Ambulatory Care Fragmentation and Incident Stroke

Lisa M. Kern, MD, MPH; Joanna B. Ringel, MPH; Mangala Rajan, MBA; Lisandro D. Colantonio, MD, PhD; Lawrence P. Casalino, MD, PhD; Evgeniya Reshetnyak, PhD; Laura C. Pinheiro, PhD; Monika M. Safford, MD

BACKGROUND: More fragmented ambulatory care (ie, care spread across many providers without a dominant provider) has been associated with excess emergency department and inpatient care. We sought to determine whether more fragmented ambulatory care is associated with an increase in the hazard of incident stroke, overall and stratified by health status and by race.

METHODS AND RESULTS: We conducted a secondary analysis of data from the REGARDS (Reasons for Geographic and Racial Differences in Stroke) study (2003–2016), including participants aged ≥65 years who had linked Medicare fee-for-service claims and no history of stroke (N=12,510). We measured fragmentation of care with the reversed Bice-Boxerman index. We used Poisson models to determine the association between fragmentation and adjudicated incident stroke. The average age of participants was 70.5 years; 53% were women, 32% were Black participants, and 16% were participants with fair or poor health. Overall, the adjusted rate of incident stroke was similar for high versus low fragmentation (8.2 versus 8.1 per 1000 person-years, respectively; P=0.89). Among participants with fair or poor self-rated health, having high versus low fragmentation was associated with a trend toward a higher adjusted rate of incident strokes (14.8 versus 10.4 per 1000 person-years, respectively; P=0.067). Among Black participants with fair or poor self-rated health, having high versus low fragmentation was associated with a higher adjusted rate of strokes (19.3 versus 10.3 per 1000 person-years, respectively; P=0.02).

CONCLUSIONS: Highly fragmented ambulatory care is independently associated with incident stroke among Black individuals with fair or poor health.

Key Words: ambulatory care ■ medicare ■ stroke

Patients who are at risk for incident stroke often see multiple ambulatory providers to manage their chronic conditions, such as diabetes mellitus, hypertension, heart disease, and atrial fibrillation.1–3 For example, patients at risk for incident stroke may have a primary care provider, cardiologist, endocrinologist, and other subspecialists who they see regularly. Patients with either diabetes mellitus or heart disease see more ambulatory providers than the median Medicare beneficiary nationally.2 Indeed, the more chronic conditions a patient has, the more providers he or she tends to see.2

Unfortunately, providers do not consistently communicate with each other about their common patients.4 In a national survey of nearly 5000 providers, 30% of primary care providers reported that they do not “always or most of the time” send information about a patient’s medical history or the reason for requesting a consultation at the time of referral.4 Similarly, 20% of specialists reported that they do not “always or most of the time” send the results of the consultation back to the referring provider.4 Thus, clinically relevant information is frequently missing at the point of care.5

Correspondence to: Lisa M. Kern, MD, MPH, Weill Cornell Medicine, 420 East 70th Street, Box 331, New York, NY 10021, USA. E-mail: lmk2003@med.cornell.edu

Supplementary Material for this article is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.120.019036

For Sources of Funding and Disclosures, see page 12.

© 2021 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

JAHA is available at: www.ahajournals.org/journal/jaha
As a result, more fragmented ambulatory care (i.e., care spread across many providers without a dominant provider) has been associated with more drug-drug interactions,\textsuperscript{6} testing,\textsuperscript{7} procedures,\textsuperscript{8} emergency department visits,\textsuperscript{9}-\textsuperscript{11} and hospitalizations,\textsuperscript{9,12} compared with less fragmented care. However, the relationship between fragmented ambulatory care and health outcomes is not well understood.\textsuperscript{13} To our knowledge, no study has explored whether fragmented ambulatory care is associated with more incident strokes.

We previously found that the association between fragmented ambulatory care and subsequent health-care utilization varies with patients’ health status.\textsuperscript{7,14} We hypothesized that the association between fragmented ambulatory care and stroke might also vary with health status. Healthy people might be able to see multiple providers without experiencing harm from gaps in communication, whereas sicker individuals might be more vulnerable to harm.

We sought to determine the association between fragmented ambulatory care and incident stroke using data from the nationwide prospective REGARDS (Reasons for Geographic and Racial Differences in Stroke) cohort study. As the name of the investigation conveys, the purpose of the REGARDS study is to explain geographic and racial disparities in stroke mortality.\textsuperscript{15} Thus, we sought to measure the association between fragmentation and incident stroke overall and to determine whether any association varied with health status, geographic region, or race.

**METHODS**

**Study Design, Population, and Data Sources**

We conducted an ancillary study to the nationwide, prospective REGARDS cohort study, using data from 2003 to 2016.\textsuperscript{15} The institutional review boards of the participating institutions approved the protocol. All participants provided written informed consent. Because of the restrictions of our data use agreement with the Centers for Medicare and Medicaid Services, the data used for this study cannot be made publicly available to other researchers for the purpose of replicating the results. However, access to REGARDS Medicare-linked data can be requested first through the REGARDS study (www.uab.edu/soph/regar dsstudy/researchers) and then through Medicare’s Research Data Assistance Center (www.resdac.org).

Between 2003 and 2007, 30,239 community-dwelling Black and White adults aged $\geq$45 years were enrolled in the REGARDS study, with oversampling of Black adults and individuals living in the Southeastern United States.\textsuperscript{15} Baseline data collection involved computer-assisted telephone interviews and in-home visits with a physical examination, blood test, urine test, ECG, and medication inventory. Participants or their proxies are contacted by telephone every 6 months to detect study end points. The report of a potential event triggers adjudication, which involves expert review of medical records, death certificates, proxy interviews, autopsy reports, Social Security Death Index, and National Death Index.\textsuperscript{16}

For this study, we used REGARDS study baseline data, REGARDS-adjudicated events, and REGARDS Medicare-linked claims.\textsuperscript{17}

**Variables**

**Exposure**

We used Medicare claims to identify ambulatory visits, which were defined using a modified National Committee for Quality Assurance (NCQA) definition\textsuperscript{18} that was restricted to Clinical Procedure Terminology codes for in-person, evaluation-and-management visits for adults in an office setting.\textsuperscript{7} The NCQA definition of ambulatory visits does not include emergency department visits. We calculated fragmentation scores for each participant using the previously validated Bice-Boxerman index, which ranges from 0 to 1 and
captures both the spread of ambulatory visits across providers and the relative share of visits by each provider (Data S1). We reverse-coded scores, calculating 1 minus Bice-Boxerman index, so that higher scores reflected more fragmentation.

Outcome

Stroke events were adjudicated by the REGARDS study according to study protocols. Briefly, stroke events were defined in part using the World Health Organization (WHO) definition as "rapidly developing clinical signs of focal, at times global, disturbance of cerebral function, lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin." Events not meeting this definition but characterized by symptoms lasting <24 hours and with neuroimaging consistent with acute ischemia or hemorrhage were also classified as "clinical strokes." We used strokes based on WHO or clinical classification, adjudicated through December 31, 2016.

Baseline Covariates

Demographics included self-reported age, sex, race, marital status, educational attainment, and annual household income; as well as geographic region and rural/urban setting using Rural/Urban Commuting Area codes based on baseline contact information. Medical conditions included hypertension (self-reported use of antihypertensive medication, systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg from the in-home visit), dyslipidemia (use of lipid-lowering medication, total cholesterol≥240 mg/dL, low-density lipoprotein cholesterol ≥160 mg/dL, or high-density lipoprotein cholesterol≤40 mg/dL from the in-home visit), diabetes mellitus (fasting glucose ≥126 mg/dL or nonfasting glucose ≥200 mg/dL from the in-home visit, or self-reported use of oral glucose-lowering medication or insulin), history of coronary heart disease (self-reported history of myocardial infarction, coronary artery bypass graft, angioplasty, or coronary stents; or evidence of myocardial infarction on ECG at baseline), and atrial fibrillation (self-reported or present on the study ECG at baseline). Medication variables included a validated measure of self-reported medication adherence; the total number of medications taken in the past 2 weeks by medication inventory; self-reported use of antihypertensive medication, insulin, and aspirin from the computer-assisted telephone interview; and statin and warfarin use from the medication inventory. Health behaviors were self-reported and included smoking status, alcohol consumption, and exercise frequency. Psychosocial variables included whether a participant reported being the primary caretaker for another individual and whether he or she saw any close friends or relatives in the past month. Depressive symptoms were defined as Center for Epidemiologic Studies Depression Scale scores ≥4. Physiological variables included body mass index, heart rate, systolic blood pressure, left ventricular hypertrophy (on ECG); total, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol; glucose; estimated glomerular filtration rate; urinary albumin to creatinine ratio; and high-sensitivity C-reactive protein. Self-rated health was assessed using self-rated general health (SF-1) from the Short-Form-12 (SF-12) survey. Hospitalization during the first year of observation was measured in Medicare claims.

Statistical Analysis

We included participants aged ≥65 years whose REGARDS study data were linked to Medicare claims at any time during the study period, allowing for staggered entry as participants aged into Medicare. We excluded participants who: (1) were eligible for Medicare on the basis of end-stage renal disease; (2) had fewer than 12 months of continuous Medicare fee-for-service coverage or had Medicare managed care; (3) were lost to follow-up before entry into this ancillary study; (4) had ≤3 ambulatory visits in the first year of observation, because calculating fragmentation based on ≤3 visits can lead to unreliable estimates; (5) had a history of stroke; or (6) had a missing value for self-rated health.

We used descriptive statistics to characterize the sample at baseline and summarize ambulatory care utilization in the first year of observation. We used the 75th percentile fragmentation score rounded to the nearest 0.05 from the first year of observation, because calculating fragmentation based on ≤3 visits can lead to unreliable estimates; and by the goal of identifying individuals who have such high scores that they might benefit from future interventions if high fragmentation is found to be associated with increased stroke risk. To compare differences between participants with high versus low fragmentation, we used Wilcoxon rank sum, Student t, and chi-square tests. We conducted sensitivity analyses changing the cutoff for high fragmentation to ≥0.80 and, separately, ≥0.90. We also conducted a sensitivity analysis treating fragmentation as a 4-level variable.

Observation for each participant began after the in-home visit with the first 12-month period for which there was continuous Medicare fee-for-service coverage, starting with calendar year 2004. Because fragmentation can change over time, we treated
Ambulatory Care Fragmentation and Incident Stroke

Kern et al Ambulatory Care Fragmentation and Incident Stroke

We used Poisson regression to estimate absolute unadjusted and adjusted rates of strokes. We used Cox proportional hazards models to estimate unadjusted and adjusted hazards ratios.\textsuperscript{34–36} Using Schoenfeld residuals, we determined that the assumption of proportional hazards was met. We included in the fully adjusted multivariate models covariates that had a bivariate association with fragmentation (\(P<0.10\)), were used in the sampling frame, or were retained because of high clinical importance (sex, coronary heart disease, atrial fibrillation, statin, aspirin, warfarin, heart rate). If 2 variables had bivariate \(P\) values <0.10, but 1 was embedded in the definition of another (eg, use of antihypertensive medication was embedded in the definition of hypertension), we adjusted only for the broader variable to avoid collinearity. To maximize power, given that some subgroups had relatively few stroke events, we also generated a more parsimonious model, which included covariates that had multivariate \(P\) values <0.10 in the fully adjusted model, were used in the sampling frame, or were retained because of high clinical importance (dyslipidemia, atrial fibrillation, aspirin).

We conducted all model analyses using stochastic regression imputation to handle missing covariates. Stochastic regression is a method that adds a residual error term to each imputed predicted value, thereby preserving uncertainty while reducing bias.\textsuperscript{37} The most frequently missing variable was income (missing for \(12\%\) of the sample).

We used self-rated health as a measure of health status.\textsuperscript{29,30} We used 3 groupings of self-rated health (excellent, very good or good, fair or poor) to detect any differences among subgroups, while maximizing statistical power. We used Wald tests to determine interactions between fragmentation and self-rated health in the overall sample, by race, and by geographic region. The Wald tests were significant for self-rated health in the overall sample (\(P=0.04\)) and by race (\(P=0.02\)) but not by geographic region (\(P=0.94\)). Thus, we conducted analyses overall and stratified by self-rated health and by race.

Analyses were conducted with SAS version 9.4 (SAS Institute Inc) and Stata version 14 (StataCorp). Multivariate \(P\) values <0.05 were considered statistically significant.

RESULTS

Study Sample

Of the 30,239 REGARDS study participants, 20,403 had linked Medicare claims and were aged \(\geq 65\) years during the study period. Of those, 12,510 met our inclusion criteria (Figure S1).

Sample Characteristics

Participants in our sample were aged 70.5 years on average; 53\% were women and 68\% were of White race (Table 1). More than half (60\%) lived in the Southeastern United States. Chronic conditions were common, with 62\% having hypertension, 62\% having dyslipidemia, 22\% having diabetes mellitus, 21\% having coronary heart disease, and 9\% having atrial fibrillation. In terms of self-rated health, 17\% reported excellent health, 67\% reported very good or good health, and 13\% reported fair or poor health. Additional characteristics are shown in Table 1. Appendices show participant characteristics stratified by self-rated health (Table S1), by race (Table S2), by sex (Table S3), and by self-rated health among Black participants (Table S4), and by self-rated health among White participants (Table S4).

Ambulatory Utilization

Participants with high fragmentation (fragmentation score \(\geq 0.85\)) in the first year of observation were younger, more likely to be of White race, and less likely to have hypertension, dyslipidemia, and diabetes mellitus than those with low fragmentation (fragmentation score <0.85). Additional differences are shown in Table 1.

Participants with high fragmentation had an average 11.1 ambulatory visits with 6.4 providers in the first year of observation, with the most frequently seen provider accounting for 29.1\% of visits (Table 2). By contrast, participants with low fragmentation had an average 9.2 ambulatory visits with 3.6 providers,
Table 1. Baseline Characteristics, Overall and Stratified by Fragmentation Score in the First Year of Observation*  

| Characteristic                                | Overall (N=12,510) | Low Fragmentation During First Year of Observation (n=9,301) | High Fragmentation During First Year of Observation (n=3,209) | P Value  |
|------------------------------------------------|--------------------|---------------------------------------------------------------|---------------------------------------------------------------|---------|
| **Demographic characteristics**                |                    |                                                               |                                                               |         |
| Age, mean (SD), y                             | 70.5 (6.0)         | 70.7 (6.0)                                                    | 70.2 (5.9)                                                    | <0.001  |
| Women, n (%)                                   | 6,623 (52.9)       | 4,896 (52.6)                                                  | 1,727 (53.8)                                                 | 0.25    |
| White race, n (%)                             | 8,513 (68.0)       | 6,108 (65.7)                                                  | 2,405 (74.9)                                                 | <0.001  |
| Marital status, married, n (%)                | 7,487 (59.8)       | 5,475 (58.9)                                                  | 2,012 (62.7)                                                 | <0.001  |
| Education, less than high school diploma, n (%)| 1,545 (12.4)       | 1,237 (13.3)                                                  | 308 (9.6)                                                    | <0.001  |
| Annual household income, <$35,000, n (%)      | 5,422 (49.5)       | 4,199 (51.5)                                                  | 1,223 (43.7)                                                 | <0.001  |
| **Geographic region, n (%)**                  |                    |                                                               |                                                               |         |
| Stroke belt†                                   | 4,551 (36.4)       | 3,334 (35.8)                                                  | 1,217 (37.9)                                                 | 0.10    |
| Stroke buckle‡                                 | 2,899 (23.2)       | 2,214 (23.8)                                                  | 685 (21.3)                                                   |         |
| Neither stroke belt nor stroke buckle          | 5,060 (40.4)       | 3,753 (40.4)                                                  | 1,307 (40.7)                                                 |         |
| Residence in urban area, n (%)                | 8,467 (75.3)       | 6,307 (75.2)                                                  | 2,160 (75.4)                                                 | 0.89    |
| **Medical conditions§**                       |                    |                                                               |                                                               |         |
| Hypertension, n (%)                            | 7,663 (61.5)       | 5,857 (63.2)                                                  | 1,806 (56.4)                                                 | <0.001  |
| Dyslipidemia, n (%)                            | 7,538 (62.3)       | 5,668 (62.9)                                                  | 1,870 (60.6)                                                 | 0.019   |
| Diabetes mellitus, n (%)                      | 2,603 (21.7)       | 2,016 (22.4)                                                  | 607 (19.6)                                                   | <0.001  |
| History of coronary heart disease, n (%)      | 2,521 (20.5)       | 1,852 (20.2)                                                  | 669 (21.2)                                                   | 0.25    |
| Atrial fibrillation, n (%)                    | 1,149 (9.4)        | 840 (9.2)                                                     | 309 (9.8)                                                    | 0.33    |
| **Medications**                                |                    |                                                               |                                                               |         |
| Medication adherence, n (%)                   | 8,302 (71.1)       | 6,205 (71.4)                                                  | 2,097 (70.3)                                                 | 0.23    |
| No. of medications, median (25th, 75th percentiles) | 6.0 (3.0, 9.0)     | 6.0 (3.0, 9.0)                                                | 6.0 (3.0, 9.0)                                               | <0.001  |
| Antihypertensive medication, n (%)            | 6,693 (55.4)       | 5,126 (57.1)                                                  | 1,567 (50.3)                                                 | <0.001  |
| Insulin use, n (%)                             | 657 (5.5)          | 483 (5.4)                                                     | 174 (5.7)                                                    | 0.62    |
| Statin use, n (%)                              | 4,439 (35.5)       | 3,297 (35.4)                                                  | 1,142 (35.8)                                                 | 0.89    |
| Aspirin use, n (%)                             | 6,084 (48.6)       | 4,509 (48.5)                                                  | 1,575 (49.1)                                                 | 0.55    |
| Warfarin use, n (%)                            | 522 (4.2)          | 402 (4.3)                                                     | 120 (3.7)                                                    | 0.16    |
| **Health behaviors**                           |                    |                                                               |                                                               |         |
| Current smoker, n (%)                         | 1,344 (10.8)       | 1,031 (11.1)                                                  | 313 (9.8)                                                    | 0.035   |
| Alcohol use, n (%)                             | 1,344 (10.8)       | 1,031 (11.1)                                                  | 313 (9.8)                                                    | 0.035   |
| Heavy                                         | 464 (3.8)          | 339 (3.7)                                                     | 125 (4.0)                                                    | <0.001  |
| Moderate                                      | 4,049 (33.0)       | 2,924 (32.0)                                                  | 1,125 (35.7)                                                 |         |
| None                                          | 7,777 (63.3)       | 5,874 (64.3)                                                  | 1,901 (60.3)                                                 |         |
| Exercise frequency, 0 times per week, n (%)   | 4,192 (34.1)       | 3,121 (34.1)                                                  | 1,071 (33.9)                                                 | 0.84    |
| **Psychosocial variables**                    |                    |                                                               |                                                               |         |
| Cares for a family member with a chronic illness or disability, n (%) | 1493 (11.9)         | 1102 (11.9)                                                  | 391 (12.2)                                                   | 0.62    |
| Lack of social support, n (%)                 | 485 (4.0)          | 343 (3.8)                                                     | 142 (4.5)                                                    | 0.073   |
| Depressive symptoms, n (%)                    | 710 (5.7)          | 528 (5.7)                                                     | 182 (5.7)                                                    | 0.99    |
| **Physiological variables**                   |                    |                                                               |                                                               |         |
| Body mass index, mean (SD), kg/m²             | 28.9 (5.8)         | 29.0 (5.8)                                                    | 28.6 (5.7)                                                   | <0.001  |
| Heart rate, beats per min, mean (SD)          | 66.6 (24.8)        | 66.5 (22.4)                                                   | 66.7 (30.8)                                                  | 0.76    |
| Systolic blood pressure, mean (SD), mm Hg     | 128.6 (16.3)       | 129.1 (16.3)                                                  | 127.2 (16.0)                                                 | <0.001  |
| Left ventricular hypertrophy, n (%)           | 1247 (10.1)        | 959 (10.4)                                                    | 286 (9.1)                                                    | 0.032   |
| Total cholesterol, mean (SD), mg/dL           | 189.9 (39.4)       | 190.5 (39.7)                                                  | 188.4 (38.3)                                                 | 0.011   |
| Low-density lipoprotein cholesterol, mean (SD), mg/dL | 111.5 (33.9)     | 112.1 (34.2)                                                  | 109.6 (32.8)                                                 | <0.001  |

(Continued)
with the most frequently seen provider accounting for 57.5% of visits (P<0.001 for each pairwise comparison). The average fragmentation score for participants with high fragmentation was 0.91, compared with 0.63 for participants with low fragmentation (P<0.001).

Participants with fair or poor self-rated health had more visits and more providers, compared with participants with very good/good self-rated health and compared with those with excellent self-rated health (P<0.001 for each comparison). However, highly fragmented care (score≥0.85) was observed in all 3 subgroups by self-rated health, affecting 25% to 28% participants in each subgroup.

Black participants had on average more visits than White participants (10.0 visits versus 9.5 visits, P<0.001) but fewer providers (4.1 providers versus 4.4 providers, P<0.001). Highly fragmented care was less common among Black participants than White participants, affecting 20% of Black participants and 28% of White participants.

## Rates of Incident Strokes

Participants were observed for a median of 5.6 years (range, 1 day to 11.8 years). We observed 611 incident strokes over 75,106 person-years, for an adjusted rate of 8.1 strokes per 1000 person-years (Table 3). The majority of strokes observed were ischemic (85%), rather than hemorrhagic (11%); stroke type was unclassifiable for 4%. Overall, the adjusted rates for incident strokes was similar for high versus low fragmentation (8.2 versus 8.1 per 1000 person-years, P=0.89). However, there were significant differences among subgroups. The subgroup with the highest adjusted rate of incident strokes was Black participants with high fragmentation and fair or poor self-rated health who had an adjusted rate of 19.3 strokes per 1000 person-years (95% CI, 11.5 to 27.2 per 1000 person-years; Figure 1).

## Hazard of Incident Stroke

Overall, there was no association between high fragmentation and the hazard of incident stroke (adjusted
Table 2. Ambulatory Utilization During the First Year of Observation, Overall and Stratified By Fragmentation Score, Self-Rated Health, and Race*

| Overall | Self-Rated Health | Fair or Poor |
|---------|------------------|--------------|
|         | Excellent | Very Good or Good | Poor | Fair or Poor |
|         | Low rBBI (<0.85) | High rBBI (≥0.85) | Total | Low rBBI (<0.85) | High rBBI (≥0.85) | Total | Low rBBI (<0.85) | High rBBI (≥0.85) | Total |
| All participants | | | | | | | | | |
| No. (%) | 12,510 (100) | 9,301 (74.4) | 3,209 (25.7) | 21,45 (100) | 15,44 (72.0) | 6,01 (28.0) | 8,363 (100) | 6,262 (74.9) | 2,101 (25.1) | 20,02 (100) |
| Visits, mean (SD) | | | | | | | | | | |
| Total | 9.68 (6.57) | 9.21 (6.28) | 11.05 (7.18) | 7.59 (4.56) | 7.36 (4.49) | 8.18 (4.70) | 9.56 (6.36) | 9.06 (6.00) | 11.06 (7.11) | 12.45 (8.13) |
| Providers, mean (SD) | | | | | | | | | | |
| Total | 4.30 (2.30) | 3.58 (1.73) | 6.40 (2.46) | 3.88 (1.85) | 3.23 (1.39) | 5.56 (1.80) | 4.25 (2.26) | 3.54 (1.68) | 6.38 (2.44) | 4.94 (2.73) |
| Percent of visits with the most frequently seen provider, mean (SD) | | | | | | | | | | |
| Total | 50.18 (19.96) | 57.45 (17.74) | 29.13 (6.74) | 49.96 (19.50) | 57.88 (16.92) | 29.62 (6.85) | 50.38 (16.89) | 57.45 (17.73) | 29.31 (6.73) | 49.59 (20.72) |
| Fragmentation score, rBBI, mean (SD) | | | | | | | | | | |
| Total | 0.70 (0.22) | 0.63 (0.22) | 0.91 (0.04) | 0.72 (0.22) | 0.64 (0.21) | 0.92 (0.05) | 0.70 (0.22) | 0.63 (0.22) | 0.91 (0.04) | 0.69 (0.23) |

White participants

| No. (%) | 8,513 (100) | 6,108 (71.6) | 2,405 (28.3) | 1,760 (100) | 1,230 (69.9) | 530 (30.1) | 5,739 (100) | 4,147 (72.3) | 1,592 (27.7) | 1,014 (100) |
| Visits, mean (SD) | | | | | | | | | | |
| Total | 9.52 (6.57) | 9.07 (6.37) | 10.66 (6.93) | 7.50 (4.50) | 7.27 (4.44) | 8.05 (4.62) | 9.53 (6.44) | 9.03 (6.18) | 10.82 (6.90) | 13.00 (8.60) |
| Providers, mean (SD) | | | | | | | | | | |
| Total | 4.38 (2.27) | 3.63 (1.73) | 6.28 (2.38) | 3.95 (1.82) | 3.28 (1.36) | 5.51 (1.79) | 4.37 (2.26) | 3.62 (1.70) | 6.32 (2.38) | 5.19 (2.73) |
| Percent of visits with the most frequently seen provider, mean (SD) | | | | | | | | | | |
| Total | 48.87 (19.25) | 56.59 (16.96) | 29.28 (6.75) | 48.80 (18.70) | 57.03 (16.00) | 29.72 (6.76) | 49.09 (19.35) | 56.64 (17.18) | 29.42 (6.75) | 47.81 (19.62) |
| Fragmentation score, rBBI, mean (SD) | | | | | | | | | | |
| Total | 0.70 (0.21) | 0.65 (0.20) | 0.91 (0.04) | 0.74 (0.20) | 0.66 (0.19) | 0.92 (0.05) | 0.72 (0.21) | 0.65 (0.21) | 0.91 (0.04) | 0.72 (0.20) |

Black participants

| No. (%) | 3,997 (100) | 3,193 (79.9) | 804 (20.1) | 385 (100) | 314 (81.6) | 71 (18.4) | 2,624 (100) | 2,115 (80.6) | 509 (19.4) | 988 (100) |
| Visits, mean (SD) | | | | | | | | | | |
| Total | 10.03 (6.55) | 9.48 (6.08) | 12.22 (7.77) | 7.97 (4.82) | 7.70 (4.71) | 9.15 (5.15) | 9.63 (6.19) | 9.11 (5.65) | 11.81 (7.69) | 11.88 (7.57) |
| Providers, mean (SD) | | | | | | | | | | |
| Total | 4.13 (2.36) | 3.48 (1.75) | 6.75 (2.66) | 3.56 (1.94) | 3.02 (1.45) | 5.93 (2.07) | 4.01 (2.24) | 3.40 (1.63) | 6.57 (2.61) | 4.67 (2.71) |
| Percent of visits with the most frequently seen provider, mean (SD) | | | | | | | | | | |
| Total | 52.97 (21.14) | 59.08 (19.03) | 28.69 (6.69) | 55.25 (22.08) | 61.21 (19.82) | 28.92 (7.51) | 53.21 (20.76) | 59.05 (18.67) | 28.98 (6.70) | 51.42 (21.66) |
| Fragmentation score, rBBI, mean (SD) | | | | | | | | | | |
| Total | 0.66 (0.24) | 0.60 (0.24) | 0.90 (0.04) | 0.64 (0.26) | 0.58 (0.25) | 0.92 (0.05) | 0.66 (0.24) | 0.61 (0.23) | 0.90 (0.04) | 0.67 (0.25) |

The reversed Bice-Boxerman index (rBBI) is equivalent to 1–Bice-Boxerman index, such that higher scores indicate more fragmentation.19

All comparisons of low vs high rBBI, overall and within self-rated health subgroup, are statistically significant (P<0.001).

*To be included in the analysis, a participant had to have ≥4 ambulatory visits in his or her first year of observation.
**Table 3. Incident Rates of Stroke, Stratified by Self-Rated General Health, Fragmentation Status, and Race**

| Sample sizes and observation time | Overall | Self-Rated General Health |  |
|----------------------------------|---------|---------------------------|---|
|                                  | No. (%) | Excellent (17)            | Very Good or Good (67) | Fair or Poor (16) |
| Range of observation time        | 1 d to 11.8 y | 11 d to 11.8 y | 2 d to 11.8 y | 1 d to 11.8 y |
| Median observation time (IQR), y | 5.6 (2.9–9.1) | 6.4 (3.2–9.9) | 5.8 (3.0–9.4) | 4.1 (2.0–7.5) |

| Event counts and rates           |          |             |           |     |
|----------------------------------|----------|-------------|----------|-----|
| All participants                 |          |             |           |     |
| Observed no. of events (% participants) | 611 (4.9) | 96 (4.5) | 399 (4.8) | 116 (5.8) |
| Observed no. of person-years     | 75 106   | 13 836      | 51 367   | 9903 |
| Unadjusted rate per 1000 person-years | 8.1      | 6.9        | 7.8      | 11.7 |
| Adjusted rate per 1000 person-years | 8.1      | 6.9        | 7.8      | 11.7 |
| Low fragmentation                |          |             |           |     |
| Observed no. of events (% participants) | 423 (5.2) | 73 (5.4) | 277 (5.1) | 73 (5.7) |
| Observed no. of person-years     | 51 053   | 9113        | 35 127   | 6813 |
| Unadjusted rate per 1000 person-years | 8.3      | 8.0        | 7.9      | 10.7 |
| Adjusted rate per 1000 person-years | 8.1      | 7.8        | 7.9      | 10.4 |
| High fragmentation               |          |             |           |     |
| Observed no. of events (% participants) | 188 (4.2) | 23 (2.9) | 122 (4.2) | 43 (5.9) |
| Observed no. of person-years     | 24 052   | 4723        | 16 239   | 3090 |
| Unadjusted rate per 1000 person-years | 7.8      | 4.9        | 7.5      | 13.9 |
| Adjusted rate per 1000 person-years | 8.2      | 5.1        | 7.5      | 14.8 |
| White participants               |          |             |           |     |
| Observed no. of events (% participants) | 431 (5.1) | 84 (4.8) | 289 (5.0) | 58 (5.7) |
| Observed no. of person-years     | 54 516   | 11 791      | 37 303   | 5422 |
| Unadjusted rate per 1000 person-years | 7.9      | 7.1        | 7.7      | 10.7 |
| Adjusted rate per 1000 person-years | 7.9      | 7.1        | 7.7      | 10.8 |
| Low fragmentation                |          |             |           |     |
| Observed no. of events (% participants) | 289 (5.5) | 63 (5.9) | 187 (5.3) | 39 (6.3) |
| Observed no. of person-years     | 35 641   | 7552        | 24 511   | 3577 |
| Unadjusted rate per 1000 person-years | 8.1      | 8.3        | 7.6      | 10.9 |
| Adjusted rate per 1000 person-years | 7.9      | 8.0        | 7.5      | 10.6 |
| High fragmentation               |          |             |           |     |
| Observed no. of events (% participants) | 142 (4.3) | 21 (3.1) | 102 (4.6) | 19 (4.8) |
| Observed no. of person-years     | 18 875   | 4239        | 12 792   | 1844 |
| Unadjusted rate per 1000 person-years | 7.5      | 5.0        | 8.0      | 10.3 |
| Adjusted rate per 1000 person-years | 7.9      | 5.3        | 8.3      | 11.1 |
| Black participants               |          |             |           |     |
| Observed no. of events (% participants) | 180 (4.5) | 12 (3.1) | 110 (4.2) | 58 (5.9) |
| Observed no. of person-years     | 20 590   | 2045        | 14 063   | 4481 |
| Unadjusted rate per 1000 person-years | 8.7      | 5.9        | 7.8      | 12.9 |
| Adjusted rate per 1000 person-years | 8.8      | 6.0        | 7.9      | 12.8 |
| Low fragmentation                |          |             |           |     |
| Observed no. of events (% participants) | 134 (4.7) | 10 (3.7) | 90 (4.6) | 34 (5.2) |
| Observed no. of person-years     | 15 413   | 1562        | 10 616   | 3235 |

(Continued)
hazard ratio [HR], 1.01; 95% CI, 0.85, 1.21) (Table 4). There was a trend suggesting that high fragmentation was associated with a higher hazard of stroke, compared with low fragmentation, among participants with fair or poor self-rated health (adjusted HR, 1.39; 95% CI, 0.95–2.04). There was no association among participants with very good or good self-rated health (adjusted HR, 1.01; 95% CI, 0.82–1.26) or excellent self-rated health (adjusted HR, 0.66; 95% CI, 0.41–1.07).

Among Black participants with fair or poor self-rated health, high fragmentation was associated with a significantly higher hazard of stroke, compared with low fragmentation (adjusted HR, 1.83; 95% CI, 1.06–3.14). Among Black participants, there was no association between fragmentation and stroke among participants

| Table 3. Continued |
|------------------|-----------------|-----------------|-----------------|
|                  | Overall         | Self-Rated General Health |
|                  |                 | Excellent | Very Good or Good | Fair or Poor |
| Unadjusted rate per 1000 person-years | 8.7 | 6.4 | 8.5 | 10.5 |
| Adjusted rate per 1000 person-years | 8.7 | 7.2 | 8.5 | 10.3 |
| High fragmentation |                 |          |                  |
| Observed no. of events (% participants) | 46 (4.1) | 2 (1.8) | 20 (2.9) | 24 (7.2) |
| Observed no. of person-years | 5177 | 484 | 3447 | 1246 |
| Unadjusted rate per 1000 person-years | 8.9 | 4.1 | 5.8 | 19.3 |
| Adjusted rate per 1000 person-years | 8.9 | 3.4 | 6.0 | 19.3 |

*Adjusted rates were derived from Poisson models that adjusted for demographics (sex, age, race, income, region), medical conditions (hyperlipidemia, myocardial infarction, atrial fibrillation), medications (aspirin use, warfarin use), health behaviors (smoking), psychosocial variables (social support), physiological variables (body mass index, systolic blood pressure, albumin to creatinine ratio, C-reactive protein), self-rated health, and hospitalization. Fragmentation status is a time-varying exposure based on the reversed Bice-Boxerman index (low <0.85, high ≥0.85). See Methods section for more details.

Figure. Adjusted rates of incident strokes per 1000 person-years with 95% CIs, stratified by healthcare fragmentation, self-rated health, and race.*

*Fragmentation is defined using the reversed Bice-Boxerman index (high ≥0.85, low <0.85) and modeled as a time-varying exposure. Adjusted rates were derived from multivariable Poisson models; see Table 3 for more details. The lower bound of the CI for low fragmentation—Black race—excellent self-rated health was equal to −1.6
with very good or good self-rated health (adjusted HR, 0.73; 95% CI, 0.45–1.19). There were too few stroke events among Black participants with excellent self-rated health to calculate a model for that subgroup. There was no association between fragmentation and stroke among White participants, overall or by self-rated health subgroup.

### Sensitivity Analyses

When we changed the cutoff for “high” fragmentation to ≥0.80 instead of ≥0.85, 46.7% of the cohort was classified as having high fragmentation (rather than 25.7%). With this alternate cutoff of ≥0.80, we did not find any association between high fragmentation and incident stroke (Table S5). When we changed the cutoff for “high” fragmentation to ≥0.90, 13.7% of the cohort was classified as having high fragmentation. With this alternate cutoff of ≥0.90, we found that the association between high fragmentation and incident stroke persisted among the subset of Black participants with fair or poor self-rated health (adjusted HR, 2.13; 95% CI, 1.15–3.95). When we modeled fragmentation as a 4-level variable, CIs widened, but the association between fragmentation and incident stroke persisted among Black participants with fair of poor self-rated health and fragmentation scores ≥0.90, compared with the reference category (adjusted HR, 2.18; 95% CI, 1.11–4.28) (Table S6).

### DISCUSSION

In this nationwide, 11-year cohort study of 12,510 Medicare beneficiaries, we found that the association between highly fragmented ambulatory care and incident stroke varied with self-rated health and race. Overall, the adjusted rate of incident stroke was similar between participants with high versus low fragmentation (8.2 versus 8.1 per 1000 person-years, \(P=0.89\)). Among participants with fair or poor self-rated health at baseline, having high versus low fragmentation was associated with a trend toward a higher adjusted rate of incident strokes (14.8 versus 10.4 per 1000 person-years, \(P=0.067\)). Among Black participants with fair or poor self-rated health, having high versus...
low fragmentation was associated with a significantly higher adjusted rate of strokes (19.3 versus 10.3 per 1000 person-years, respectively; \( P=0.02 \)), which was equivalent to a significantly increased adjusted hazard of stroke (HR, 1.83; 95% CI, 1.06–3.14).

This study creates a novel bridge across several existing bodies of work. There is one body of work documenting physiologic risk factors for stroke, such as age, hypertension, diabetes mellitus, atrial fibrillation, coronary heart disease, and left ventricular hypertrophy, which our analysis includes. There is a second body of work linking self-rated health with stroke incidence and all-cause mortality. There is a third body of work documenting racial disparities in stroke incidence, with Black individuals experiencing a disproportionate number of strokes. There is a fourth body of work documenting racial disparities in the delivery of health care. This study is a novel addition, contributing new data on how fragmented ambulatory care relates to incident strokes, by self-rated health and by race, after accounting for physiologic risk factors.

The exact mechanism by which fragmentation increases the hazard of stroke among Black individuals with fair or poor self-rated health cannot be fully elucidated by the data in this study. Previous work has shown that fragmented care can lead to gaps in communication across providers caring for the same patient. Such gaps in communication have been shown to be associated with an increased risk of drug–drug interactions, including drug–drug interactions that could inadvertently worsen blood pressure control or worsen anticoagulation control among individuals at risk for stroke. Additional factors to be considered include that Black adults may be cared for by less well-trained physicians than White adults, Black adults may have less access to specialist providers than White adults (even with similar Medicare insurance), Black adults have reason to distrust the healthcare system, and Black adults may face explicit and/or implicit bias in the care they receive. In this context, Black adults with fair or poor health may be particularly vulnerable to any adverse consequences of fragmented care.

If future interventions were to try to reduce fragmentation, by how much would care patterns need to change in order to reduce fragmentation scores? To illustrate this, we provide a nomogram (Figure S2), which shows all possible patterns of providers for individuals with 12 visits (the average number of visits for Black participants with fair or poor health). The nomogram shows all possible patterns of providers (1 to 12 providers) and all possible distributions of visits across those providers. The nomogram illustrates how fragmentation scores decrease as the proportion of visits with the most frequently seen provider increases. Although the nomogram illustrates only patterns of care for individuals with 12 visits, this negative correlation holds for any visit count. In our study, participants with high fragmentation often had average fragmentation scores of \(0.90\), whereas participants with low fragmentation often had fragmentation scores of \(0.60\). Using the nomogram, we can see that, for individuals with 12 visits, a changing a fragmentation score from \(0.90\) to \(0.60\) would involve increasing the proportion of visits with the most frequently seen provider from \(25\%\) to \(58\%\). The nomogram also shows how fragmentation scores vary with the distribution of visits to the other providers, not just the most frequently seen provider.

This study has several strengths, including the national sampling frame and large sample size, with oversampling of Black individuals to ensure robust subgroup analysis, the long follow-up period, the uniform insurance coverage through Medicare fee-for-service, the previously validated measure of fragmentation, the treatment of fragmentation as a time-varying exposure, adjudicated stroke events, and clinically detailed potential confounders that were collected through standardized protocols.

This study has several limitations. First, this is an observational study, so we cannot infer causation or rule out unmeasured confounding. There were differences in the characteristics for participants with high versus low fragmentation; the reasons for these differences are not known. However, the direction of many of these differences (such as lower rates of cardiovascular risk factors in the high fragmentation group) would bias our study toward the null. Second, we do not have data on communication among providers, so fragmentation cannot be interpreted as the definite absence of communication. Third, we cannot determine the clinical appropriateness of the ambulatory visit patterns that we observed. Fourth, we measured self-rated health and clinical covariates at baseline, and it is possible that they change over time. However, self-rated health at baseline was a significant predictor of incident stroke.

CONCLUSIONS

High fragmentation of ambulatory care was associated with an increase in the hazard of incident stroke for Black individuals with fair or poor self-rated health, compared with low fragmentation (adjusted HR, 1.83; 95% CI, 1.06–3.14). Future research is needed to better understand how fragmentation affects Black adults with fair or poor health, in order to inform the design of future interventions to prevent unnecessary fragmentation and prevent excess strokes.

ARTICLE INFORMATION

Received August 18, 2020; accepted February 16, 2021.

Affiliations

From the Weill Cornell Medicine, New York, NY (L.M.K., J.B.R., M.R., L.P.C., E.R.; L.C.P., M.M.S.); and University of Alabama at Birmingham, Birmingham, AL (L.D.C.).
Acknowledgments
The authors thank the other investigators, the staff, and the participants of the REGARDS study for their valuable contributions. A full list of participating REGARDS study investigators and institutions can be found at http://www.regardsstudy.org.

Sources of Funding
The REGARDS study is funded by the National Institute of Neurological Disorders and Stroke and the National Institute on Aging, of the National Institutes of Health, Department of Health and Human Services (U01 NS041588). The ancillary study on healthcare fragmentation and cardiovascular outcomes was funded by the National Heart, Lung, and Blood Institute (R01 HL135199). The funding agencies played no role in the design or conduct of the study, and no role in data management, data analysis, interpretation of data, or preparation of the article. The REGARDS Executive Committee reviewed and approved this article before submission, ensuring adherence to standards for describing the REGARDS study.

Disclosures
Dr. Kern is a consultant to Mathematica, Inc. Ms. Rajan is a consultant to Veterans Biomedical Research Institute. Dr. Saiford reports a grant from Aman, Inc. Dr. Colantonio reports a grant from Aman, Inc. The remaining authors have no disclosures to report.

Supplementary Material
Data S1-S2
Supplemental Methods
Figures S1-S2
Tables S1-S6

REFERENCES
1. Chambless LE, Heiss G, Shahar E, Earp MJ, Tooie J. Prediction of ischemic stroke risk in the Atherosclerosis Risk in Communities Study. Am J Epidemiol. 2004;160:259–269. DOI: 10.1093/aje/kwh189.
2. Pham HH, Schrag D, O’Malley AS, Wu B, Bach PB. Care patterns in Medicare and their implications for pay for performance. N Engl J Med. 2007;356:1130–1139. DOI: 10.1056/NEJMsa062997.
3. Wolf PA, D’Agostino RB, Belanger AJ, Kannel WB. Probability of stroke: a risk profile from the Framingham Study. Stroke. 1991;22:312–318. DOI: 10.1161/01.STR.22.3.312.
4. O’Malley AS, Reschovsky JD. Referral and consultation communication between primary care and specialist physicians: finding common ground. Arch Intern Med. 2011;171:56–65. DOI: 10.1001/archinternmed.2010.480.
5. Smith PC, Arauya-Guerra R, Bubltz C, Parnes B, Dickinson LM, Van Vorst RM, Westfall JM, Pace WD. Missing clinical information during primary care. J Gen Intern Med. 2004;19:1103–1108. DOI: 10.1111/j.1525-1497.2005.00291.x.
6. Katz MA, McCoy KD, Vaughn-Sarrazin MS. Does greater continuity of Veterans Administration primary care reduce emergency department visits and hospitalization in older Veterans? J Am Geriatr Soc. 2015;63:2510–2519. DOI: 10.1111/jgs.13841.
11. Liu CW, Einstadter D, Cebul RD. Care fragmentation and emergency department use among complex patients with diabetes. Am J Manag Care. 2010;16:413–420.
12. Nyeideje DJ, Anthony DL, Byrum JP, Strawderman RL, Weeks WB, Casalino LP, Fisher ES. Continuity of care and the risk of preventable hospitalization in older adults. JAMA Intern Med. 2013;173:1679–1685. DOI: 10.1001/jama.2013.10059.
34. Chang HG, Lininger LL, Doyle JT, Maccubbin PA, Rothenberg RB. Application of the Cox model as a predictor of relative risk of coronary heart disease in the Albany Study. Stat Med. 1990;9:287–292. DOI: 10.1002/sim.4780090311.

35. Fisher LD, Lin DY. Time-dependent covariates in the Cox proportional-hazards regression model. Annu Rev Public Health. 1999;20:145–157. DOI: 10.1146/annurev.publheal.20.1.145.

36. Fleming TR, Harrington DP. Counting Process and Survival Analysis. Hoboken, NJ: John Wiley & Sons, Inc.; 2005.

37. Rubin DB, Schenker N. Multiple imputation in health-care databases: an overview and some applications. Stat Med. 1991;10:585–598. DOI: 10.1002/sim.4780100410.

38. Mavaddat N, van der Linde R, Parker R, Savva G, Kimmonth AL, Brayne C, Mant J. Relationship of self-rated health to stroke incidence and mortality in older individuals with and without a history of stroke: a longitudinal study of the MRC Cognitive Function and Ageing (CFAS) Population. PLoS One. 2016;11:e0150178. DOI: 10.1371/journal.pone.0150178.

39. Smedley BD, Stith AY, Nelson AR, eds. Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care. Washington, DC: National Academies Press; 2003.

40. Kern LM, Safford MM, Slavin MJ, Makovkina E, Fudl A, Carrillo JE, Abramson EL. Patients’ and providers’ views on the causes and consequences of healthcare fragmentation. J Gen Intern Med. 2019;34:899–907. DOI: 10.1007/s11606-019-04859-1.

41. Bach PB, Pham HH, Schrag D, Tate RC, Hargraves JL. Primary care physicians who treat blacks and whites. N Engl J Med. 2004;351:575–584. DOI: 10.1056/NEJMsa040609.

42. Blustein J, Weiss LJ. Visits to specialists under Medicare: socioeconomic advantage and access to care. J Health Care Poor Underserved. 1998;9:153–169. DOI: 10.1353/hpu.2010.0451.

43. Ferrer RL. Pursuing equity: contact with primary care and specialist clinicians by demographics, insurance, and health status. Ann Fam Med. 2007;5:492–502. DOI: 10.1370/afm.746.

44. Boulware LE, Cooper LA, Ratner LE, LaVeist TA, Powe NR. Race and trust in the health care system. Public Health Rep. 2003;118:358–365. DOI: 10.1016/S0033-3549(04)50262-5.

45. Cooper LA, Roter DL, Carson KA, Beach MO, Sabin JA, Greenwald AG, Inui TS. The associations of clinicians’ implicit attitudes about race with medical visit communication and patient ratings of interpersonal care. Am J Public Health. 2012;102:979–987. DOI: 10.2105/AJPH.2011.300558.
SUPPLEMENTAL MATERIAL
Data S1. Supplemental Methods. Formula for the Bice-Boxerman Index (BBI)*

\[ BBI = \frac{\left( \sum_{i=1}^{p} n_i^2 \right) - n}{n (n - 1)} \]

where  
- \( n \) = total number of visits in the 12-month period  
- \( n_i \) = number of visits to provider \( i \)  
- \( p \) = total number of providers

* The BBI is a continuous index that ranges from 0 to 1. We have reversed the direction of the Index, calculating 1 minus BBI, so that higher scores reflect more fragmentation.
Data S2. Supplemental Methods. Schematic diagram of analytic approach*

REGARDS = Reasons for Geographic and Racial Differences in Stroke.

*This schematic diagram illustrates a longitudinal design that treats the exposure (healthcare fragmentation) as time-varying. Observation continues until a stroke occurs, censoring occurs, or the end of the study period is reached. Note that the periods of time for the outcome do not overlap with each other, but they are contiguous (with the next one starting where the previous one left off).

†Observation began after the in-home visit with the first 12-month period for which there was continuous Medicare fee-for-service coverage, starting as early as January 1, 2004. The study continued (as shown in the schematic diagram) until the end of the study period, which was December 31, 2016.
Figure S1. Derivation of the study sample

All REGARDS participants
(N = 30,239)

Those participants ≥65 years old whose cohort data were linked to Medicare claims at any time in the study period
(N = 20,403)

Excluded for end-stage renal disease
(N = 1,431)

Excluded for having <12 months of continuous Medicare fee-for-service or for having Medicare managed care
(N = 3,816)

Excluded for being lost to follow-up before entry into this ancillary study
(N = 1,137)

Excluded for having ≤3 ambulatory visits in the first year of observation
(N = 551)

Excluded for evidence of stroke prior to or during the first year of observation
(N = 930)

Excluded for missing data for self-rated health
(N = 28)

Study sample
(N = 12,510)

Key: REGARDS = Reasons for Geographic and Racial Differences in Stroke
Table S1. Baseline characteristics, overall and stratified by self-rated health*

| Characteristic                                      | Overall (N = 12,510) | Excellent (N = 2,145) | Very good or good (N= 8,363) | Fair or poor (N = 2,002) | p-value |
|-----------------------------------------------------|----------------------|-----------------------|------------------------------|--------------------------|---------|
| **Demographic characteristics**                     |                      |                       |                              |                          |         |
| Age, years, mean (SD)                               | 70.5 (6.0)           | 70.4 (5.9)            | 70.6 (5.9)                   | 70.5 (6.2)               | 0.38    |
| Gender, female, N (%)                               | 6623 (52.9%)         | 994 (46.3%)           | 4425 (52.9%)                 | 1204 (60.1%)             | <0.001  |
| Race, white, N (%)                                  | 8513 (68.0%)         | 1760 (82.1%)          | 5739 (68.6%)                 | 1014 (50.6%)             | <0.001  |
| Marital status, married, N (%)                      | 7487 (59.8%)         | 1432 (66.8%)          | 5049 (60.4%)                 | 1006 (50.2%)             | <0.001  |
| Education, less than high school diploma, N (%)     | 1545 (12.4%)         | 127 (5.9%)            | 889 (10.6%)                  | 529 (26.4%)              | <0.001  |
| Annual household income, <$35,000, N (%)            | 5422 (49.5%)         | 652 (33.9%)           | 3568 (48.8%)                 | 1202 (69.8%)             | <0.001  |
| **Geographic region, N (%)**                        |                      |                       |                              |                          |         |
| Stroke Belt†                                        | 4551 (36.4%)         | 783 (36.5%)           | 2980 (35.6%)                 | 788 (39.4%)              | 0.015   |
| Stroke Buckle‡                                       | 2899 (23.2%)         | 490 (22.8%)           | 1941 (23.2%)                 | 468 (23.4%)              |         |
| Neither Stroke Belt nor Stroke Buckle               | 5060 (40.4%)         | 872 (40.7%)           | 3442 (41.2%)                 | 746 (37.3%)              |         |
| Residence in urban area, N (%)                      | 8467 (75.3%)         | 1412 (73.5%)          | 5711 (75.8%)                 | 1344 (75.0%)             | 0.003   |
| **Medical conditions§**                            |                      |                       |                              |                          |         |
| Hypertension, N (%)                                 | 7663 (61.5%)         | 874 (40.8%)           | 5256 (63.1%)                 | 1533 (76.8%)             | <0.001  |
| Dyslipidemia, N (%)                                 | 7538 (62.3%)         | 1109 (53.6%)          | 5082 (62.9%)                 | 1347 (69.4%)             | <0.001  |
| Diabetes, N (%)                                     | 2623 (21.7%)         | 166 (8.1%)            | 1665 (20.6%)                 | 792 (40.8%)              | <0.001  |
| History of coronary heart disease, N (%)            | 2521 (20.5%)         | 227 (10.7%)           | 1642 (20.0%)                 | 652 (33.1%)              | <0.001  |
| Atrial fibrillation, N (%)                          | 1149 (9.4%)          | 94 (4.4%)             | 723 (8.8%)                   | 332 (17.0%)              | <0.001  |
| **Medications**                                     |                      |                       |                              |                          |         |
| Medication adherence, N (%)                         | 8302 (71.1%)         | 1437 (75.2%)          | 5591 (71.2%)                 | 1274 (66.8%)             | <0.001  |
| Number of medications, median (IQR)                | 6.0 (3.0, 9.0)       | 4.0 (2.0, 7.0)        | 6.0 (3.0, 8.0)               | 8.0 (5.0, 11.0)          | <0.001  |
| Anti-hypertensive medication, N (%)                 | 6693 (55.4%)         | 671 (32.4%)           | 4602 (56.9%)                 | 1420 (73.5%)             | <0.001  |
| Insulin use, N (%)                                  | 657 (5.5%)           | 23 (1.1%)             | 355 (4.4%)                   | 279 (14.9%)              | <0.001  |
| Statin use, N (%)                                   | 4439 (35.5%)         | 547 (25.5%)           | 3074 (36.8%)                 | 818 (40.9%)              | <0.001  |
| Aspirin use, N (%)                                  | 6084 (48.6%)         | 967 (45.1%)           | 4112 (49.2%)                 | 1005 (50.2%)             | <0.001  |
| Warfarin use, N (%)                                 | 522 (4.2%)           | 40 (1.9%)             | 339 (4.1%)                   | 143 (7.1%)               | <0.001  |
| **Health behaviors**                                |                      |                       |                              |                          |         |
| Current smoker, N (%)                               | 1344 (10.8%)         | 144 (6.8%)            | 877 (10.5%)                  | 323 (16.2%)              | <0.001  |
| Alcohol use, N (%)                                  |                      |                       |                              |                          |         |
| Heavy                                               | 464 (3.8%)           | 113 (5.3%)            | 314 (3.8%)                   | 37 (1.9%)                | <0.001  |
| Moderate                                            | 4049 (33.0%)         | 851 (40.2%)           | 2791 (34.0%)                 | 407 (20.7%)              |         |
| None                                                | 7775 (63.3%)         | 1152 (54.4%)          | 5103 (62.2%)                 | 1520 (77.4%)             |         |
| Exercise, 0 times per week, N (%)                   | 4192 (34.1%)         | 419 (19.8%)           | 2740 (33.3%)                 | 1033 (52.4%)             | <0.001  |
| **Psychosocial variables**                          |                      |                       |                              |                          |         |
| Cares for a family member with a chronic illness or disability, N (%) | 1493 (11.9%)         | 242 (11.3%)           | 990 (11.9%)                  | 261 (13.0%)              | 0.20    |
| Lack of social support, N (%)                       | 485 (4.0%)           | 73 (3.5%)             | 320 (3.9%)                   | 92 (4.7%)                | 0.13    |
| Depressive symptoms, N (%)                          | 710 (5.7%)           | 54 (2.5%)             | 368 (4.4%)                   | 288 (14.4%)              | <0.001  |
| **Physiological variables**                         |                      |                       |                              |                          |         |
| Body mass index, kg/m², mean (SD)                   | 28.9 (5.8)           | 26.8 (4.5)            | 28.9 (5.6)                   | 31.2 (6.8)               | <0.001  |
| Measures                                                                 | 66.6 (24.8) | 65.4 (36.6) | 66.1 (18.2) | 70.0 (31.9) | <0.001 |
|-------------------------------------------------------------------------|-------------|-------------|-------------|-------------|-------|
| Heart rate, beats per min, mean (SD)                                    | 128.6 (16.3)| 125.7 (15.0)| 128.8 (16.1)| 130.9 (17.6)| <0.001|
| Systolic blood pressure, mm Hg, mean (SD)                               | 198.9 (39.4)| 193.3 (36.9)| 189.5 (39.4)| 188.0 (41.6)| <0.001|
| Left ventricular hypertrophy, N (%)                                     | 1247 (10.1%)| 136 (6.4%)  | 846 (10.3%) | 265 (13.4%) | <0.001|
| Total cholesterol, mg/dL, mean (SD)                                     | 189.9 (39.4)| 193.3 (36.9)| 189.5 (39.4)| 188.0 (41.6)| <0.001|
| Low-density lipoprotein cholesterol, mg/dL, mean (SD)                   | 111.5 (33.9)| 114.5 (31.8)| 111.2 (34.0)| 109.5 (35.4)| <0.001|
| High-density lipoprotein cholesterol, mg/dL, mean (SD)                  | 51.6 (16.3) | 53.9 (17.0) | 51.5 (16.2) | 49.6 (15.6) | <0.001|
| Glucose, mg/dL, mean (SD)                                               | 103.8 (33.7)| 96.5 (22.6) | 103.2 (32.6)| 114.0 (44.3)| <0.001|
| Estimated glomerular filtration rate, mL/min/1.73 m², mean (SD)        | 80.6 (18.9) | 82.3 (15.3) | 80.8 (18.5) | 77.9 (23.2) | <0.001|
| Urinary albumin-to-creatinine ratio, mg/g, median (IQR)                 | 7.8 (4.9, 16.7) | 6.4 (4.3, 11.3) | 7.9 (4.9, 16.8) | 10.2 (5.7, 30.2) | <0.001|
| C-reactive protein, mg/L, median (IQR)                                  | 7.8 (4.9, 16.7) | 6.4 (4.3, 11.3) | 7.9 (4.9, 16.8) | 10.2 (5.7, 30.2) | <0.001|
| Mental component summary score, mean (SD)                               | 55.1 (7.6) | 56.9 (5.5)  | 55.6 (6.9)  | 50.9 (10.4) | <0.001|
| Physical component summary score, mean (SD)                             | 46.6 (10.3) | 54.1 (5.4)  | 47.6 (8.5)  | 34.0 (10.3) | <0.001|
| Healthcare utilization                                                   |             |             |             |             |       |
| Hospitalization in the first year of observation, N (%)                 | 1245 (10.0%)| 153 (7.1%)  | 803 (9.6%)  | 289 (14.4%) | <0.001|

* Missing data: education (N=4), income (1,554), residence in urban area (N=1,261), medication count (N=12), smoking (N=48), exercise (N= 207), caregiver status (N= 12), lack of social support (N= 308), depressive symptoms (N= 72), body mass index (N=65), heart rate (111), systolic blood pressure (N=34), total cholesterol (N=454), low density lipoprotein (N=680), high-density lipoprotein (N=529), glucose (N=456), estimated glomerular filtration rate (N=454), urinary albumin-to-creatinine ratio (N=505), C-reactive protein (N=724), mental component summary score (N=591), and physical component summary score (N=591).
† Stroke Belt = North Carolina, South Carolina, Georgia, Tennessee, Mississippi, Alabama, Louisiana, and Arkansas (except for 153 coastal counties that constitute the Stroke Buckle).15
‡ Stroke Buckle = 153 coastal counties in North Carolina, South Carolina, and Georgia.15,21
§ See methods section for detailed definitions of variables.
Key: rBBI = reversed Bice-Boxerman Index (BBI), equivalent to 1 – BBI, such that higher scores indicate more fragmentation.19 IQR = interquartile range. SF = short-form survey.32 Percentages may not sum to 100 due to rounding.
Table S2. Baseline characteristics, overall and stratified by race*

| Characteristic                                                                 | Overall (N = 12,510) | Black (N = 3,997) | White (N = 8,513) | p-value |
|-------------------------------------------------------------------------------|----------------------|-------------------|-------------------|---------|
| **Demographic characteristics**                                               |                      |                   |                   |         |
| Age, years, mean (SD)                                                         | 70.5 (6.0)           | 70.2 (5.8)        | 70.7 (6.0)        | <0.001  |
| Gender, female, N (%)                                                         | 6623 (52.9%)         | 2531 (63.3%)      | 4092 (48.1%)      | <0.001  |
| Marital status, married, N (%)                                                | 7487 (59.8%)         | 1767 (44.2%)      | 5720 (67.2%)      | <0.001  |
| Education, less than high school diploma, N (%)                              | 1545 (12.4%)         | 912 (22.8%)       | 633 (7.4%)        | <0.001  |
| Annual household income, <$35,000, N (%)                                      | 5422 (49.5%)         | 2269 (64.6%)      | 3153 (42.4%)      | <0.001  |
| Geographic region, N (%)                                                      |                      |                   |                   |         |
| Stroke Belt†                                                                 | 4551 (36.4%)         | 1345 (33.7%)      | 3206 (37.7%)      | <0.001  |
| Stroke Buckle‡                                                                | 2899 (23.2%)         | 809 (20.2%)       | 2090 (24.6%)      |         |
| Neither Stroke Belt nor Stroke Buckle                                         | 5060 (40.4%)         | 1843 (46.1%)      | 3217 (37.8%)      |         |
| Residence in urban area, N (%)                                                | 8467 (75.3%)         | 3299 (89.5%)      | 5168 (68.3%)      | <0.001  |
| **Medical conditions§**                                                       |                      |                   |                   |         |
| Hypertension, N (%)                                                           | 7663 (61.5%)         | 2990 (75.0%)      | 4673 (55.1%)      | <0.001  |
| Dyslipidemia, N (%)                                                           | 7538 (62.3%)         | 2250 (58.9%)      | 5288 (63.9%)      | <0.001  |
| Diabetes, N (%)                                                              | 2621 (20.5%)         | 1270 (33.1%)      | 1353 (16.4%)      | <0.001  |
| History of coronary heart disease, N (%)                                      | 2521 (20.5%)         | 693 (17.6%)       | 1828 (21.8%)      | <0.001  |
| Atrial fibrillation, N (%)                                                    | 1149 (9.4%)          | 312 (8.0%)        | 837 (10.0%)       | <0.001  |
| **Medications**                                                              |                      |                   |                   |         |
| Medication adherence, N (%)                                                   | 8302 (71.1%)         | 2620 (70.7%)      | 5682 (71.3%)      | 0.53    |
| Number of medications, median (IQR)                                          | 6.0 (3.0, 9.0)       | 5.0 (3.0, 8.0)    | 6.0 (3.0, 9.0)    | <0.001  |
| Anti-hypertensive medication, N (%)                                          | 6693 (55.4%)         | 2699 (69.8%)      | 3994 (48.6%)      | <0.001  |
| Insulin use, N (%)                                                           | 657 (5.5%)           | 374 (9.9%)        | 283 (3.5%)        | <0.001  |
| Statin use, N (%)                                                            | 4439 (35.5%)         | 1304 (32.6%)      | 3135 (36.8%)      | <0.001  |
| Aspirin use, N (%)                                                           | 6084 (48.6%)         | 1749 (43.8%)      | 4335 (50.9%)      | <0.001  |
| Warfarin use, N (%)                                                          | 522 (4.2%)           | 101 (2.5%)        | 421 (5.0%)        | <0.001  |
| **Health behaviors**                                                          |                      |                   |                   |         |
| Current smoker, N (%)                                                        | 1344 (10.8%)         | 510 (12.8%)       | 834 (9.8%)        | <0.001  |
| Alcohol use, N (%)                                                           |                      |                   |                   | <0.001  |
| Heavy                                                                        | 464 (3.8%)           | 79 (2.0%)         | 385 (4.6%)        |         |
| Moderate                                                                     | 4049 (33.0%)         | 906 (23.2%)       | 3143 (37.5%)      |         |
| None                                                                         | 7775 (63.3%)         | 2920 (74.8%)      | 4855 (57.9%)      |         |
| Exercise frequency, 0 times per week, N (%)                                  | 4192 (34.1%)         | 1515 (38.6%)      | 2677 (32.0%)      | <0.001  |
| **Psychosocial variables**                                                    |                      |                   |                   |         |
| Cares for a family member with a chronic illness or disability, N (%)        | 1493 (11.9%)         | 531 (13.3%)       | 962 (11.3%)       | 0.001   |
| Lack of social support, N (%)                                                 | 485 (4.0%)           | 154 (4.0%)        | 331 (4.0%)        | 0.99    |
| Depressive symptoms, N (%)                                                   | 710 (5.7%)           | 306 (7.7%)        | 404 (4.8%)        | <0.001  |
| **Physiological variables**                                                  |                      |                   |                   |         |
| Body mass index, kg/m², mean (SD)                                            | 28.9 (5.8)           | 30.6 (6.3)        | 28.1 (5.4)        | <0.001  |
| Heart rate, beats per minute, mean (SD)                                       | 66.6 (24.8)          | 68.0 (23.8)       | 65.9 (25.3)       | <0.001  |
| Systolic blood pressure, mm Hg, mean (SD)                                    | 128.6 (16.3)         | 131.8 (17.0)      | 127.1 (15.7)      | <0.001  |
| Left ventricular hypertrophy, N (%)                                          | 1247 (10.1%)         | 643 (16.3%)       | 604 (7.2%)        | <0.001  |
| Total cholesterol, mg/dL, mean (SD)                                          | 189.9 (39.4)         | 192.9 (40.9)      | 188.5 (38.6)      | <0.001  |
| Low-density lipoprotein cholesterol, mg/dL, mean (SD)                         | 111.5 (33.9)         | 116.4 (36.1)      | 109.2 (32.5)      | <0.001  |
| Parameter                                      | Group 1 | Group 2 | Group 3 | p-value |
|-----------------------------------------------|---------|---------|---------|---------|
| High-density lipoprotein cholesterol, mg/dL, mean (SD) | 51.6 (16.3) | 53.9 (15.8) | 50.6 (16.4) | <0.001 |
| Glucose, mg/dL, mean (SD)                     | 103.8 (33.7) | 109.7 (41.9) | 101.1 (28.8) | <0.001 |
| Estimated glomerular filtration rate, mL/min/1.73 m², mean (SD) | 80.6 (18.9) | 83.9 (22.4) | 79.1 (16.8) | <0.001 |
| Urinary albumin-to-creatinine ratio, mg/g, median (IQR) | 2.1 (0.9, 4.8) | 2.9 (1.2, 6.4) | 1.9 (0.9, 4.1) | <0.001 |
| C-reactive protein, mg/L, median (IQR)        | 7.8 (4.9, 16.7) | 8.3 (4.9, 20.2) | 7.6 (4.9, 15.4) | <0.001 |

**Self-rated health**

| Self-rated general health (SF-1), N (%)          |        |
|------------------------------------------------|--------|
| Excellent                                      | 2145 (17.1%) | 385 (9.6%) | 1760 (20.7%) |
| Very good                                      | 3940 (31.5%) | 943 (23.6%) | 2997 (35.2%) |
| Good                                           | 4423 (35.4%) | 1681 (42.1%) | 2742 (32.2%) |
| Fair                                           | 1669 (13.3%) | 843 (21.1%) | 826 (9.7%) |
| Poor                                           | 333 (2.7%) | 145 (3.6%) | 188 (2.2%) |

| Mental component summary score, mean (sd)       |        |
|------------------------------------------------|--------|
|                                                      | 55.1 (7.6) | 54.2 (8.4) | 55.5 (7.2) |

| Physical component summary score, mean (sd)      |        |
|------------------------------------------------|--------|
|                                                      | 46.6 (10.3) | 45.1 (10.4) | 47.2 (10.1) |

**Healthcare utilization**

| Hospitalization in the first year of observation, N (%) |        |
|---------------------------------------------------------|--------|
|                                                        | 1245 (10.0%) | 454 (11.4%) | 791 (9.3%) |

|                  |        |
|------------------|--------|
| Healthcare utilization | <0.001 |
Table S3. Baseline characteristics among black participants, overall and stratified by self-rated health

| Characteristic                                                                 | Overall (N = 3,997) | Excellent (N = 385) | Very good or good (N = 2624) | Fair or poor (N = 988) | p-value |
|--------------------------------------------------------------------------------|---------------------|----------------------|-------------------------------|------------------------|---------|
| **Demographic characteristics**                                                 |                     |                      |                               |                        |         |
| Age, years, mean (SD)                                                          | 70.2 (5.8)          | 70.0 (5.5)           | 70.2 (5.7)                    | 70.3 (6.2)             | 0.7     |
| Gender, female, N (%)                                                          | 2531 (63.3%)        | 207 (53.8%)          | 1644 (62.7%)                  | 680 (68.8%)            | <0.001  |
| Marital status, married, N (%)                                                 | 1767 (44.2%)        | 174 (45.2%)          | 1207 (46.0%)                  | 386 (39.1%)            | <0.001  |
| Education, less than high school diploma, N (%)                               | 912 (22.8%)         | 59 (15.3%)           | 499 (19.0%)                   | 354 (35.8%)            | <0.001  |
| Annual household income, <$35,000, N (%)                                       | 2269 (64.6%)        | 175 (51.0%)          | 1434 (61.7%)                  | 660 (78.0%)            | <0.001  |
| **Geographic region, N (%)**                                                   | 1345 (33.7%)        | 125 (32.5%)          | 869 (33.1%)                   | 351 (35.5%)            | 0.46    |
| **Residence in urban area, N (%)**                                            | 3299 (89.5%)        | 322 (90.7%)          | 2199 (90.8%)                  | 778 (85.6%)            | <0.001  |
| **Medical conditions§**                                                       |                     |                      |                               |                        |         |
| Hypertension, N (%)                                                           | 2990 (75.0%)        | 216 (56.1%)          | 1937 (74.1%)                  | 837 (84.8%)            | <0.001  |
| Dyslipidemia, N (%)                                                            | 2250 (58.9%)        | 177 (48.6%)          | 1440 (57.6%)                  | 633 (66.1%)            | <0.001  |
| Diabetes, N (%)                                                               | 1270 (33.1%)        | 69 (18.8%)           | 759 (30.2%)                   | 442 (46.1%)            | <0.001  |
| History of coronary heart disease, N (%)                                       | 693 (17.6%)         | 34 (9.1%)            | 384 (14.9%)                   | 275 (28.3%)            | <0.001  |
| Atrial fibrillation, N (%)                                                    | 312 (8.0%)          | 9 (2.4%)             | 162 (6.3%)                    | 141 (14.8%)            | <0.001  |
| **Medications**                                                               |                     |                      |                               |                        |         |
| Medication adherence, N (%)                                                   | 2620 (70.7%)        | 247 (75.1%)          | 1742 (71.4%)                  | 631 (67.5%)            | 0.016   |
| Number of medications, median (IQR)                                           | 5.0 (3.0, 8.0)      | 3.0 (1.0, 5.0)       | 5.0 (3.0, 7.0)                | 7.0 (5.0, 10.0)        | <0.001  |
| Anti-hypertensive medication, N (%)                                           | 2699 (69.8%)        | 173 (45.6%)          | 1743 (68.9%)                  | 783 (81.6%)            | <0.001  |
| Insulin use, N (%)                                                            | 374 (9.9%)          | 14 (3.8%)            | 196 (7.9%)                    | 164 (17.7%)            | <0.001  |
| Statin use, N (%)                                                             | 1304 (32.6%)        | 73 (19.0%)           | 842 (32.1%)                   | 389 (39.4%)            | <0.001  |
| Aspirin use, N (%)                                                            | 1749 (43.8%)        | 135 (35.1%)          | 1141 (43.5%)                  | 473 (47.9%)            | <0.001  |
| Warfarin use, N (%)                                                           | 101 (2.5%)          | 4 (1.0%)             | 54 (2.1%)                     | 43 (4.4%)              | <0.001  |
| **Health behaviors**                                                          |                     |                      |                               |                        |         |
| Current smoker, N (%)                                                         | 510 (12.8%)         | 46 (12.1%)           | 306 (11.7%)                   | 158 (16.0%)            | 0.002   |
| Alcohol use, N (%)                                                            | 79 (2.0%)           | 10 (2.7%)            | 50 (2.0%)                     | 19 (2.0%)              |         |
| Heavy                                                                         | 906 (23.2%)         | 88 (23.4%)           | 667 (26.0%)                   | 151 (15.6%)            |         |
| Moderate                                                                      | 2920 (74.8%)        | 278 (73.9%)          | 1845 (72.0%)                  | 797 (82.4%)            | <0.001  |
| None                                                                          | 1515 (38.6%)        | 89 (23.7%)           | 917 (35.6%)                   | 509 (52.3%)            | <0.001  |
| Exercise, 0 times per week, N (%)                                            |                     |                      |                               |                        |         |
| **Psychosocial variables**                                                    |                     |                      |                               |                        |         |
| Cares for a family member with a chronic illness or disability, N (%)         | 531 (13.3%)         | 39 (10.1%)           | 362 (13.8%)                   | 130 (13.2%)            | 0.14    |
| Lack of social support, N (%)                                                 | 154 (4.0%)          | 12 (3.2%)            | 103 (4.1%)                    | 39 (4.1%)              | 0.72    |
| Depressive symptoms, N (%)                                                    | 306 (7.7%)          | 15 (3.9%)            | 145 (5.6%)                    | 146 (14.8%)            | <0.001  |
| **Physiological variables**                                                   |                     |                      |                               |                        |         |
| Body mass index, kg/m², mean (SD)                                             | 30.6 (6.3)          | 28.5 (5.1)           | 30.3 (6.0)                    | 32.3 (6.9)             | <0.001  |
|                                | 68.0 (23.8) | 68.5 (48.8) | 67.3 (21.4) | 69.5 (12.4) | 0.041 |
|--------------------------------|-------------|-------------|-------------|-------------|-------|
| Heart rate, beats per min, mean (SD) | 68.0 (23.8) | 68.5 (48.8) | 67.3 (21.4) | 69.5 (12.4) | 0.041 |
| Systolic blood pressure, mm Hg, mean (SD) | 131.8 (17.0) | 129.2 (16.1) | 131.7 (16.8) | 133.1 (17.8) | <0.001 |
| Left ventricular hypertrophy, N (%) | 643 (16.3%) | 50 (13.2%) | 406 (15.7%) | 187 (19.1%) | 0.01 |
| Total cholesterol, mg/dL, mean (SD) | 192.9 (40.9) | 198.9 (39.2) | 192.9 (40.9) | 190.7 (41.4) | 0.005 |
| Low-density lipoprotein cholesterol, mg/dL, mean (SD) | 116.4 (36.1) | 122.3 (34.6) | 116.3 (36.1) | 114.5 (36.7) | 0.002 |
| High-density lipoprotein cholesterol, mg/dL, mean (SD) | 53.9 (15.8) | 55.4 (16.4) | 54.2 (15.8) | 52.4 (15.6) | 0.002 |
| Glucose, mg/dL, mean (SD) | 109.7 (41.9) | 102.0 (31.4) | 108.2 (39.8) | 116.6 (49.4) | <0.001 |
| Estimated glomerular filtration rate, mL/min/1.73 m², mean (SD) | 83.9 (22.4) | 88.0 (18.9) | 84.5 (21.6) | 80.6 (25.2) | <0.001 |
| Urinary albumin-to-creatinine ratio, mg/g, median (IQR) | 2.9 (1.2, 6.4) | 6.5 (4.3, 11.7) | 8.1 (4.8, 18.6) | 10.9 (5.5, 36.8) | <0.001 |
| C-reactive protein, mg/L, median (IQR) | 8.3 (4.9, 20.2) | 2.0 (0.8, 4.3) | 2.8 (1.3, 6.0) | 3.9 (1.5, 8.2) | <0.001 |
| Self-rated health | 54.2 (8.4) | 56.7 (6.0) | 55.4 (7.2) | 50.2 (10.6) | <0.001 |
| Mental component summary score, mean (SD) | 45.1 (10.4) | 54.1 (5.4) | 47.3 (8.5) | 35.7 (10.2) | <0.001 |
| Physical component summary score, mean (SD) | 45.1 (10.4) | 54.1 (5.4) | 47.3 (8.5) | 35.7 (10.2) | <0.001 |
| Healthcare utilization | 454 (11.4%) | 39 (10.1%) | 280 (10.7%) | 135 (13.7%) | 0.03 |
Table S4. Baseline characteristics among white participants, overall and stratified by self-rated health

| Characteristic                                      | Overall (N = 8,513) | Excellent (N = 1,760) | Very good or good (N = 5,739) | Fair or poor (N = 1,014) | p-value |
|-----------------------------------------------------|---------------------|-----------------------|-----------------------------|--------------------------|---------|
| **Demographic characteristics**                     |                     |                       |                             |                          |         |
| Age, years, mean (SD)                               | 70.7 (6.0)          | 70.5 (6.0)            | 70.8 (6.0)                  | 70.7 (6.2)               | 0.22    |
| Gender, female, N (%)                               | 4092 (48.1%)        | 787 (44.7%)           | 2781 (48.5%)                | 524 (51.7%)              | 0.001   |
| Marital status, married, N (%)                      | 5720 (67.2%)        | 1258 (71.5%)          | 3842 (66.9%)                | 620 (61.1%)              | <0.001  |
| Education, less than high school diploma, N (%)     | 633 (7.4%)          | 68 (3.9%)             | 390 (6.8%)                  | 175 (17.3%)              | <0.001  |
| Annual household income, <$35,000, N (%)            | 3153 (42.4%)        | 477 (30.2%)           | 2134 (42.8%)                | 542 (61.9%)              | <0.001  |
| **Geographic region, N (%)**                         |                     |                       |                             |                          |         |
| Stroke Belt†                                        | 3206 (37.7%)        | 658 (37.4%)           | 2111 (36.8%)                | 437 (43.1%)              |         |
| Stroke Buckle‡                                       | 2090 (24.6%)        | 409 (23.2%)           | 1419 (24.7%)                | 262 (25.8%)              | <0.001  |
| Neither Stroke Belt nor Stroke Buckle                | 3217 (37.8%)        | 693 (39.4%)           | 2209 (38.5%)                | 315 (31.1%)              |         |
| **Residence in urban area, N (%)**                  | 5168 (68.3%)        | 1090 (69.6%)          | 3512 (68.7%)                | 566 (64.1%)              | 0.003   |
| **Medical conditions§**                             |                     |                       |                             |                          |         |
| Hypertension, N (%)                                  | 4673 (55.1%)        | 658 (37.5%)           | 3319 (58.0%)                | 696 (69.0%)              | <0.001  |
| Dyslipidemia, N (%)                                  | 5288 (63.9%)        | 932 (54.7%)           | 3642 (65.2%)                | 714 (72.6%)              | <0.001  |
| Diabetes, N (%)                                      | 1353 (16.4%)        | 97 (5.7%)             | 906 (16.3%)                 | 350 (35.6%)              | <0.001  |
| History of coronary heart disease, N (%)            | 1828 (21.8%)        | 193 (11.1%)           | 1258 (22.3%)                | 377 (37.9%)              | <0.001  |
| Atrial fibrillation, N (%)                           | 837 (10.0%)         | 85 (4.9%)             | 561 (10.0%)                 | 191 (19.2%)              | <0.001  |
| **Medications**                                      |                     |                       |                             |                          |         |
| Ideal medication adherence                          | 5682 (71.3%)        | 1190 (75.2%)          | 3849 (71.1%)                | 643 (66.1%)              | <0.001  |
| Number of medications, median (IQR)                 | 6.0 (3.0, 9.0)      | 4.0 (2.0, 7.0)        | 6.0 (4.0, 9.0)              | 9.0 (6.0, 12.0)          | <0.001  |
| Anti-hypertensive medication, N (%)                  | 3994 (48.6%)        | 498 (29.5%)           | 2859 (51.4%)                | 637 (65.5%)              | <0.001  |
| Insulin use, N (%)                                   | 283 (3.5%)          | 9 (0.5%)              | 159 (2.9%)                  | 115 (12.2%)              | <0.001  |
| Statin use, N (%)                                    | 3135 (36.8%)        | 474 (26.9%)           | 2232 (38.9%)                | 429 (42.3%)              | <0.001  |
| Aspirin use, N (%)                                   | 4335 (50.9%)        | 832 (47.3%)           | 2971 (51.8%)                | 532 (52.5%)              | 0.002   |
| Warfarin use, N (%)                                  | 421 (5.0%)          | 36 (2.1%)             | 285 (5.0%)                  | 100 (9.9%)               | <0.001  |
| **Health behaviors**                                 |                     |                       |                             |                          |         |
| Current smoker, N (%)                                | 834 (9.8%)          | 98 (5.6%)             | 571 (10.0%)                 | 165 (16.3%)              | <0.001  |
| Alcohol use, N (%)                                   |                     |                       |                             |                          |         |
| Heavy                                               | 385 (4.6%)          | 103 (5.9%)            | 264 (4.7%)                  | 18 (1.8%)                | <0.001  |
| Moderate                                             | 3143 (37.5%)        | 763 (43.9%)           | 2124 (37.6%)                | 256 (25.7%)              | <0.001  |
| None                                                 | 4855 (57.9%)        | 874 (50.2%)           | 3258 (57.7%)                | 723 (72.5%)              |         |
| Exercise, 0 times per week, N (%)                    | 2677 (32.0%)        | 330 (19.0%)           | 1823 (32.3%)                | 524 (52.6%)              | <0.001  |
| **Psychosocial variables**                           |                     |                       |                             |                          |         |
| Cares for a family member with a chronic illness or disability, N (%) | 962 (11.3%)          | 203 (11.5%)           | 628 (11.0%)                | 131 (12.9%)              | 0.18    |
| Lack of social support, N (%)                        | 331 (4.0%)          | 61 (3.6%)             | 217 (3.9%)                  | 53 (5.3%)                | 0.061   |
| Depressive symptoms, N (%)                           | 404 (4.8%)          | 39 (2.2%)             | 223 (3.9%)                  | 142 (14.1%)              | <0.001  |
| **Physiological variables**                          |                     |                       |                             |                          |         |
| Body mass index, kg/m², mean (SD)                    | 28.1 (5.4)          | 26.4 (4.2)            | 28.2 (5.3)                  | 30.1 (6.5)               | <0.001  |
|                                | Mean (SD)        | Mean (SD)        | Mean (SD)        | Mean (SD)        | Mean (SD)        | p-value  |
|--------------------------------|------------------|------------------|------------------|------------------|------------------|----------|
| Heart rate, beats per min.     | 65.9 (25.3)      | 64.7 (33.3)      | 65.5 (16.5)      | 70.4 (43.1)      | <0.001           |          |
| Systolic blood pressure, mm Hg | 127.1 (15.7)     | 124.9 (14.6)     | 127.5 (15.7)     | 128.8 (17.1)     | <0.001           |          |
| Left ventricular hypertrophy, N| 604 (7.2%)       | 86 (4.9%)        | 440 (7.8%)       | 78 (7.8%)        | <0.001           |          |
| Total cholesterol, mg/dL       | 188.5 (38.6)     | 192.1 (36.3)     | 188.0 (38.6)     | 185.4 (41.7)     | <0.001           |          |
| Low-density lipoprotein cholesterol, mg/dL | 109.2 (32.5)     | 112.8 (30.9)     | 108.9 (32.7)     | 104.6 (33.3)     | <0.001           |          |
| High-density lipoprotein cholesterol, mg/dL | 50.6 (16.4)      | 53.6 (17.1)      | 50.3 (16.2)      | 46.9 (15.0)      | <0.001           |          |
| Glucose, mg/dL                 | 101.1 (28.8)     | 95.3 (20.0)      | 101.0 (28.6)     | 111.4 (38.7)     | <0.001           |          |
| Estimated glomerular filtration rate, mL/min/1.73 m² | 79.1 (16.8)      | 81.1 (14.1)      | 79.2 (16.7)      | 75.2 (20.7)      | <0.001           |          |
| Urinary albumin-to-creatinine ratio, mg/g, median (IQR) | 1.9 (0.9, 4.1)   | 6.3 (4.4, 11.1)  | 7.8 (4.9, 16.2)  | 9.9 (5.8, 25.0)  | <0.001           |          |
| C-reactive protein, mg/L, median (IQR) | 7.6 (4.9, 15.4) | 1.3 (0.7, 3.0)   | 1.9 (0.9, 4.1)   | 3.0 (1.3, 7.0)   | <0.001           |          |
| Self-rated health              |                  |                  |                  |                  |                  |          |
| Mental component summary score | 55.5 (7.2)       | 56.9 (5.4)       | 55.7 (6.8)       | 51.6 (10.1)      | <0.001           |          |
| Physical component summary score | 47.2 (10.1)      | 54.0 (5.4)       | 47.7 (8.4)       | 32.4 (10.2)      | <0.001           |          |
| Healthcare utilization         |                  |                  |                  |                  |                  |          |
| Hospitalization in the first year of observation, N (%) | 791 (9.3%)       | 114 (6.5%)       | 523 (9.1%)       | 154 (15.2%)      | <0.001           |          |
Table S5. Fully adjusted hazard of incident stroke, comparing high to low fragmentation, overall and stratified by self-rated general health and race, with sensitivity analyses varying the cut-off for high fragmentation*

| Cut-off for high fragmentation | N (%) classified as high fragmentation | Self-rated general health | Adjusted hazard ratios (95% confidence intervals) |
|--------------------------------|----------------------------------------|--------------------------|-----------------------------------------------|
|                                | Overall | Excellent | Very Good or Good | Fair or Poor |
| ALL PARTICIPANTS               | N = 12,510 | 1.03 (0.88, 1.21) | 1.09 (0.89, 1.33) | 1.11 (0.77, 1.61) |
| ≥0.80                          | 5,838 (46.7%) | 0.72 (0.48, 1.09) | --- | --- |
| ≥0.85 (base case)              | 3,209 (25.7%) | 0.66 (0.41, 1.07) | 1.01 (0.82, 1.26) | 1.39 (0.95, 2.04) |
| ≥0.90                          | 1,713 (13.7%) | 0.80 (0.45, 1.42) | 0.96 (0.72, 1.27) | 1.69 (1.07, 2.67) |
| WHITE PARTICIPANTS             | N = 8,513 | 1.02 (0.84, 1.23) | 1.16 (0.92, 1.48) | 0.87 (0.51, 1.46) |
| ≥0.80                          | 4,289 (50.4%) | 0.76 (0.49, 1.17) | --- | --- |
| ≥0.85 (base case)              | 2,405 (28.3%) | 0.67 (0.40, 1.10) | 1.11 (0.87, 1.42) | 1.01 (0.58, 1.76) |
| ≥0.90                          | 1,326 (15.6%) | 0.75 (0.41, 1.39) | 0.99 (0.72, 1.36) | 0.83 (0.49, 1.40) |
| BLACK PARTICIPANTS             | N = 3,997 | 1.02 (0.75, 1.37) | --- | 0.91 (0.62, 1.34) | 1.34 (0.79, 2.29) |
| ≥0.80                          | 1,549 (38.8%) | --- | 0.73 (0.45, 1.19) | 1.83 (1.06, 3.14) |
| ≥0.85 (base case)              | 804 (20.1%) | 1.05 (0.74, 1.46) | --- | 0.80 (0.42, 1.54) | 2.13 (1.15, 3.95) |
| ≥0.90                          | 387 (9.7%) | 1.26 (0.83, 1.91) | --- | --- |

* Results were derived from Cox proportional hazards models that treat fragmentation as a time-varying exposure, consider 12 months of the exposure at a time and outcomes that occur in the 3 months immediately following the exposure period, and occur over up to 11.8 years of follow-up. Fragmentation is measured with the reversed Bice-Boxerman Index. We were not able to calculate results for black participants with excellent self-rated health because they had too few events.
Table S6. Fully adjusted hazard of incident stroke, overall and stratified by self-rated general health and race, modeling fragmentation as a variable with four levels*

| Fragmentation score | N (%)† | Number of strokes† | Overall | Self-rated general health |
|---------------------|--------|--------------------|---------|--------------------------|
|                     |        |                    |         | Excellent | Very Good or Good | Fair or Poor |
|                     |        |                    | Adjusted hazard ratios (95% confidence intervals) | |
| ALL PARTICIPANTS    | N = 12,510 |                    |         |            |            |            |
| ≤0.80               | 6672 (53.3%) | 324 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| 0.81-0.84           | 2629 (21.0%) | 138 | 1.04 (0.84, 1.28) | 0.85 (0.51, 1.42) | 1.14 (0.89, 1.47) | 0.81 (0.47, 1.39) |
| 0.85-0.89           | 1496 (12.0%) | 77  | 1.00 (0.79, 1.26) | 0.55 (0.27, 1.12) | 1.10 (0.82, 1.46) | 1.06 (0.63, 1.80) |
| ≥0.90               | 1713 (13.7%) | 72  | 1.06 (0.84, 1.34) | 0.70 (0.38, 1.27) | 1.01 (0.75, 1.37) | 1.63 (1.00, 2.67) |
| WHITE PARTICIPANTS  | N = 8,513 |                    |         |            |            |            |
| ≤0.80               | 4224 (49.6%) | 218 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| 0.81-0.84           | 1884 (22.1%) | 108 | 1.05 (0.82, 1.34) | 0.92 (0.54, 1.58) | 1.17 (0.86, 1.58) | 0.76 (0.36, 1.62) |
| 0.85-0.89           | 1079 (12.7%) | 51  | 1.02 (0.78, 1.33) | 0.61 (0.30, 1.26) | 1.24 (0.90, 1.71) | 0.77 (0.36, 1.64) |
| ≥0.90               | 1326 (15.6%) | 54  | 0.98 (0.74, 1.30) | 0.68 (0.35, 1.30) | 1.08 (0.77, 1.53) | 1.13 (0.54, 2.35) |
| BLACK PARTICIPANTS  | N = 3,997 |                    |         |            |            |            |
| ≤0.80               | 2448 (61.2%) | 106 | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) | 1.00 (ref) |
| 0.81-0.84           | 745 (18.6%) | 30  | 0.98 (0.66, 1.45) | --- | 1.10 (0.69, 1.74) | 0.79 (0.35, 1.76) |
| 0.85-0.89           | 417 (10.4%) | 26  | 0.88 (0.54, 1.42) | --- | 0.71 (0.37, 1.40) | 1.41 (0.67, 2.96) |
| ≥0.90               | 387 (9.7%) | 18  | 1.23 (0.79, 1.90) | --- | 0.78 (0.40, 1.54) | 2.18 (1.11, 4.28) |

* Results were derived from Cox proportional hazards models that treat fragmentation as a time-varying exposure, consider 12 months of the exposure at a time and outcomes that occur in the 3 months immediately following the exposure period, and occur over up to 11.8 years of follow-up. Fragmentation is measured with the reversed Bice-Boxerman Index. We were not able to calculate results for black participants with excellent self-rated health because they had too few events.

† The sample size should be interpreted as the number of participants with the given level of fragmentation in the first year of observation. The number of strokes should be interpreted as the event count for the participants who had the given level of fragmentation in the first year of observation. The models, however, treat fragmentation as a time-varying exposure.
Figure S2. An illustrative nomogram showing how fragmentation scores (reversed Bice-Boxerman scores*) vary with the proportion of visits with the most frequently seen provider, among those with 12 ambulatory visits†

*Higher scores reflect more fragmentation of care.
†Republished with permission of MJH Life Sciences, from eAppendix D in Kern et al., Fragmented ambulatory care and subsequent emergency department visits and hospital admissions among Medicaid beneficiaries. Am J Manage Care 2019 Mar;25(3):107-112; permission conveyed through Copyright Clearance Center, Inc.