ARIC Manuscript Proposal Form

ARIC Publication Admin Use Only

Publication Committee Review Date: **1/27/2026**
ARIC Manuscript Proposal Number: **#4809**

1.a. Full Title:

Associations of Brain Care Score Trajectories with Incident Stroke and Dementia in the ARIC Study

b. Abbreviated Title (Length 26 characters):

BCS and Stroke/Dementia

2. Writing Group [please provide a middle initial if available; EX: Adam L Williams]:

Writing group members: Evy M Reinders MD (first author), Jonathan Rosand MD MSc, Sanjula Singh MD PhD (co-senior author), Christopher D Anderson MD MSc, William C.P. Brebner MD, Mariya Vodyanyk MA, Andrew Lim, Niklas Jung, Alexa Walter PhD, Andrea L.C. Schneider MD PhD (co-senior author), Sabrina Abbruzzese MS (data analyst), James Russell Pike MBA, Rebecca F. Gottesman MD PhD, Michelle C. Johansen MD PhD, Others Welcome

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. EMR **[please confirm with your initials electronically or in writing]**

First author [please provide a middle initial; EX: Adam L Williams]:

Evy	M.	Reinders
First name	Middle initial	Last name

Address: 399 Revolution Drive
Somerville, MA 02145

Phone: 617-309-0873
E-mail: ereinders@mgh.harvard.edu

ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (The ARIC author should be involved enough in ARIC to be able to point the lead author to appropriate ancillary study PIs and to be able to search ARIC manuscript proposals if the lead author doesn't have the access needed to do such a search).

Name: Andrea L.C. Schneider MD PhD

Address: 3535 Market Street, Room 724
Philadelphia, Pennsylvania 19335

Phone: 443-827-2352
E-mail: Andrea.Schneider@pennmedicine.upenn.edu

3. Timeline:

The proposed analysis will utilize currently available data. Analysis, abstract submission, and manuscript creation will take place in the 6-12 months following manuscript proposal approval.

4. Rationale:

A large body of research indicates that over 80% of stroke-related disability-adjusted life years globally are attributable to modifiable risk factors.[1] Furthermore, an estimated 45% of dementia cases could be prevented by adequate risk factor control.[2] The Brain Care Score (BCS) was developed as a tool to engage individuals in addressing 12 shared modifiable risk factors for dementia and stroke. The BCS consists of four physical components (blood pressure, Hb1Ac, body mass index, cholesterol), five lifestyle factors (nutrition, physical activity, smoking, alcohol, sleep), and three social-emotional factors (relationships, stress, and purpose in life).[3] To assess the prospective validity of the BCS, Cox proportional hazard models were performed amongst approximately 400,000 UK Biobank participants with a median follow-up of 13 years.[4] Statistically significant and clinically meaningful associations between an increased BCS at baseline and decreased incidence of stroke and dementia were found: a five-point higher BCS at baseline was associated with a 48% (HR: 0.52 [95% CI: 0.44–0.61]) lower incidence of stroke and a 59% (HR: 0.41 [95% CI:0.28–0.60]) lower risk of dementia among individuals aged ≤50 years at baseline, with similar findings among older aged individuals.[4] In a subgroup analysis using polygenic risk scores for stroke and APOE status for dementia, a higher BCS was associated with a decreased risk of stroke and dementia across all genetic risk strata.[5] A 5-point higher BCS at baseline was associated with neuroimaging markers of small vessel diseases (SVD), including with a 25% lower white matter hyperintensity volumes, 18% higher fractional anisotropy, and 9% decreased mean diffusivity.[6] The validation of the BCS' associations with stroke has been replicated in diverse populations, showing similar risk reductions in the Women's Health Study (43% [HR: 0.57, 95%CI:0.47-0.68] lower risk of stroke or TIA)[7], COSMOS database (36% [HR: 0.64, 95%CI:0.48-0.84] lower risk of stroke)[8], and REGARDS Cohort (53% [HR: 0.47, 95%CI:0.36–0.61] lower risk of stroke in Black and 25% [HR:0.75, 95%CI:0.62–0.92] lower risk of stroke in White individuals; in press).

These validation studies of the BCS have relied almost exclusively on cross-sectional BCS measurements, demonstrating that a higher BCS at a single timepoint is associated with substantially lower risk of incident stroke, dementia, cognitive impairment, and small vessel disease across multiple cohorts. However, the modifiable risk factors in the BSC fluctuate substantially over the life course, and individuals frequently transition between risk strata as their health behaviors and clinical factors change.[2,9,10] As the BCS is intended not only as a risk-assessment tool but also as an ongoing behavioral and clinical monitoring framework, it is essential to determine whether changes in BCS over time—rather than baseline levels alone—are

associated with long-term brain health outcomes. The ARIC Study offers a uniquely powerful setting for this longitudinal validation. ARIC's extended longitudinal depth enables evaluation of i) trajectories of BCS scores across life stages and ii) how improvements or declines in BCS are associated with subsequent risk of stroke and dementia. This work will give insight into the critical timing of modifiable risk factor control. Longitudinal validation in ARIC will therefore address key unanswered questions about the temporal dynamics of the BCS, establish its utility as a repeated measure for population surveillance and intervention tracking, and strengthen its foundation as a tool for promoting lifelong brain health.

5. Main Hypothesis/Study Aims:

Aim 1: Describe trajectories of BCS scores from mid-life through late life (using data from Visit 2 through Visit 11).

Aim 2: Evaluate associations of BCS trajectories from mid-life through early late life (using data from Visit 2 through Visit 5) with incident stroke and dementia (occurring post-Visit 5).

6. Design and analysis - please address the following aspects:

a) Inclusion/exclusion

Visit 2 is the first visit where there is information on all BCS components. All ARIC Study participants who attended Visit 2 will be included in Aim 1. All ARIC Study participants who attended Visit 5 without prevalent stroke or dementia will be included in Aim 2.

b) Study design

Prospective cohort study. Aim 1 will use data from Visit 2 through Visit 11. Aim 2 will use data from Visit 2 through Visit 5 to define the BCS with follow-up post-Visit 5 extending through the latest administrative censoring date.

c) Outcome and other variables of interest with specific reference to the time of their collection

Brain Care Score (BCS): The BCS (range of possible scores: 0-21, where higher scores are indicative of better health) will be calculated using data from each in-person visit, starting at ARIC Visit 2 (1990-1992).

The BCS contains four physical components (blood pressure, Hb1Ac, body mass index, cholesterol), which are scored as follows:[3]

Physical	Blood Pressure	Resting blood pressure greater than 140/90, with or without treatment	0	
		Resting blood pressure 120-139/80-89, with or without treatment	2	
		Resting blood pressure less than 120/80	3	
	Blood Sugar	Hemoglobin A1c greater than 6.4	0	
		Hemoglobin A1c between 5.7 and 6.4	1	
		Hemoglobin A1c less than 5.7	2	
	Cholesterol	190 or higher	0	
		No treatment required or less than 190mg/dL	1	
		For people with cardiovascular disease, LDL in accordance with CDC recommendations	1	
	BMI	Lower than 18.5 kg/m^2	1	
		18.5-25 kg/m^2	2	
		25-29.9 kg/m^2	1	
		Greater than 30 kg/m^2	0	

In ARIC, **blood pressure** is measured at every in-person visit and will be scored identically to the BCS instructions above. Sitting blood pressure was measured 2-3 times after a 5-minute rest period, using a random zero sphygmomanometer; two of the measurements were averaged and will be used in analyses. **Blood sugar** will be modified from the BCS instructions above as HbA1c is not available at all in-person visits. HbA1c will be scored in accordance with the BCS instructions (at visits where it is available). At visits where HbA1c is not available, we will consider fasting glucose (which is available at all study visits), scored as 0 for ≥126 mg/dl, 1 for 100-125 mg/dl and 2 for <100 mg/dl. Serum blood glucose levels were measured using the hexokinase/glucose-6-phosphate dehydrogenase procedure and HbA1c was measured using the Tosoh 2.2 Plus HPLC instrument and the Tosoh G7 HPLC instrument. **Cholesterol** and **body mass index** are measured at every in-person visit and will be scored identically to the BCS instructions above. Total cholesterol was measured using standardized enzymatic methods and cholesterol-lowering medication use within the past two weeks was assessed by self-report or from prescription bottles. BMI was calculated as weight (kg) divided by height squared (m^2).

The BCS contains five lifestyle factors (nutrition, physical activity, smoking, alcohol, sleep), which are scored as follows:[3]

Lifestyle	Nutrition	Dietary habits: • 4 – 5 servings of fruit and vegetables per day • 2 servings of lean protein per day • 3 or more servings of whole grains per day • Less than 1,500 mg of sodium per day • Less than 36 oz of sugar sweet beverages (soda, juice, etc.) per week	
		Typical weekly diet does not include at least 2 of the recommendations above	0
		Typical weekly diet includes 2 or more of the recommendations above	1
		Typical weekly diet includes 3 or more of the recommendations above	2
	Alcohol	4 or more alcoholic drinks per week	0
		2-3 alcoholic drinks per week	1
		0-1 alcoholic drinks per week	2
	Smoking	Current smoker	0
		Never smoked or quit more than a year ago	3
	Aerobic Activities	Less than 150 minutes of moderate or 75 minutes of high intensity physical activity per week	0
		At least 150 minutes of moderate physical activity (ex. walking) or 75 minutes of high intensity physical activity per week	1
	Sleep	Untreated sleep disorder and/or sleeps <7hrs per night	0
		Treated sleep disturbances and 7-8 hours of sleep per night	1

In ARIC, **nutrition** data was collected at Visit 1, Visit 2, and Visit 3 using a modified version of the 66-item Harvard food frequency questionnaire[11], which asks participants how frequently they eat certain quantities of specific foods (scored as > 6 per day, 4–6 per day, 2–3 per day, 1 per day, 5–6 per week, 2–4 per week, 1 per week, 1–3 per month, and almost never). We will modify the BCS scoring above to 2-3 servings per day for whole grains as there is not an option for 3+ servings per day; other dietary habits will be scored according to the BCS instructions. **Alcohol consumption** is self-reported at all visits and will be scored in accordance with the BCS instructions. **Smoking** is self-reported at all visits, but ARIC does not have information on how long ago someone quit smoking, so we will modify the scoring to 0 for current smoker and 3 for former or never smoker. **Physical activity** was ascertained at Visit 1, Visit 3, and Visits 5-7 using the Baecke questionnaire.[12] The self-reported answers to this questionnaire were converted to metabolic equivalents (METs) per the Compendium of Physical Activities, and weekly minutes of moderate-to-vigorous physical activity was calculated by multiplying the duration of weekly physical activity by the number of months per year. We will modify the BCS scoring above to 1 point for at least 150 minutes of aerobic moderate or vigorous intensity per week, with intensity based on reported activities of at least 3 METS, and 0 points for less physical activity.[13] Information on **sleep** was self-reported via several different questionnaires at different in-person visits; sleep scores will be modified from the BCS scoring above. At Visit 2, sleep quality was assessed using the first three questions of the Maastricht Vital Exhaustion Questionnaire[14]: 1) Do you often feel tired? 2) Do you often have trouble falling asleep? and 3) Do you wake up repeatedly during the night? If participants answered at least one of these questions with a "yes," they will receive a score of 0, if all questions were "no," the score will be 1. At Visits 5, 6, 9, and 10, we will use the question, "my sleep was restless" from the Center for Epidemiologic Studies Depression Scale (CES-D)[15], with "yes" receiving a score of 0 and "no" receiving a score of 1. At Visits 6, 7, and 11, we will also incorporate the Epworth Sleepiness Scale (ESS), which is a self-reported measure of daytime sleepiness that correlates strongly with sleep disorder diagnosis and OSA severity.[16] ESS scores range from 0 to 24 with a score ≥11

representing excessive daytime sleepiness, which will receive a BCS score of 0 and ESS scores <11 will receive a BCS score of 1.

The BCS contains three social-emotional factors (relationships, stress, and purpose in life), which are scored as follows:[3]

Social Emotional	Stress	High level of stress that often makes it difficult to function	0
		Moderate level of stress that occasionally makes it difficult to function	1
		Manageable level of stress that rarely makes it difficult to function	2
	Social Relationships	I have few or no close connections other than my spouse or children	0
		I have at least two people, other than my spouse or children, that I feel close with and could talk about private matters or call upon for help	1
	Meaning in life	I often struggle to find value or purpose in my life	0
		I generally feel that my life has meaning and/or purpose	1

In ARIC, most of the social emotional factors will require modification in the scoring. **Stress** was assessed at Visit 2 using the question "Do you have the feeling that you can't cope with everyday problems as well as you used to?" from the Maastricht Vital Exhaustion Questionnaire.[14] This question can be answered as yes or no; yes will result in a score of 1.5 and no will result in a score of 0. At Visits 5 and 6, stress was assessed with the question, "How much of the time during the past week did you feel calm and peaceful?" This question will be scored as a 0 for answers of "none of the time" or "a little of the time," a 1 for answers of "some of the time," or "a good bit of the time," and a 2 for answers of "most of the time," or "all of the time." **Social relationships** were assessed at Visit 2 using the Interpersonal Support Evaluation List[17] questions "how many relatives do you feel close to? that is, how many of them do you feel at ease with, can talk to about private matters, or can call on for help?" (variable: hpaa21) and "do you have any close friends? that is, do you have any friends with whom you feel at ease, can talk to about private matters, or can call on for help?" (variable: HPAA22). These questions have answer choices of 0, 1, 2, 3-4, 5-8, 9+ and will be scored in accordance with the BSC scoring above.

At Visits 5 and 6, social relationships will be using the following 2 questions" "Can you count on anyone to help you when you need to make difficult decisions or talk problems over?" and" Can you count on anyone to help you with daily tasks like grocery shopping, housecleaning, cooking, telephoning or giving you a ride?" These questions will be scored as a 0 for "yes" and 1 for "no." **Meaning in life** was assessed at Visit 2 using the Interpersonal Support Evaluation List[17] question, "how satisfied are you with the meaning and purpose of your life?" (variable: HPAA02). This question was answered on a 0 to 10 scale, with 0 being most satisfied. Scores <5 will be scored as 0 and scores ≥5 will be scored as 1. At Visits 5, 6, 9, and 10, we will use the CES-D question, "I enjoyed life" with responses of "much or most of the time or some of the time" being scored as 0 and responses of "hardly ever or never" being scored as 1.

Stroke: Possible stroke events were identified via surveillance of hospitalizations occurring in ARIC study communities and self-report of hospitalizations during telephone follow-up calls (after which medical records were obtained), and, for deaths, by linkage to State vital statistics registers and the National Death Index.[18,19] These possible stroke events were identified using International Classification of Diseases, Ninth Revision (ICD-9) codes 430–438 and

International Classification of Diseases, Tenth Revision (ICD-10) codes G45.X, I60.X, I61.X, I62.X, I63.X, I65.X, I66.X, I67.X. Stroke events were preliminarily classified by a computer-generated algorithm, with adjudication by study physicians. Definite/probable all-cause (ischemic, hemorrhagic) stroke will be the outcome used in the present analyses.

Dementia: The ARIC study uses a 3-level dementia ascertainment protocol[20]. Level 1 includes adjudicated dementia status defined from in-person cognitive evaluations starting at ARIC visit 5 (2011-2013). Level 2 adds telephone data from participants who did not attend visit 5 or later visits and data from informants of participants who died. Level 3 adds continuously collected dementia cases identified from hospitalization ICD-9/10 codes or death certificate codes. Level 3 dementia will be the outcome used in the present analyses because it is available over the entire study duration and is not dependent on visit attendance, which minimizes potential biases due to attrition and the competing risk of death.

Covariates: In Aim 2, we will adjust for the following covariates in our statistical model: age (continuous, years), sex (male; female), race/center (MN White race; MD White race; NC White race; NC Black race; MS Black race), education (less than high school; high school or vocational school or GED; some college or more), and APOE ε4 genotype (0 alleles; 1 or 2 alleles). We will also consider adjustment for baseline BCS score.

d) Summary of data analysis

Aim 1: Population characteristics at analysis baseline (Visit 2) will be calculated as means and standard deviations for continuous normally distributed data, medians and 25^{th}-75^{th} percentiles for continuous non-normally distributed data, and numbers and percentages for categorical data. The BCS will be calculated for each participant at each visit that was attended using data from Visit 2 through Visit 11 – if a component is not available at a visit, the last observed data for that factor will be carried forward. Next, we will explore trajectories of BCS descriptively within individuals over time using several approaches: 1) to evaluate individual-level variability, we will visualize randomly sampled spaghetti plots and use heatmaps to show patterns overtime, 2) to obtain population level trajectories, we will obtain marginal means (95% CIs) at each visit from linear mixed effects models with random intercept, random slopes, and unstructured covariance matrix. In this model, we will consider non-linearity using spline or quadratic terms. 3) to explore subgroup patterns, we will create distribution-based categories for changes in scores over time (e.g., stable, increasing, decreasing, etc.). Alternatively, we could consider latent class growth models.

Aim 2: Population characteristics at analysis baseline (Visit 5) will be calculated as means and standard deviations for continuous normally distributed data, medians and 25^{th}-75^{th} percentiles for continuous non-normally distributed data, and numbers and percentages for categorical data. The BCS will be calculated for each participant at Visits 2, 3, 4, and 5 – if a component is not available at a visit, the last observed data for that factor will be carried forward. We will obtain individual level slopes of the BCS from Visit 2 through Visit 5 from linear mixed effects models with random intercept, random slopes, and unstructured covariance matrix. In this model, we will consider non-linearity using spline or quadratic terms. The individual level slopes of the BCS from Visit 2 through Visit 5 will then serve as the exposure (modeled continuously and in

quartiles) in our Cox proportional hazards models to evaluate associations of BCS trajectory with incident stroke and dementia (separately, and as a composite outcome). We will assess the proportional hazards assumption using Schoenfeld residuals. We will also consider Fine and Gray models to account for the competing risk of mortality. Models will be adjusted for age, sex, race/center, education, and APOE ε4 genotype. We will also consider adjustment for baseline BCS score.

e) Any anticipated methodologic limitations or challenges if present

Not all BCS metrics were ascertained at each ARIC Study visit (e.g., physical activity, nutrition, etc.), which will require us to carry-forward the last observed score for factor the BCS is updated at each visit and assume that the factor is the same as at the last visit where it was measured. As a sensitivity analysis, we can fill in values from the nearest time of ascertainment (either before or after the visit where the BCS is being calculated). We will also consider an overall score that just includes the components that are available in at least 50% of study visits. As another sensitivity analyses, we can consider the four physical components, five lifestyle factors, and three social-emotional factors separately. The four physical components are available at each in-person visit, whereas the five lifestyle factors and three social-emotional factors are not.

f) Will the author need Limited data to complete the proposed manuscript? ☐ Yes, Limited data is needed (Provide a brief (2-3 sentences) justification for requesting PHI data) . ☒ No, De-identified data will be sufficient.

*Please note, Limited dataset access is strict and rarely provided. Limited data includes identifiable information such as dates (birthdays, visit dates, etc.). CMS, Genomic, Geocoded, Proteomics/Somalogic, and other -omic data all fall under the limited data category. De-identified data does not include dates. All dates are date adjusted to "Days since Visit 1".

7.a. Will the data be used for non-ARIC analysis or by a for-profit organization in this manuscript? (Non-ARIC analysis means that the authors are not regarded as ARIC investigators and the "ARIC author" is essentially just a facilitator rather than an integral part of the writing group.) ☐ Yes ☒ No

b. If Yes, is the author aware that the current derived consent file ICTDER05 must be used to exclude persons with a value RES_OTH and/or RES_DNA = "ARIC only" and/or "Not for Profit" ? ☐ Yes ☐ No
(The file ICTDER is distributed to ARIC PIs annually, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? ☒ Yes ☐ No – APOE ε4 genotype

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the current derived consent file ICTDER05 must be used to exclude those with value RES_DNA = "No use/storage DNA"? ☒ Yes ☐ No

9. **The lead author or the "sponsoring" ARIC author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status.** ARIC Investigators have access to the publications lists under the Study Members Area of the website at: https://aric.cscc.unc.edu/aric9/proposalsearch [ARIC Website□Publications□Proposal Search]

☒ Yes ☐ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

- MSP #2120C: Associations Between Midlife Vascular Risk Factors and 25-Year Incident Dementia in the Atherosclerosis Risk in Communities (ARIC) Cohort (Gottesman)
- MSP #2139: Social Isolation, Social Support, and the Risk of Incident Stroke: the Atherosclerosis Risk in Communities Study (Nagayoshi)
- MSP #3513: Social Isolation, Social Support, and the Risk of Incident Dementia and MCI: The Atherosclerosis Risk in Communities (ARIC) Study (Liu)
- MSP #3672: Association of Ischemic Stroke Incidence, Severity, and Recurrence With Dementia in the Atherosclerosis Risk in Communities Cohort Study (Koton)
- MSP #3677: Genetic Risk, Midlife Life's Simple 7, and Incident Dementia in the Atherosclerosis Risk in Communities Study (Tin)
- MSP #3776: Association of change in cardiovascular risk factors with incident dementia (Sedaghat)
- MSP #3811: Genetic Risk, Midlife Life's Simple 7 And Incident Ischemic Stroke In the Atherosclerosis Risk In Communities Study (Enduru)
- MSP #3965A: Contribution of Modifiable Midlife and Late-Life Vascular Risk Factors to Incident Dementia (Smith)
- MSP #4131: Associations of psychosocial factors and cardiovascular health measured by Life's Essential 8: The Atherosclerosis Risk in Communities (ARIC) study (Peter-Marske)

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or does it use current [or ongoing] ancillary study data (this includes ACHIEVE)? ☒ Yes ☐ No → Skip to question 12

11.b. If yes to 11.a., is the proposal

☒ **A. primarily the result of an ancillary study**

☐ **B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables)**

11.c. If yes to 11.a., list number*ARIC-NCS 2008.06_

*ancillary studies are listed by number
https://aric.cscc.unc.edu/aric9/researchers/ancillary_studies/approved_ancillary_studies [ARIC Website Ancillary Studies Approved Ancillary Studies]

12a. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

Understood.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is **your responsibility to upload manuscripts to PubMed Central** whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in https://aric.cscc.unc.edu/aric9/publications/policies_forms_and_guidelines [ARIC Website Publications, Publication Policies, Forms, and Guidelines].
http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.

Understood.

References

1. GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Neurol*. 2021;20(10):795-820. doi:10.1016/S1474-4422(21)00252-0

2. Livingston G, Huntley J, Sommerlad A, et al. Dementia Prevention, Intervention, and Care: 2020 Report of the Lancet Commission. *The Lancet*. 2020;396(10248):413-446. doi:10.1016/S0140-6736(20)30367-6

3. Singh SD, Gutierrez-Martinez L, Newhouse A, Sonni A, Chemali Z, Rosand J. Brain health begins with brain care. *The Lancet Neurology*. 2022;21(11):961-962. doi:10.1016/S1474-4422(22)00397-0

4. Singh SD, Oreskovic T, Carr S, et al. The predictive validity of a Brain Care Score for dementia and stroke: data from the UK Biobank cohort. *Front Neurol*. 2023;14:1291020. doi:10.3389/fneur.2023.1291020

5. Marini S, Kimball TN, Mayerhofer E, et al. Health-Related Behaviors and Risk of Common Age-Related Brain Diseases Across Severities of Genetic Risk. *Neurology*. 2024;103(10):e210014. doi:10.1212/WNL.0000000000210014

6. Rivier CA, Singh S, Senff J, et al. Brain Care Score and Neuroimaging Markers of Brain Health in Asymptomatic Middle-Age Persons. *Neurology*. 2024;103(4):e209687. doi:10.1212/WNL.0000000000209687

7. Choksi D, Gutiérrez-Martínez L, Rist PM, et al. Use of the Brain Care Score to Estimate the Risk of Incident Cerebrovascular Events in Middle-Aged Women. *Neurology*. 2025;104(11):e213674. doi:10.1212/WNL.0000000000213674

8. Senff JR, Tack RWP, Tan BYQ, et al. Assocation Between a Brain Care Score Derived from Participant Responses and Incident Stroke from the COSMOS Study. *Am J Lifestyle Med*. Published online August 22, 2025:15598276251368345. doi:10.1177/15598276251368345

9. Ding M, Fitzmaurice GM, Arvizu M, et al. Associations between patterns of modifiable risk factors in mid-life to late life and longevity: 36 year prospective cohort study. *bmjmed*. 2022;1(1). doi:10.1136/bmjmed-2021-000098

10. Pedamallu H, Zmora R, Perak AM, Allen NB. Life Course Cardiovascular Health: Risk Factors, Outcomes, and Interventions. *Circulation Research*. 2023;132(12):1570-1583. doi:10.1161/CIRCRESAHA.123.321998

11. Willett WC, Sampson L, Stampfer MJ, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. *Am J Epidemiol*. 1985;122(1):51-65. doi:10.1093/oxfordjournals.aje.a114086

12. Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in epidemiological studies. *Am J Clin Nutr*. 1982;36(5):936-942. doi:10.1093/ajcn/36.5.936

13. Palta P, Heiss G, Sharrett AR, et al. Mid- and Late-Life Leisure-Time Physical Activity and Global Brain Amyloid Burden: The Atherosclerosis Risk in Communities (ARIC)-PET Study. *J Alzheimers Dis*. 2020;76(1):139-147. doi:10.3233/JAD-200152

14. Appels A, Höppener P, Mulder P. A questionnaire to assess premonitory symptoms of myocardial infarction. *Int J Cardiol*. 1987;17(1):15-24. doi:10.1016/0167-5273(87)90029-5

15. Radloff LS. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. *Applied Psychological Measurement*. 1977;1(3):385-401. doi:10.1177/014662167700100306

16. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep*. 1991;14(6):540-545. doi:10.1093/sleep/14.6.540

17. Cohen S, Hoberman HM. Positive Events and Social Supports as Buffers of Life Change Stress[1]. *J Applied Social Pyschol*. 1983;13(2):99-125. doi:10.1111/j.1559-1816.1983.tb02325.x

18. Koton S, Schneider ALC, Rosamond WD, et al. Stroke incidence and mortality trends in US communities, 1987 to 2011. *JAMA*. 2014;312(3):259-268. doi:10.1001/jama.2014.7692

19. Koton S, Sang Y, Schneider ALC, Rosamond WD, Gottesman RF, Coresh J. Trends in Stroke Incidence Rates in Older US Adults: An Update From the Atherosclerosis Risk in Communities (ARIC) Cohort Study. *JAMA Neurol*. 2020;77(1):109-113. doi:10.1001/jamaneurol.2019.3258

20. Knopman DS, Gottesman RF, Sharrett AR, et al. Mild Cognitive Impairment and Dementia Prevalence: The Atherosclerosis Risk in Communities Neurocognitive Study (ARIC-NCS). *Alzheimers Dement (Amst)*. 2016;2:1-11. doi:10.1016/j.dadm.2015.12.002

To view publications materials, click "Log in" at the top right of the ARIC website. Click "Forgot Password" if you are experiencing issues with logging in.