by race, sex, and age divided at 65 years.

RESULTS Among 1051 (7%) participants with incident stroke, there were 929 with incident ischemic stroke and 140 with incident hemorrhagic stroke (18 participants had both during the study period). Crude incidence rates were 3.73 (95% CI, 3.51-3.96) per 1000 person-years for total stroke, 3.29 (95% CI, 3.08-3.50) per 1000 person-years for ischemic stroke, and 0.49 (95% CI, 0.41-0.57) per 1000 person-years for hemorrhagic stroke. Stroke incidence decreased over time in white and black participants (age-adjusted IRRs per 10-year period, 0.76 [95% CI, 0.66-0.87]; absolute decrease of 0.93 per 1000 person-years overall). The decrease in age-adjusted incidence was evident in participants age 65 years and older (age-adjusted IRR per 10-year period, 0.69 [95% CI, 0.59-0.81]; absolute decrease of 1.35 per 1000 person-years) but not evident in participants younger than 65 years (age-adjusted IRR per 10-year period, 0.97 [95% CI, 0.76-1.25]; absolute decrease of 0.09 per 1000 person-years) (P = .02 for interaction). The decrease in incidence was similar by sex. Of participants with incident stroke, 614 (58%) died through 2011. The mortality rate was higher for hemorrhagic stroke (68%) than for ischemic stroke (57%). Overall, mortality after stroke decreased over time (hazard ratio [HR], 0.80 [95% CI, 0.66-0.98]; absolute decrease of 8.09 per 100 strokes after 10 years [per 10-year period]). The decrease in mortality was mostly accounted for by the decrease at younger than age 65 years (HR, 0.65 [95% CI, 0.46-0.93]; absolute decrease of 14.19 per 100 strokes after 10 years [per 10-year period]), but was similar across race and sex.

CONCLUSIONS AND RELEVANCE In a multicenter cohort of black and white adults in US communities, stroke incidence and mortality rates decreased from 1987 to 2011. The decreases varied across age groups, but were similar across sex and race, showing that improvements in stroke incidence and outcome continued to 2011.

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Corresponding Author: Josef Coresh, MD, PhD, Departments of Epidemiology, Biostatistics, & Medicine, Johns Hopkins University, 2024 E Monument, Ste 2-630, Baltimore, MD 21287 (coresh@jhu .edu). troke ranks fourth among all causes of death in the United States¹ and is recognized as a leading cause of serious physical and cognitive long-term disability in adults.² Almost 800 000 US residents experience an incident or recurrent stroke each year, and more than 600 000 of these are first-ever events.³ Stroke incidence varies by sex and ethnic group.⁴-6

A decrease in stroke incidence rates in recent decades has been shown in several countries.7-10 However, reports on changes in sex-specific and race-specific incidence and casefatality rates over time are not consistent. The reported ageadjusted incidence of first ischemic stroke is more than twice as high in black as in white participants. The black vs white incidence rate ratio (IRR) is highest at midlife and decreases thereafter.3 Studies from the United States and the United Kingdom have generally shown a decline in stroke incidence for the white population. 5,11,12 Some studies 5,12 have shown no changes in stroke incidence in the black population, whereas others reported a decline in stroke incidence in black women, but not men.11 Trends in incidence and 30-day mortality over several decades in 9152 Framingham Heart Study participants show a decrease in lifetime risk of stroke, along with a decline in 30day mortality in men between 1950 and 2004.4 The ageadjusted rate of mortality after stroke decreased by 37% from 1999 to 2009 in the United States. The decline in mortality was greater for men than women overall, but lower in black men compared with other groups.3

Previous studies from the Atherosclerosis Risk in Communities (ARIC) study cohort found the highest age-adjusted stroke incidence rates among black men, followed by black women, white men, and white women. ¹³ Age-adjusted casefatality rates tended to be higher among black participants and men. We report here long-term temporal trends through 2011 in stroke incidence and subsequent short- and long-term mortality by race, sex and age-group, based on 24 years of follow-up among black and white adults in the ARIC prospective cohort study.

Methods

Study Population

The Atherosclerosis Risk in Communities (ARIC) study is a prospective study of 15 792 residents in 4 US communities aged 45 to 64 years at baseline (1987-1989), 13 designed to investigate variation in cardiovascular diseases by race, sex, location, and date. Informed consent was obtained and procedures were approved by institutional review boards at all centers from which there were participants. Information on cardiovascular risk factors and self-reported race was collected at baseline through interviews and physical examinations. 14 Follow-up was carried out through examinations (1990-1992, 1993-1995, and 1996-1998), annual phone interviews, and active surveillance of discharges from local hospitals.

Ascertainment of Stroke Events and Vital Status

All stroke hospitalizations and deaths from 1987 to 2011 occurring in ARIC participants were identified. Hospital records for possible stroke-related hospitalizations were obtained (*International Classification of Diseases, Ninth Revision [ICD-9*] codes 430-438 until 1997 and codes 430-436 afterwards) and stroke deaths were ascertained through linkage with the National Death Index. Physician reviewers adjudicated all possible strokes and classified them as definite or probable ischemic or hemorrhagic events. ^{13,14}

Definition of Stroke Incidence and Subsequent Short- and Long-term Mortality

An incident stroke was defined as a first definite or probable stroke in a participant with no physician-diagnosed stroke at the baseline interview. Subsequent short- and long-term mortality were defined as hazard of death due to all causes within 30-day, 1-year, and 5-year periods and by the end of follow-up after the incident stroke.

Definition of Covariates

Sociodemographic and behavioral risk factors were selfreported at baseline and updated during follow-up examinations and phone interviews. Smoking status was classified in 3 categories: never, former, or current. Participants were screened for hypertension and diabetes at the study visits, as well as asked for use of medications for these conditions. For hypertension, the average of last 2 of 3 seated blood pressure levels measured after 5 minutes of rest using a random-zero sphygmomanometer was reported. Prevalent hypertension was defined as average systolic of at least 140 mm Hg or average diastolic blood pressure of at least 90 mm Hg, self-reported diagnosis of hypertension by a physician, or use of hypertension medication. Prevalent diabetes was defined by selfreported diagnosis of diabetes by a physician or treatment for diabetes, a fasting glucose level of at least 126 mg/dL, or a casual blood glucose level of at least ≥200 mg/dL. Coronary heart disease (CHD) was defined by self-reported physician diagnosis of myocardial infarction (MI) or coronary revascularization, or by electrocardiographic evidence of a prior MI. Cholesterol-lowering medications use was self-reported and confirmed by review of medications brought to each follow-up visit. Time-varying hypertension and diabetes were updated using annual telephone calls based on self-reported physician diagnosis or use of hypertension or diabetes medication. CHD, cholesterol-lowering medications use, and smoking status were time-varying covariates as well.

Statistical Analysis

Characteristics of participants at baseline (ARIC visit 1, 1987-1989) and follow-up (ARIC visit 4, 1996-1998) were presented for the entire sample as well as for the 55- to 64-year-old group, which overlaps all time periods. Prevalence of time-varying risk factors at baseline and visit 4 was compared using ageadjusted prevalence rate ratios (RRs) and 95% CIs.

Incidence rates (IRs) and 95% CIs of total and ischemic definite or probable stroke per 1000 person-years were calculated and modeled with Poisson regression, stratifying age by 5-year groups and calendar time by 3-year periods corresponding to the ARIC visit intervals. In order to include the most updated data available, the last period was defined as a 4-year

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period (2008-2011). Tables presenting IRs report the 1990-2011 time frame, after recruitment was complete. Incidence rate ratio estimates were adjusted for age and calendar time period in model 1, additionally adjusted for sex and race/center (demographic variables) and hypertension, diabetes, CHD, cholesterol-lowering medications use, and smoking status (timevarying prevalence of risk factors) in model 2, and were computed overall and stratified by race, sex, and age (categorized as younger than 65 years and 65 and older). These subgroup comparisons were preplanned. Interactions between linearly modeled calendar time and race, sex, and age-group were assessed. The adjusted IRRs (95% CIs) were graphed for incident stroke for the age groups of younger than 65 years and also for 65 years and older, with calendar time modeled categorically and linearly.

Thirty-day, 1-year, 5-year and end of follow-up hazard ratios (HRs) and 95% CIs were analyzed using Cox proportional hazards regression models, adjusting for time-dependent prevalent risk-factors. No violations of proportionality were observed. Models stratified by race, sex, and age at stroke incidence (<65 and ≥65 years) were presented and interactions tested.

All participants included in this analysis had complete baseline data for age, sex, race, center, smoking status, hypertension, diabetes, CHD, and cholesterol-lowering medications use. If a participant missed a visit or a follow-up telephone call, the last value for time-varying smoking status, diabetes, hypertension, and cholesterol-lowering medications use was carried forward. Missing data rate was less than 2.5% for each of these variables at the visits and less than 10% at each annual follow-up call. Based on the low rates of missing data for covariates, this analysis used a complete data model. All tests were 2-sided and a *P* value of less than .05 was considered statistically significant. Stata version 13 (StataCorp) was used for data analysis.

Results

Participants' Characteristics

The present analysis included 14 357 ARIC participants after excluding individuals with prevalent stroke (n = 779), individuals who were not black or white (suburban Minneapolis Minnesota and Washington County, Maryland limited to white participants; n = 96), or individuals with missing data on prevalence of CHD (n = 271), diabetes (n = 122), hypertension (n = 76), cholesterol-lowering medications use (n = 79), or smoking status (n = 12). Demographic characteristics of participants and prevalence of cardiovascular risk factors are shown in Table 1. At baseline, mean (SD) age was 54.1 (5.8) years and 55.4% of the participants were women. Hypertension was present in more than one-third of participants, 11.6% had diabetes, 2.8% used cholesterol-lowering medications, and 25.9% reported current smoking. At 9-year follow-up (visit 4), reported use of cholesterol-lowering medications was more than 5 times higher than at baseline (14.3% vs 2.8%). In addition, there was a 40% increase in the proportion of hypertension and diabetes, and 80% increase in CHD prevalence, while the rate of current smoking substantially decreased to 14.7%. Comparison of a subset of participants in the same age-group (55-64 years) at both visits showed a 3.3-fold increase in cholesterol-lowering medications use, but similar proportions of hypertension, diabetes, and CHD in both visits. The rate of smoking was lower and education and income were significantly higher among participants in the younger birth cohort (age 55-64 years at visit 4). Age-adjusted prevalence rate ratios for the entire study period (visit 1-end of follow-up) (PRRs, 95% CIs) for timevarying risk-factors were 0.66 (95% CI, 0.64-0.68) for current smoking, 1.24 (95% CI, 1.23-1.26) for hypertension, 1.36 (95% CI, 1.33-1.39) for diabetes, 1.01 (95% CI, 0.98-1.04) for CHD and 3.03 (95% CI, 2.96-3.09) for cholesterol-lowering medications use.

Stroke Incidence

Definite or probable incident stroke was diagnosed in 1051 of 14 357 participants (7%) during 282 097 person-years of follow-up from 1987 to 2011. In total, 929 participants had incident ischemic stroke and 140 had incident hemorrhagic stroke. Eighteen of the 1051 participants with incident stroke had both a first-ever ischemic and a first-ever hemorrhagic stroke during the study period. Median (interquartile range [IQR]) length of follow-up was 22.5 (17.4-23.5) years. Losses to follow-up were less than 1% annually for the follow-up calls used to determine hospitalization and hence stroke incidence. From recruitment (1987-1989) to the end of follow-up for this study (December 31, 2011), the cumulative loss to follow-up (participants alive with no stroke and censored before December 31, 2011) was 4.4% (638/14 357 participants). Crude incidence rates were 3.73 (95% CI, 3.51-3.96) per 1000 person-years for total stroke, 3.29 (95% CI, 3.08-3.50) per 1000 person-years for ischemic stroke, and 0.49 (0.41-0.57) per 1000 person-years for hemorrhagic stroke. Incidence rates were greater with increasing age and often decreased across calendar time periods within a given age category, with the clearest pattern at age 70 to 79 years, and less clear patterns in other rows including a suggestion of less decline at younger ages and random variation in some small cells (Table 2). Crude incidence rates of ischemic stroke showed similar trends (eTable 1 in the Supplement). The decrease in risk of stroke with time was reflected by the incidence rate ratios (IRRs) shown in Table 3. IRRs per 10-year period were 0.76 (95% CI, 0.66-0.87; absolute decrease of 0.93 per 1000 personyears) adjusted for age and 0.71 (95% CI, 0.62-0.83; absolute decrease of 1.16 per 1000 person-years) adjusted for age, other demographic variables, and time-varying prevalence of riskfactors. Stroke IRRs for a 10-year increase in age were 2.15 (95% CI, 1.93-2.39; absolute increase of 1.82 per 1000 person-years) adjusted for calendar time and 2.03 (95% CI, 1.82-2.26; absolute decrease of 1.72 per 1000 person-years) additionally adjusted for demographic variables and time-varying prevalence of risk factors. Stroke incidence was strongly related to older age, male sex, black race, hypertension, diabetes, CHD, and current smoking, and negatively associated with cholesterol-lowering medications use.

In the stratified analysis (Table 3), age-adjusted IRR per 10-year period was 0.71 (95% CI, 0.59-0.85; absolute decrease of 0.83 per 1000 person-years) for white participants and 0.75 (95%

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Table 1. Characteristics of ARIC Participants at Baseline and at 9-Year Follow-up

	0\	verall ^a	Age 55-64 ^a		
	Visit 1 (1987-1989) (N = 14 357)	Visit 4 (1996-1998) (n = 10 700)	Visit 1 (1987-1989) (n = 6614)	Visit 4 1996-1998) (n = 5866)	
Age, mean (SD), y	54.1 (5.8)	62.8 (5.7)	59.3 (2.9)	59.4 (2.8)	
Women, No. (%)	7955 (55.4)	5974 (55.8)	3448 (52.1)	3384 (57.7)	
Race and center, No. (%)					
White, Minneapolis, Minnesota	3844 (26.8)	3139 (29.3)	1719 (26.0)	1786 (30.5)	
White, Washington County, Maryland	3382 (23.6)	2705 (25.3)	1707 (25.8)	1439 (24.5)	
White, Forsyth County, North Carolina	3331 (23.2)	2446 (22.9)	1637 (24.8)	1213 (20.7)	
Black, Forsyth County, North Carolina	442 (3.1)	241 (2.3)	217 (3.3)	119 (2.0)	
Black, Jackson, Mississippi	3358 (23.4)	2169 (20.3)	1334 (20.2)	1309 (22.3)	
Education, No. (%)					
<high school<="" td=""><td>3300 (23.0)</td><td>2008 (18.8)</td><td>1903 (28.8)</td><td>920 (15.7)</td></high>	3300 (23.0)	2008 (18.8)	1903 (28.8)	920 (15.7)	
High school, GED, or vocational school	5868 (40.9)	4486 (41.9)	2625 (39.7)	2516 (42.9)	
College, graduate, or professional school	5172 (36.0)	4194 (39.2)	2079 (31.4)	2424 (41.3)	
Annual family income, \$ US, No. (%)					
<35 000	7436 (51.8)	5166 (48.3)	3960 (59.9)	2491 (42.5)	
≥35 000	6086 (42.4)	4951 (46.3)	2296 (34.7)	3045 (51.9)	
Not reported	835 (5.8)	583 (5.5)	358 (5.4)	330 (5.6)	
Smoking status, No. (%)					
Never	5995 (41.8)	4384 (41.0)	2691 (40.7)	2385 (40.7)	
Former	4651 (32.4)	4647 (43.4)	2381 (36.0)	2465 (42.0)	
Current	3711 (25.9)	1569 (14.7)	1542 (23.3)	963 (16.4)	
Alcohol consumption, No. (%)					
Never	3577 (24.9)	2188 (20.5)	1755 (26.5)	1102 (18.8)	
Former	2650 (18.5)	3138 (29.3)	1298 (19.6)	1626 (27.7)	
Current	8083 (56.3)	5275 (49.3)	3533 (53.4)	3086 (52.6)	
BMI, median (IQR) ^b	26.9 (24.0-30.4)	28.0 (24.9-31.6)	27.0 (24.1-30.4)	28.2 (25.1-32.0)	
Hypertension, No. (%)	4886 (34.0)	5058 (47.3)	2725 (41.2)	2514 (42.9)	
Blood pressure, mm Hg, median (IQR)					
Systolic	119 (108-131)	125 (114-139)	123 (112-135)	123 (112-136)	
Diastolic	73 (66-80)	71 (64-78)	73 (66-80)	72 (66-79)	
Hypertension medication use, No. (%)	4241 (29.5)	4645 (43.4)	2351 (35.6)	2319 (39.5)	
Diabetes, No. (%)	1662 (11.6)	1761 (16.5)	952 (14.4)	900 (15.3)	
Coronary heart disease, No. (%)	649 (4.5)	884 (8.3)	443 (6.7)	387 (6.6)	
Cholesterol, mg/dL, median (IQR)					
Total	212 (186-239)	199 (176-223)	217 (192-245)	199 (177-223)	
HDL	49 (39-61)	47 (38-59)	48 (39-60)	47 (38-60)	
LDL	135 (111-161)	120 (100-143)	140 (115-166)	120 (100-143)	
Triglycerides	109 (78-156)	122 (89-174)	115 (84-162)	122 (88-172)	
Cholesterol-lowering medication use, No. (%)	404 (2.8)	1527 (14.3)	251 (3.8)	743 (12.7)	

Abbreviations: ARIC, Atherosclerosis Risk in Communities; BMI, body mass index; GED, general equivalency diploma; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein.

CI, 0.61-0.92; absolute decrease of 1.75 per 1000 personyears) for black participants. The decrease in stroke incidence per 10-year period was similar by sex. Analysis by age group showed decreases in incidence over time only in participants older than age 65 years. Age-adjusted IRRs per 10year period for the group younger than 65 years was 0.97 (95% CI, 0.76-1.25; absolute decrease of 0.09 per 1000 personyears) vs 0.69 (95% CI, 0.59-0.81; absolute decrease of 1.35 per 1000 person-years) for the group aged 65 years and older (P = .02 for interaction). Fully adjusted IRRs per 10-year period for the group younger than 65 years was 0.88 (95% CI, 0.67-1.16; absolute decrease of 0.38 per 1000 person-years) vs 0.64 (95% CI, 0.54-0.77; absolute decrease of 1.66 per 1000 personyears) for the group aged 65 years and older (P = .04 for interaction), with linear trends as well as IRRs for 3-year periods compared to 1999-2001 shown in the Figure. Sensitivity analy-

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^b BMI was calculated as weight in kilograms divided by height in meters squared.

^a Missing data rate was less than 2.5% for all variables.

Table 2. Crude Total Stroke Incidence Rates (per 1000 Person-Years) Stratified by 5-Year Age Group and 3-Year Calendar Period of Follow-up

	Calendar Period of Follow-up ^a								
Age Group, y	1990-1992	1993-1995	1996-1998	1999-2001	2002-2004	2005-2007	2008-2011 ^b		
45-49									
IR (95% CI)	1.2 (0.5-2.6) ^c								
Cases/person-years	6/5131	0/411							
50-54									
IR (95% CI)	1.7 (1.1-2.6)	1.2 (0.7-2.2)	0.7 (0.2-2.7) ^c						
Cases/person-years	19/11 386	11/9180	2/2920	0/56					
55-59									
IR (95% CI)	2.4 (1.7-3.6)	1.7 (1.1-2.7)	2.1 (1.4-3.2)	2.9 (1.9-4.5)	3.2 (1.2-8.6) ^c				
Cases/person-years	26/10 664	19/10 904	23/10 832	20/6922	4/1245				
60-64									
IR (95% CI)	3.1 (2.2-4.4)	3.2 (2.3-4.6)	3.2 (2.2-4.5)	2.8 (1.9-4.0)	2.9 (2.0-4.2)	1.1 (0.5-2.7) ^c	5.9 (1.5-23.5)°		
Cases/person-years	30/9706	32/9890	32/10 109	29/10 386	28/9620	5/4498	2/340		
65-69									
IR (95% CI)	3.1 (1.9-5.0)	5.5 (4.1-7.3)	5.5 (4.1-7.3)	3.3 (2.3-4.7)	5.1 (3.8-6.8)	2.9 (2.0-4.2)	2.1 (1.3-3.3)		
Cases/person-years	16/5193	47/8609	49/8935	30/9177	48/9428	28/9616	19/9063		
70-74									
IR (95% CI)		5.2 (2.7-10.0) ^c	6.9 (5.0-9.3)	6.4 (4.8-8.4)	5.5 (4.1-7.5)	4.2 (3.0-5.9)	4.4 (3.3-5.8)		
Cases/person-years	0/29	9/1738	41/5982	50/7829	44/7940	35/8261	50/11 380		
75-79									
IR (95% CI)				10.4 (7.1-15.1)	6.3 (4.6-8.7)	6.7 (5.0-9.0)	6.8 (5.3-8.7)		
Cases/person-years			0/179	27/2603	37/5883	44/6599	62/9146		
80-85									
IR (95% CI)					8.1 (3.0-21.5) ^c	8.3 (5.6,-12.2)	8.8 (6.9-11.1)		
Cases/person-years					4/495	25/3022	69/7866		

Abbreviation: IR, incidence rate.

ses limited to participants aged 60 to 69 years at the start of each follow-up interval, which included ARIC participants during the entire 1990-2011 period, showed similar results to the overall ARIC cohort (eTable 2 in the Supplement).

Mortality

Stroke as the underlying cause of death was reported in 4.8% of all deaths in this study cohort, and in 36.2% of deaths following a stroke. Cumulative mortality rates were 10.47% at the 30-day time point (110/1051 of all incident strokes), 21.24% at 1-year (213/1003 strokes occurring before 2011 [ie, with ≥1 year of follow-up]), 39.83% at 5-year (319/801 strokes occurring before 2007), and 58.42% at the end of follow-up (614/1051 strokes occurring before end of follow-up, December 31, 2011). Mortality rates were higher after an incident hemorrhagic stroke (95/140; 67.86% of patients) than after an incident ischemic stroke (533/929; 57.37%). Loss to follow-up for stroke mortality was 2.4% (25/1051 participants with stroke censored alive before December 31, 2011). HRs for all-cause mortality after stroke at each of these periods are presented in Table 4, and hazard estimates related to covariates are shown in eTable 3 in the Supplement. Overall, age-adjusted mortality after stroke decreased over time (HR, 0.80; 95% CI, 0.66-0.98 per 10-year period; absolute decrease of 8.09 per 100 strokes after 10 years).

Precision increased along with longer follow-up, and the decrease in mortality was mostly accounted for by the decrease for the younger than 65 years age group (HR, 0.65; 95% CI, 0.46-0.93; absolute decrease of 14.19 per 100 strokes after 10 years), but was similar across sex and race, except for a suggestion of steeper decline among white participants in the full followup. Adjustment did not significantly change the results; however, use of cholesterol-lowering medications was associated with lower mortality (HR, 0.69; 95% CI, 0.57-0.84), whereas higher mortality hazards were associated with diabetes (HR, 1.48; 95% CI, 1.25-1.75), CHD (HR, 1.45; 95% CI, 1.22-1.73), and current smoking (HR, 1.37; 95% CI, 1.07-1.75). Test for interaction suggests that differences in 30-day mortality by age may be large, but precision was limited; and that long-term mortality (>5-year) trends may be less steep in black participants. Secondary analysis of the trends in stroke, as the underlying cause of death among all participants, showed a decline over time as well (HR, 0.64; 95% CI, 0.46-0.89 per 10 years).

Discussion

In this cohort of 4 US communities, this study demonstrated a significant decrease in stroke incidence from 1987 to 2011 in

^a Total participants (N = 14 357) with (n = 1051) incident stroke cases over 282 097 person-years of follow-up.

^b Last period includes 4 years of follow-up (2008-2011).

 $^{^{\}rm c}$ Data were based on fewer than 10 cases.

white and black participants and in men and women. However, the decrease in stroke incidence was observed only at ages older than 65 years. Stroke mortality decreased as well. This decrease was generally similar in men and women and by race. In contrast to incidence trends, the steepest stroke mortality decrease was found at younger age.

Comparison With Other Studies

Trends in Stroke Incidence

Substantial decreases in stroke incidence had been reported in the United States before the establishment of the ARIC study. 15,16 Data from the Framingham Study 4 and the Greater Cincinnati/Northern Kentucky Stroke Study⁵ showed the de-

Table 3. Total Stroke Incidence Rates and Incidence Rate Ratios per 10-Year Calendar Time and Age Overall and Stratified by Race, Sex, and Age Group

		Race		S	Sex		Age Group	
	Overall	White	Black	Men	Women	<65 y	≥65 y	
No. of events/ No. of person-years	1051/282 097	626/211 452	425/70 645	518/120 967	533/161 130	312/142 303	739/139 795	
Total crude IR (95% CI) per 1000 person-years	3.73 (3.51-3.96)	2.96 (2.74-3.20)	6.02 (5.47-6.62)	4.28 (3.93-4.67)	3.31 (3.04-3.60)	2.19 (1.96-2.45)	5.29 (4.92-5.68)	
Model 1, IRR (95% CI) ^a							
Calendar time per 10 y	0.76 (0.66-0.87)	0.71 (0.59-0.85)	0.75 (0.61-0.92)	0.76 (0.62-0.91)	0.79 (0.65-0.96)	0.97 (0.76-1.25)	0.69 (0.59-0.81) ^b	
Age per 10 y	2.15 (1.93-2.39)	2.69 (2.32-3.10)	1.81 (1.54-2.13) ^b	2.02 (1.74-2.36)	2.24 (1.92-2.60)	1.97 (1.48-2.63)	2.11 (1.79-2.49)	
Model 2, IRR (95% CI) ^a							
Calendar time per 10 y	0.71 (0.62-0.83)	0.66 (0.55-0.81)	0.80 (0.63-1.00)	0.70 (0.57-0.87)	0.72 (0.59-0.89)	0.88 (0.67-1.16)	0.64 (0.54-0.77) ^b	
Age per 10 y	2.03 (1.82-2.26)	2.42 (2.08-2.80)	1.62 (1.37-1.92) ^b	1.92 (1.64-2.25)	2.14 (1.84-2.51)	1.64 (1.22-2.19)	2.08 (1.76-2.45)	
Sex								
Women	1 [Reference]	1 [Reference]	1 [Reference]			1 [Reference]	1 [Reference]	
Men	1.22 (1.08-1.39)	1.27 (1.07-1.50)	1.21 (0.99-1.48)			1.28 (1.02-1.62)	1.20 (1.03-1.40)	
Race and center								
White, Minneapolis, Minnesota	1 [Reference]	1 [Reference		1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	
White, Washington County, Maryland	1.06 (0.88-1.28)	1.07 (0.88-1.29) ^c		0.98 (0.76-1.27)	1.17 (0.88-1.54)	1.13 (0.76-1.68)	1.03 (0.83-1.28)	
White, Forsyth County, North Carolina	0.97 (0.79-1.18)	0.96 (0.79-1.17) ^c		1.01 (0.78-1.32)	0.91 (0.67-1.24)	1.06 (0.70-1.60)	0.93 (0.74-1.16)	
Black, Forsyth County, North Carolina	1.35 (0.95-1.91)		0.75 (0.53-1.04) ^c	1.50 (0.92-2.45)	1.22 (0.74-2.00)	1.88 (1.03-3.44)	1.17 (0.76-1.80)	
Black, Jackson, Mississippi	1.89 (1.58-2.25)		1 [Reference]	1.72 (1.34-2.20)	2.01 (1.56-2.59)	2.49 (1.77-3.52)	1.66 (1.35-2.04) ^b	
Time-varying risk factors ^d								
Hypertension	2.39 (2.02-2.84)	2.05 (1.68-2.51)	3.45 (2.39-4.96) ^b	2.65 (2.09-3.35)	2.15 (1.68-2.76)	2.57 (1.95-3.39)	2.13 (1.71-2.64)	
Diabetes	1.73 (1.52-1.97)	1.55 (1.30-1.85)	2.01 (1.65-2.46) ^b	1.55 (1.29-1.87)	1.90 (1.58-2.29)	2.57 (2.03-3.25)	1.48 (1.27-1.72) ^b	
Coronary heart disease	1.93 (1.65-2.26)	1.66 (1.36-2.02)	2.43 (1.88-3.13) ^b	1.55 (1.26-1.92)	2.65 (2.10-3.34) ^b	2.91 (2.17-3.91)	1.67 (1.39-2.01) ^b	
Smoking status								
Never	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]	
Former	1.02 (0.88-1.17)	1.05 (0.87-1.26)	1.00 (0.79-1.25)	0.94 (0.76-1.15)	1.11 (0.91-1.35)	1.18 (0.89-1.56)	0.97 (0.82-1.14)	
Current	1.95 (1.64-2.31)	2.12 (1.68-2.69)	1.76 (1.36-2.27)	1.81 (1.40-2.33)	2.02 (1.59-2.56)	2.12 (1.60-2.80)	1.88 (1.50-2.36)	
Cholesterol- lowering medication use	0.85 (0.73-0.99)	1.01 (0.83-1.22)	0.67 (0.51-0.87) ^b	0.86 (0.69-1.08)	0.84 (0.68-1.03)	0.77 (0.54-1.09)	0.93 (0.78-1.10)	

Abbreviations: IR, incidence rate; IRR, incidence rate ratio. MD, Maryland; MN, Minnesota; NC, North Carolina.

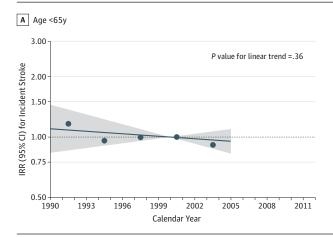
^a Model 1 was adjusted for calendar year and age. Model 2 was adjusted for calendar year, age, demographic variables, and time-varying risk factors.

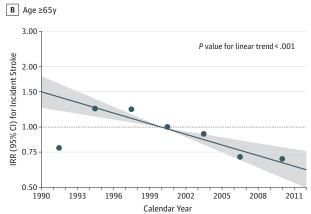
^b The *P* value was less than .05 for interaction in a model containing both groups and interaction terms for all variables.

 $^{^{\}rm c}$ Washington County, MD and Forsyth County, NC were both adjusted for center.

^d Prevalence at baseline as reference.

Figure. Adjusted Stroke Incidence Rate Ratios vs Calendar Time





Models are adjusted for age, sex, race and center, hypertension, diabetes, coronary heart disease, cholesterol-lowering medication use, and smoking. Dots represent adjusted incidence rate ratio point estimates from model run using a categorical calendar time variable, plotted at midpoint of each 3-year

calendar time category, with 1999-2001 as the reference category. The dotted line represents the linear trend in adjusted incidence rate ratios and the shaded area represents the 95% CI with 2000 as the reference point. Models included all study data, but plots exclude time periods in which there were few events.

crease in stroke incidence continued to the early 2000s. Decreasing trends have been reported in Europe, ¹⁷⁻¹⁹ New Zealand, ⁷ Western Australia, ⁸ and Japan. ²⁰ The analysis of this study, which adjusted for calendar time and age simultaneously, showed a significant decrease in stroke incidence from 1987 to 2011 in the ARIC cohort. The decrease in rates was not consistent for all age groups. In fact, no decrease in incidence rates was observed for younger participants (aged <65 years). This is consistent with a study from Sweden, ²¹ which reported a decrease in stroke incidence limited to older ages as well as with other reports of a lower mean age at stroke. ^{22,23}

Data from the Greater Cincinnati/Northern Kentucky Stroke Study showed a significant decrease in stroke incidence in 2005, when compared with 1993-1994 and 1999, driven by a decrease in incidence in white participants only. In ARIC, the decrease in stroke incidence was similar in black and white participants. Among black participants, discordance in trend estimates across studies could be due to differences in risk factors distribution in geographically diverse communities. The ARIC data provided new evidence that at least among some black communities in the South, stroke incidence had declined from 1987 to 2011. Similarity by sex in this study was consistent with previous reports on US stroke trends. In the South of the stroke incidence of the stroke trends.

Trends in Mortality After Stroke

Mortality after stroke in ARIC decreased by approximately 10% to 20% over time, with much of the decrease accounted by a steeper decline at age younger than 65 years compared with little decline at age older than 65 years. Previous reports have not been consistent. Data from the Framingham Study showed a significant decrease in case-fatality rate from 25% to 14% between 1950 and 2004 in men, but no significant changes in women. In Minneapolis-St. Paul, stroke mortality substantially declined during the 1980s. In Oxfordshire, United Kingdom and Perth, Australia, no changes in stroke case-fatality were observed in the last decades, while a 40% de-

cline between 1981-1982 and 2002-2003 was reported in Auckland, New Zealand. ²⁵ More recent data were only available for Denmark, where case-fatality rate decreased by approximately 45% from 1994-1998 to 2009-2011. ²⁶ Mortality due to stroke as the underlying cause of death showed a similar decline to the 37% decline from 1999 to 2009 reported by the Centers for Disease Control and Prevention. ¹ Within ARIC, mortality after stroke declined at younger age while stroke incidence declined at older age.

Potential Reasons for the Decrease in Stroke Incidence and Mortality

More successful control of risk factors in the last decades (mainly hypertension control starting in the 1970s and later hypertension treatment combined with smoking cessation, control of diabetes and dyslipidemia, and treatment of atrial fibrillation) may have resulted in lower stroke incidence and less severe strokes,27 which may account for the observed lower mortality rates. 25 In the cohort for this study, age-adjusted rates of hypertension and diabetes increased between ARIC visits. Use of cholesterol-lowering medications, which decreased stroke risk and mortality in trials^{28,29} and showed similar associations in ARIC, increased. In contrast to hypertension and diabetes, current smoking decreased, so the overall effect of adjustment for prevalent risk factors was relatively small; however, this study could not quantify the intensity of treatment for risk factors. In addition to better control of risk factors, the use of reperfusion therapy for acute ischemic stroke has increased since treatment with tissue plasminogen activator was approved in the United States in 1996 and postacute management strategies have improved over time.

Factors related to short- and long-term mortality after stroke differ. Comorbidities and factors associated with atherosclerotic vascular disease have been shown to predict long-term mortality, whereas stroke characteristics have been associated with short-term mortality.³⁰ The increased hazards

Table 4. Total Cumulative Incidence and Mortality Risk Estimates of All-Cause Mortality After Stroke, at 30 Days, 1 Year, 5 Years, and End of Follow-upa

		Race		Sex		Age Group	
	Overall	White	Black	Men	Women	<65 y	≥65 y
30-d Mortality, No. of	deaths (n = 110)/N	o. of strokes until De	ecember 31, 2011 (ı	n = 1051)			
No. of events/ No. of person-months	110/960	71/569	39/391	47/479	63/481	34/283	76/677
Crude 30-d cumulative incidence (95% CI)	0.10 (0.09-0.12)	0.11 (0.09-0.14)	0.09 (0.07-0.12)	0.09 (0.07-0.12)	0.12 (0.09-0.15)	0.11 (0.08-0.15)	0.10 (0.08-0.13)
HR (95% CI) per 10 year	ars calendar time of	stroke incidence					
Age adjusted	1.12 (0.73-1.71)	1.31 (0.77-2.26)	0.80 (0.39-1.64)	1.16 (0.61-2.17)	1.05 (0.59-189)	0.57 (0.24-1.36)	1.42 0.81-2.49) ^b
Fully adjusted	1.11 (0.71-1.75)	1.32 (0.75-2.33)	0.81 (0.37-1.78)	1.12 (0.57-2.19)	1.20 (0.64-2.24)	0.48 (0.19-1.21)	1.49 (0.83-2.67) ^b
1-y Mortality, No. of d	eaths (n = 213)/No.	of strokes occurring	g before 2011 (n = 1	1003)			
No. of events/ No. of person-years	213/841	123/497	90/344	99/422	114/419	57/267	156/574
Crude 1-y cumulative incidence (95% CI)	0.21 (0.19-0.24)	0.21 (0.18-0.24)	0.22 (0.18-0.26)	0.20 (0.17-0.24)	0.23 (0.19-0.26)	0.18 (0.14-0.23)	0.23 (0.20-0.26)
HR (95% CI) per 10 year	ars calendar time of	stroke incidence					
Age adjusted	0.87 (0.63-1.19)	0.83 (0.54-1.27)	0.84 (0.52-1.38)	0.81 (0.52-1.28)	0.90 (0.58-1.41)	0.60 (0.32-1.14)	0.94 (0.64-1.39)
Fully adjusted	0.87 (0.62-1.22)	0.86 (0.54-1.36)	0.84 (0.50-1.42)	0.75 (0.45-1.23)	1.03 (0.64-1.66)	0.52 (0.26-1.04)	0.97 (0.64-1.47)
5-y Mortality, No. of d	eaths (n = 319)/No.	of strokes occurring	g before 2007 (n = 8	301)			
No. of events/ No. of person-years	319/2889	164/1664	155/1225	158/1500	161/1389	105/1157	214/1732
Crude 5-y cumulative incidence (95% CI)	0.40 (0.37-0.43)	0.37 (0.33-0.42)	0.44 (0.39-0.49)	0.37 (0.34-0.44)	0.41 (0.36-0.46)	0.34 (0.29-0.40)	0.44 (0.39-0.48)
HR (95% CI) per 10 year	ars calendar time of	stroke incidence					
Age adjusted	0.87 (0.65-1.16)	0.79 (0.52-1.20)	0.85 (0.57-1.29)	1.07 (0.71-1.63)	0.69 (0.46-1.03)	0.63 (0.40-0.99)	1.05 (0.71-1.55)
Fully adjusted	0.96 (0.70-1.31)	0.98 (0.63-1.52)	0.89 (0.57-1.39)	1.19 (0.76-1.87)	0.76 (0.49-1.18)	0.62 (0.37-1.03)	1.18 (0.77-1.80)
End of follow-up mort	ality, No. of deaths (n = 614)/No. of str	okes occurring until	December 31, 2011	(n = 1051)		
No. of events/ No. of person-years	614/6120	344/3552	270/2569	307/3212	307/2908	187/2730	427/3360
Crude 10-y cumulative incidence (95% CI)	0.60 (0.56-0.63)	0.58 (0.53-0.62)	0.62 (0.57-0.67)	0.58 (0.53-0.63)	0.61 (0.56-0.66)	0.49 (0.43-0.55)	0.66 (0.62-0.70)
HR (95% CI) per 10 year	ars calendar time of	stroke incidence					
Age adjusted	0.80 (0.66-0.98)	0.68 (0.51-0.90)	0.91 (0.68-1.23)	0.78 (0.58-1.03)	0.82 (0.62-1.09)	0.65 (0.46-0.93)	0.94 (0.73-1.22)
Fully adjusted	0.90 (0.72-1.11)	0.77 (0.57-1.07)	1.01 (0.73-1.39)	0.84 (0.62-1.16)	0.92 (0.68-1.25)	0.73 (0.49-1.08)	1.02 (0.77-1.34)

Abbreviation: HR, hazard ratio.

of mortality at 5 years and over after stroke incidence observed in association with diabetes and CHD support these previous findings.

In contrast with the greater decline in stroke incidence at age older than 65 years, the decrease in short- and long-term mortality, adjusted for age and other time-varying prevalent risk factors, was driven by reductions at age younger than 65 years rather than at age of 65 years and older. Less improvement in mortality after strokes at older ages may be related to estimates that withdrawal of care accounted for approximately 40% of the observed early stroke excess mortality among older patients compared with younger ones.31

Strengths and Limitations

The prospective ARIC cohort study allows for collection of accurate data on time-varying prevalence of cardiovascular risk factors, stroke incidence, and mortality in 4 US communities. The prolonged follow-up of this large biracial cohort provided detailed information for the study of stroke trends by sex, age-group, race, and study center. ARIC was designed to

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^a Baseline risk for attributable risk calculations is a cumulative mortality of 0.09, 0.19, 0.37 and 0.54 at 30 days, 1 year, 5 years, and 10 years for a stroke patient aged 65 years in 2000. Fully adjusted models were adjusted for age, sex, race and center, hypertension, diabetes, smoking, and cholesterol-lowering medication use

 $^{^{\}rm b}$ P < .05 for interaction in a model containing both groups and interaction terms for all variables (for race interactions, a difference in the age association with mortality by race contributed to differences in the race calendar time by race interaction).

allow adequate power to make comparisons across white and black races; however, comparisons between races are confounded by geography. Complete adjudication of stroke events and the consistency in methods across study centers and calendar time are important strengths of this study. Still, some change over time in the classification of cases was possible due to increasing availability of computed tomography and magnetic resonance imaging.

Declines in stroke incidence likely reflect changes in lifetime risk factor levels, whereas improved survival may be attributed to time trends in medical care, in stroke severity, or both. To allow for updating over the full follow-up period, risk factors are self-reported in ARIC. Factors beyond the major cardiovascular risk factors leading to the observed trends, including intensity of treatment, were not examined in this study. Analyses were conducted for total stroke, whereas supplementary analysis by stroke type was limited to ischemic stroke due to the small number of hemorrhagic events. Also, this study focused on adjudicated stroke and did not include transient

ischemic attack for which validation was not possible. As a closed cohort, ARIC is limited in having fewer older participants at early follow-up and fewer younger participants in later follow-up, and for some estimates precision is limited.

Conclusions

In a large multicenter cohort of black and white adults in US communities, validated total stroke incidence rates decreased from 1987 to 2011. The decline in incidence was similar in white and black participants, as well as in men and women, but was seen only at age 65 years and older, with younger participants experiencing stable stroke incidence rates. Mortality also decreased during the last 2 decades, mostly due to a decrease among participants younger than age 65 years. Thus, the overall decline in stroke mortality is a combination of different decreases in stroke incidence and mortality across age.

ARTICLE INFORMATION

Author Contributions: Drs Coresh and Koton had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Koton, Schneider, Rosamond, Coresh.

Acquisition, analysis, or interpretation of data: Koton, Schneider, Rosamond, Shahar, Sang, Gottesman.

Drafting of the manuscript: Koton, Coresh.
Critical revision of the manuscript for important
intellectual content: Koton, Schneider, Shahar, Sang,
Gottesman, Rosamond, Coresh.

Statistical analysis: Koton, Schneider, Sang, Coresh.

Obtained funding: Rosamond, Coresh.

Administrative, technical, or material support: Sang.

Study supervision: Koton, Coresh.

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