CLINICAL/SCIENTIFIC NOTE

Association of Modifiable Risk Factors Measured With the Brain Care Score and Incident Stroke in the REGARDS Cohort

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Abstract

Objectives

Stroke disproportionately affects Black individuals in the United States. We aimed to assess differences between Black and White individuals in the associations between health-related behaviors, measured with the Brain Care Score (BCS; a tool encompassing 12 modifiable risk factors), and incident stroke.

Methods

We analyzed data from REGARDS, a prospective US cohort of Black and White adults aged 45 years or older. Participants who were stroke free at baseline with complete BCS data were included. We assessed the BCS (range: 0–21; higher indicating healthier behaviors) and its associations with incident stroke in Black vs White individuals. Cox proportional hazard models were stratified by race (Black vs White) and adjusted for demographics and socioeconomic factors. Effect sizes were compared using Z-statistics.

Results

Among 10,861 participants (30.6% Black, 57.4% female, mean age: 63.2 years), 696 strokes occurred over a median of 15.9 years. A five-point higher BCS was associated with lower stroke risk in both groups, with larger magnitude among Black vs White individuals (HR: 0.47 [95% CI 0.36–0.61] vs 0.75 [95% CI 0.62–0.92]; Z-statistic p value = 0.0045).

Discussion

The BCS is associated with incident stroke in a biracial US cohort and shows larger effect sizes within Black compared with White individuals, suggesting that BCS improvement may yield greater stroke prevention benefits for Black populations.

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Supplementary Material

Introduction

Stroke disproportionately affects Black individuals in the United States, who face a 2–3 times higher risk between the ages of 45 and 65 years compared with White individuals[1-3] and are reported to experience greater post-stroke disability.[4] These disparities are largely attributed to socioeconomic inequities, including differential access to care and suboptimal control of modifiable risk factors.[1,2,4-6] Notably, over 80% of strokes in Black individuals in the United States are attributable to modifiable risk factors, emphasizing the potential for targeted prevention efforts.[7]

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The Brain Care Score (BCS) was developed as a comprehensive tool to address 12 modifiable risk factors associated with stroke, dementia, and late-life depression.[8] Previous validation in over 400,000 UK Biobank participants (with over 95% of participants having a self-reported White ethnicity) demonstrated that a higher BCS, indicating better brain care, is associated with a lower incidence of stroke,[9] reduced burden of cerebral small vessel disease,[10] and decreased risk of other age-related brain diseases, including dementia and late-life depression.[11]

In this study, we examined differences between Black and White individuals in the association between health-related behaviors—captured by the BCS—and incident stroke in a biracial US cohort.

Methods

Study Population

The Reasons for Geographic and Racial Differences in Stroke (REGARDS) study is a prospective US cohort of 30,239 adults aged 45 years or older, with robust representation of Black individuals (~42%).[12] Using a commercial database, participants were recruited by mail and telephone (2003–2007). Participants self-reported race and sex during enrollment. Baseline data were collected by computer-assisted telephone interview (CATI) and in-home visits. Participants or proxies are contacted every 6 months by CATI to identify cerebrovascular and other health events.[12] For this study, participants who were stroke free at baseline with complete BCS data were included.

Derivation of the BCS

The development of the BCS has been described elsewhere.[8] In brief, it contains 12 modifiable risk factors of stroke, dementia, and late-life depression across 3 domains: (1) physical (blood pressure, blood sugar, cholesterol, and BMI), (2) lifestyle (nutrition, alcohol consumption, smoking, physical activity, and sleep), and (3) social-emotional (stress, social relationships, and meaning in life). Scores range from 0 to 21, with higher scores indicating better brain care. Proxies for all BCS components in the REGARDS cohort were identified through author consensus (J.R.S., R.W.P.T., B.Y.Q.T.; eTable 1).

Outcome

The primary outcome was incident stroke (ischemic and hemorrhagic, including subarachnoid hemorrhage). Suspected events were identified through telephone follow-ups and confirmed by physician-adjudicated medical record reviews. Proxy-reported events were included for deceased or incapacitated participants. Stroke adjudication methods in the REGARDS study have been documented elsewhere.[13] Strokes occurring through October 2022 were included.

Statistical Analysis

Baseline characteristics were summarized using appropriate descriptive statistics. Only participants with a complete BCS were included for analyses.[10,11,14] The associations between the BCS and incident stroke were assessed using race-stratified Cox proportional hazard models. Exploratory subtype models (ischemic vs hemorrhagic) were fit, although hemorrhagic analyses were underpowered. Hazard ratios (HRs) and 95% CIs were calculated for a five-point higher BCS, which is considered a clinically relevant (40% lower stroke risk[14]) and achievable brain health improvement, for example, by (1) improving diet and lowering blood pressure or (2) reducing alcohol and quitting smoking.[14] Models were adjusted for a priori selected confounders, including age, sex, socioeconomic factors (income, education, insurance), and living situation (urban vs rural).[1,14,15] Proportional hazards were assessed using scaled Schoenfeld residuals.

Differences in effect sizes between Black and White participants were assessed using Z-statistics from adjusted Cox models. A cause-specific Cox model assessed stroke risk, treating death as a censoring event and adjusting for the aforementioned confounders.

Sensitivity Analyses

We conducted the following sensitivity analyses: (i) addressing missing BCS components using multiple imputation with chained equations and (ii) excluding BCS components available only during follow-up (sleep, social relationships, and meaning in life).

All analyses were conducted using R 4.4.2, and statistical significance was defined as a 2-tailed p value <0.05. The article was written following the STROBE guidelines.

Standard Protocol Approvals, Registrations, and Patient Consents

REGARDS was approved by the institutional review boards (IRBs) of all participating centers (coordinating IRB: University of Alabama at Birmingham, FWA00005960). All participants provided written informed consent.

Data Availability

REGARDS data are not publicly available because of ethical and legal restrictions. To abide by its obligations with NIH/NINDS and the Institutional Review Board of the University of Alabama at Birmingham, REGARDS facilitates data sharing through data use agreements. Any investigator is welcome to access the REGARDS data, including statistical code, through this process. Requests for data access may be sent to regardsadmin@uab.edu.

Results

Among 30,183 participants, 10,861 participants were stroke free at baseline and had a complete BCS (eFigure 1). Included participants had a mean age of 63.2 (SD: 8.4) years, 57.4% (N = 6,234) were female, and 30.6% (N = 3,319) were Black (Table 1). Excluded participants were older, were more often

male, had lower income and education levels, and had slightly lower insurance coverage (eTable 2).

The BCS ranged from 0 to 21 (eTables 3 and 4), with a mean of 14.4 (SD: 2.4). Black individuals had significantly lower baseline BCS compared with White individuals (13.8 [SD: 2.5] vs 14.7 [SD: 2.3], $p < 0.001$; Figure 1).

Over a median of 15.9 years (Q1–Q3: 13.5–17.5), 696 incident strokes occurred (6.2% overall; 6.2% in both Black [N = 216] and White [N = 480] participants; Figure 2). Cox model diagnostics were satisfactory; in the White model, sex showed borderline nonproportionality ($p = 0.045$) without affecting the BCS estimate (eTable 5). A five-point increase in BCS was associated with a 53% lower risk of stroke in Black individuals (HR: 0.47; 95% CI 0.36–0.61; c-statistic: 0.695 [SE = 0.016]) and 25% lower risk in White individuals (HR: 0.75; 95% CI 0.62–0.92; c-statistic: 0.670 [SE = 0.012]). The magnitude of the association was significantly stronger among Black individuals (Z-statistic; $p = 0.0045$). Ischemic stroke models showed consistent findings; hemorrhagic models were imprecise and nonsignificant (eTable 6).

Using the cause-specific Cox model, a five-point higher BCS was associated with a 53% lower stroke risk in Black individuals (HR:0.47 [95% CI 0.36–0.61]) and 27% lower risk in White individuals (HR:0.73 [95% CI 0.60–0.89]). Excluding variables not obtained at baseline, the following associations remained: 49% lower risk in Black individuals (HR: 0.51 [95% CI 0.41–0.63]) and 32% lower risk in White individuals (HR: 0.68 [95% CI 0.58–0.80]). Sensitivity analyses using multiple imputation showed nonsubstantial differences (eTable 7).

Discussion

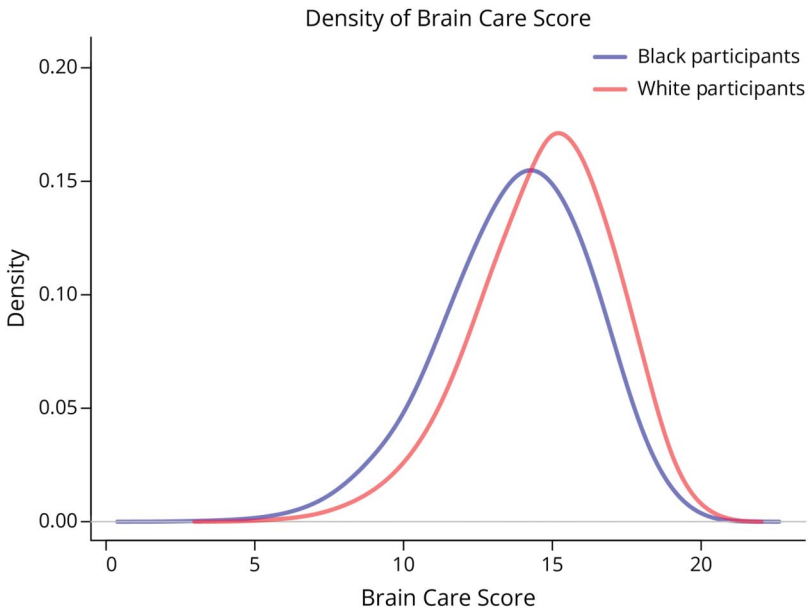
In this study, we demonstrated that the BCS is associated with stroke in a multi-ethnic US cohort and exhibits larger effect sizes for the association with future stroke among Black

Table 1 Baseline Characteristics

Baseline variables	Total, N = 10,861	Black, N = 3,319	White, N = 7,542
Age, mean (SD)	63.2 (8.4)	62.3 (8.1)	63.6 (8.5)
Sex, N (%)			
Female	6,238 (57.4)	2,276 (68.6)	3,962 (52.5)
Male	4,623 (42.6)	1,043 (31.4)	3,580 (47.5)
Income, N (%)			
Less than $20,000	1,215 (11.2)	637 (19.2)	578 (7.7)
$20,000–34,000	2,356 (21.7)	856 (25.8)	1,500 (19.9)
$35,000–74,000	3,777 (34.8)	1,118 (33.7)	2,659 (35.3)
More than $75,0000	2,387 (22.0)	423 (12.7)	1,964 (26.0)
Refused	1,126 (10.4)	285 (8.6)	841 (11.2)
Education, N (%)			
Less than high school	658 (6.1)	348 (10.5)	310 (4.1)
High school	2,482 (22.9)	866 (26.1)	1,616 (21.4)
Some college	2,911 (26.8)	980 (29.5)	1,931 (25.6)
College and above	4,810 (44.3)	1,125 (33.9)	3,685 (48.9)
Rural/urban[a], N (%)			
Small rural	658 (6.7)	113 (3.7)	545 (8.1)
Large rural	1,143 (11.7)	256 (8.4)	887 (13.2)
Urban	7,767 (79.2)	2,668 (87.2)	5,099 (75.6)
Isolated	237 (2.4)	24 (0.8)	213 (3.2)
Insurance, N (%)			
Yes	10,268 (94.6)	3,005 (90.6)	7,263 (96.3)
No	591 (5.4)	313 (9.4)	278 (3.7)

[a] The total number of participants for the rural/urban variable differs because of missing responses (total, N = 9,805; Black, N = 3,061; White, N = 6,744).

Figure 1 Density of the BCS Stratified into Black and White Participants

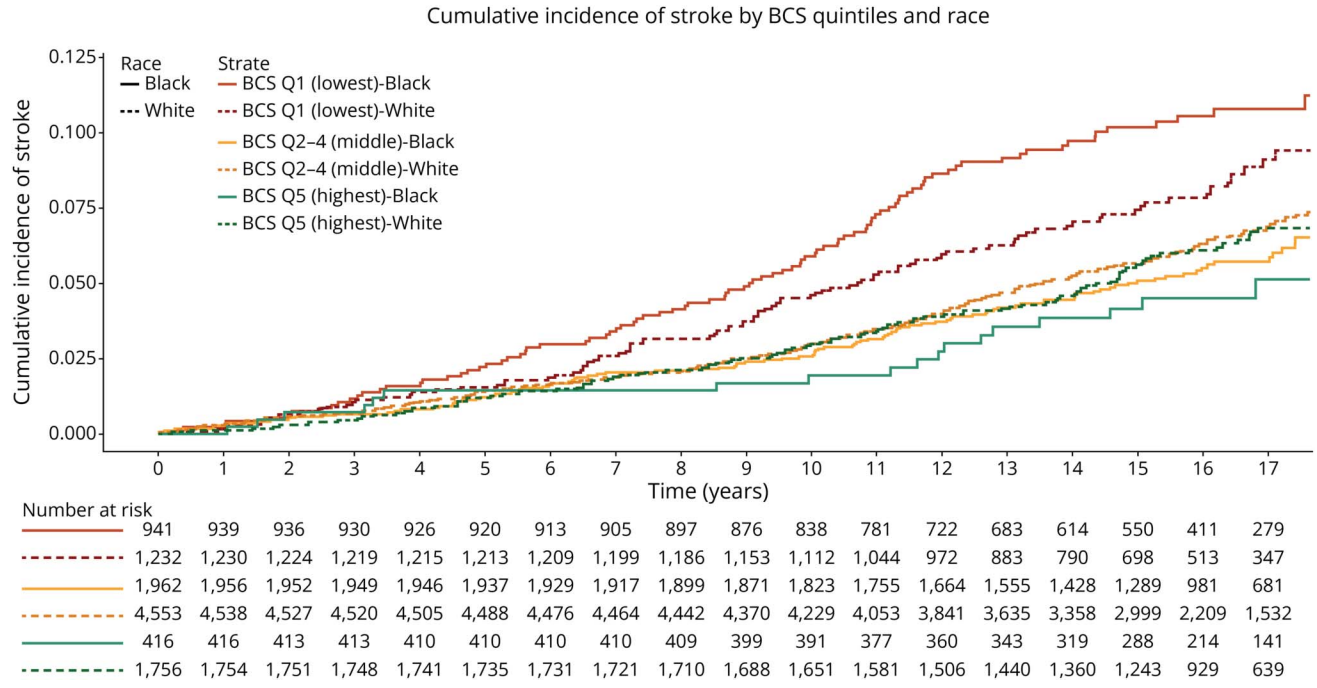


Black participants are denoted with the blue line, and White participants are denoted with the red line. The mean BCS for Black participants was 13.8 (SD 2.5). The mean BCS for White participants was 14.7 (SD 2.3). BCS = Brain Care Score.

compared with White individuals. This study confirms the association of BCS with incident stroke[11,14] and highlights its potential use in addressing racial disparities.

Black individuals were found to have a significantly lower BCS compared with White individuals, reflecting the previously described higher burden of vascular risk factors.[2] Similar disparities are observed using comparable cardiovascular metrics, such as Life's Simple Seven (LS7), where Black participants also exhibit significantly less favorable scores.[15] However, our study also identified racial differences in the magnitude of the association between the BCS and stroke

Figure 2 Cumulative Incidence of Stroke



The plot is stratified by (1) BCS quintiles: Q1, lowest BCS (range 0–12) in red; Q2–Q4, middle BCS (range 12–16) in yellow; and Q5, highest BCS (range 16–21) in green) and (2) race: Black participants indicated as solid lines and White participants indicated as dotted lines. BCS = Brain Care Score.

risk, unlike LS7.[15] This might be due to BCS including a more comprehensive list of modifiable risk factors, including alcohol consumption, sleep, and social-emotional factors.[8,16]

Some limitations should be considered when interpreting our results. Selection bias may have been introduced by excluding participants without complete BCS data. Statistically significant demographic differences between included and excluded participants limit external generalizability of our findings. However, we found nonsubstantial differences in sensitivity analyses using multiple imputation. Furthermore, not all BCS components were available at baseline; 3 factors—sleep, social relationships, and meaning in life—were included only at follow-up years later, potentially introducing reverse causality. However, sensitivity analyses excluding these follow-up factors yielded consistent results. Finally, although we adjusted for demographic differences and socioeconomic factors previously linked to stroke disparities, residual confounding or genetic factors may still influence the results.[1,2,15]

In conclusion, the BCS is associated with stroke in this biracial cohort and shows larger effect sizes among Black compared with White individuals. Given its potential to significantly affect stroke risk in more vulnerable groups, the BCS represents a promising tool for reducing disparities and improving population health.

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Author Contributions

E.M. Reinders: drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data. J.R. Senff: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data. R.W.P. Tack: drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data. B.Y.Q. Tan: drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data. T.N. Kimball: drafting/revision of the manuscript for content, including medical writing for content; study concept or design. S. Prapiadou: drafting/revision of the manuscript for content, including medical writing for content; study concept or design. M.-G. Duperron: drafting/revision of the manuscript for content, including medical writing for content; study concept or design. D. Choksi: drafting/revision of the manuscript for content, including medical writing for content; study concept or design. K. Sherman: drafting/revision of the manuscript for content, including medical writing for content; study concept or design. S. Mendez: drafting/revision of the manuscript for content, including medical writing for content; study concept or design. R. Moran: drafting/revision of the manuscript for content, including medical writing for content; study concept or design. A. Tinoble: drafting/revision of the manuscript for content, including medical writing for content; study concept or design. M. Maulik: drafting/revision of the manuscript for content, including medical writing for content; study concept or design. V.J. Howard: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design. R.M. Lazar: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design. C.D. Anderson: drafting/revision of the manuscript for content, including medical writing for content; study concept or design; analysis or interpretation of data. J. Rosand: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design. G. Howard: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data. S. Dhillon Singh: drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data.

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