Healthcare Fragmentation and Incident Acute Coronary Heart Disease Events: a Cohort Study

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BACKGROUND: Highly fragmented ambulatory care (i.e., care spread across many providers without a dominant provider) has been associated with excess tests, procedures, emergency department visits, and hospitalizations. Whether fragmented care is associated with worse health outcomes, or whether any association varies with health status, is unclear.

OBJECTIVE: To determine whether fragmented care is associated with the risk of incident coronary heart disease (CHD) events, overall and stratified by self-rated general health.

DESIGN AND PARTICIPANTS: We conducted a secondary analysis of the nationwide prospective Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort study (2003–2016). We included participants who were ≥ 65 years old, had linked Medicare fee-for-service claims, and had no history of CHD ($N = 10,556$).

MAIN MEASURES: We measured fragmentation with the reversed Bice-Boxerman Index. We used Cox proportional hazards models to determine the association between fragmentation as a time-varying exposure and adjudicated incident CHD events in the 3 months following each exposure period.

KEY RESULTS: The mean age was 70 years; 57% were women, and 34% were African-American. Over 11.8 years of follow-up, 569 participants had CHD events. Overall, the adjusted hazard ratio (HR) for the association between high fragmentation and incident CHD events was 1.14 (95% confidence interval (CI) 0.92, 1.39). Among those with very good or good self-rated health, high fragmentation was associated with an increased hazard of CHD events (adjusted HR 1.35; 95% CI 1.06, 1.73; $p = 0.01$). Among those with fair or poor self-rated health, high fragmentation was associated with a trend toward a decreased hazard of CHD events (adjusted HR 0.54; 95% CI 0.29, 1.01; $p = 0.052$). There was no association among those with excellent self-rated health.

CONCLUSION: High fragmentation was associated with an increased independent risk of incident CHD events among those with very good or good self-rated health.

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INTRODUCTION

Receiving ambulatory care from multiple providers is common.¹ For example, 50% of Medicare beneficiaries nationally see 7 or more different physicians each year.¹ This may be clinically appropriate, but it creates challenges, as providers often do not communicate with each other regarding their common patients.^{2,3} As a result, clinically relevant information, such as the results of tests ordered by another physician, is missing in 1 out of every 7 visits.⁴ More fragmented ambulatory care (that is, care spread across many providers without a dominant provider) has been associated with more testing,⁵ more procedures,⁶ more emergency department visits,^{7–9} and more hospitalizations,^{7,10} compared to less fragmented care. However, the relationship between fragmented ambulatory care and health outcomes is unclear.¹¹

We previously found that the association between fragmented ambulatory care and subsequent healthcare utilization varies with patients' health status.^{5,12} We hypothesize that the association between fragmented ambulatory care and health outcomes 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.

Prior to a myocardial infarction (MI), many patients have cardiovascular risk factors,¹³ such as hypertension and diabetes, which are often managed by multiple ambulatory providers (primary care physicians, cardiologists, endocrinologists, and others).¹⁴ We sought to determine whether more fragmented ambulatory care is associated with an increased risk of incident coronary heart disease (CHD) events, overall and by health status.

METHODS

Study Design, Population, and Data Sources

We conducted an ancillary study to the nationwide, prospective Reasons for Geographic and Racial Differences in Stroke

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(REGARDS) cohort study, using data from 2003 to 2016.¹⁵ Institutional review boards of the participating institutions approved the protocol. All participants provided written informed consent.

Between 2003 and 2007, 30,239 community-dwelling African-American and white adults ≥ 45 years old were enrolled in the REGARDS study, with oversampling of African-American adults and individuals living in the Southeastern U.S.¹⁵ Baseline data collection involved computer-assisted telephone interviews (CATI) and in-home visits with a physical examination, blood test, urine test, electrocardiogram (ECG), and medication inventory. Participants or their proxies are contacted by telephone every 6 months to detect study endpoints. The report of a potential event triggers adjudication, which involves an expert review of medical records, death certificates, proxy interviews, autopsy reports, the Social Security Death Index, and the National Death Index (NDI).¹⁶

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

Variables

Exposure. We used Medicare claims to identify ambulatory visits, which were defined using a modified National Committee for Quality Assurance (NQCA) definition¹⁸ restricted to Clinical Procedure Terminology (CPT) codes for in-person, evaluation-and-management visits for adults in an office setting.⁵ The NQCA definition of ambulatory visits does not include emergency department visits. We calculated fragmentation scores for each participant, using the previously validated^{7,10} Bice-Boxerman Index (BBI, Appendix 1).¹⁹ This index was originally labeled as a measure of “continuity,” but—as its originators intended—it actually measures more than consistency of care with a single provider. It captures both “dispersion” (the spread of visits across providers) and “density” (the relative share of visits by each provider).²⁰ Values of the original BBI range from 0 (least continuity, or most fragmentation) to 1 (most continuity, or least fragmentation). Patients receive a raw score of 0 if each ambulatory visit is with a different provider and a raw score of 1 if all visits are with the same provider. Other patterns of visits and providers receive intermediate scores; patterns with high dispersion (many providers) and low density (a relatively low proportion of visits by each provider) receive worse scores (indicating more fragmentation) than patterns with low dispersion and high density. To facilitate interpretation, we reversed the scores, calculating 1 minus BBI, so that higher scores reflect more fragmentation.^{5,9,12}

Outcome. An incident CHD event was defined as a definite or probable fatal or non-fatal MI or CHD death. Adjudication of MI followed national guidelines and was based on a clinical presentation suggestive of ischemia; cardiac biomarkers, usually troponin, exhibiting a rising and/or falling pattern to at least twice the upper limit of normal over at least 6 h; or imaging

suggestive of acute ischemia.^{16,21,22} Adjudication of CHD death included sudden cardiac death and deaths for which insufficient information could be gathered to adjudicate an MI but where the NDI cause of death was an acute coronary event. We used events adjudicated through December 31, 2016.

Baseline Covariates. Demographics included self-reported age, gender, race, marital status, educational attainment, and annual household income; geographic region from baseline contact information; and rural/urban setting using rural/urban commuting area codes.²³ Medical conditions included hypertension (self-reported use of anti-hypertensive medication, systolic blood pressure ≥ 140 mmHg, or diastolic blood pressure ≥ 90 mmHg from the in-home visit), hyperlipidemia (use of lipid-lowering medication, total cholesterol ≥ 240 mg/dL, low-density lipoprotein cholesterol (LDL) ≥ 160 mg/dL, or high-density lipoprotein (HDL) cholesterol ≤ 40 mg/dL from the in-home visit), diabetes (fasting glucose ≥ 126 mg/dL or non-fasting glucose ≥ 200 mg/dL from the in-home visit, or self-reported use of oral glucose-lowering medication or insulin), atrial fibrillation (self-reported or present on the study ECG at baseline), and stroke (self-reported). Medications included the total number of prescription medications taken in the past 2 weeks by medication inventory, self-reported use of anti-hypertensive medication and insulin from the CATI, and statin use from the medication inventory. Health behaviors were self-reported and included smoking status, alcohol consumption,²⁴ 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 (CES-D) scores ≥ 4 .²⁵ Physiological variables included body mass index (BMI); systolic blood pressure; total, LDL, and HDL cholesterol; glucose; estimated glomerular filtration rate (eGFR);²⁶ urinary albumin-to-creatinine ratio (ACR);²⁷ and high-sensitivity C-reactive protein. Self-rated health was assessed using self-rated general health (SF-1) from the 12-Item Short Form Health Survey (SF-12).^{28–31}

Statistical Analysis

We included participants ≥ 65 years old whose REGARDS data were linked to Medicare claims at any time during the study period, allowing for staggered entry as younger participants aged into Medicare when they turned 65.³² 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 prior to entry into this ancillary study, (4) had ≤ 3 ambulatory visits in the first year of observation,¹⁰ (5) had evidence of CHD (self-report of MI or coronary revascularization, ECG, or adjudicated MI) prior to or during the first year of observation, 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 from the first year of observation (0.85) to dichotomize fragmentation into high (≥ 0.85) and low (< 0.85). This approach was informed by our previous studies^{5,12} 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 CHD risk. To compare differences between participants with and without high fragmentation, we used Wilcoxon rank-sum tests, *t* tests, and chi-square tests.

Because fragmentation can change over time, we treated fragmentation as a time-dependent exposure.^{10,12,33} Because the effects of fragmentation are hypothesized to occur relatively quickly (for example, if different doctors unknowingly prescribe drugs that interact, the subsequent drug-drug interaction would be an acute event), previous studies have measured the occurrence of outcomes (e.g., ED visits and hospitalizations) in the 1 month following exposure to ambulatory fragmentation.^{12,33} For this study of CHD events, we lengthened the period of observation for outcomes to 3 months following the exposure to ambulatory fragmentation and conducted a sensitivity analysis lengthening it further to 6 months. We did not lengthen the outcome period beyond 6 months, because any exposure period and its corresponding outcome period are mutually exclusive; thus, the longer the outcome period, the more that ambulatory utilization (from the outcome period) is inadvertently omitted from the calculation of the exposure.

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. For each participant, we calculated a fragmentation score for the first 12 months of his or her observation period and then determined whether a CHD event occurred in the 3 months immediately following the exposure period (months 13–15). If no event occurred, we moved the window of observation forward by 3 months, measuring fragmentation in months 4–15 and any event in months 16–18, and so on (Appendix 2). If the number of visits in any 12-month exposure period fell below 4, we carried forward the last fragmentation score based on ≥ 4 visits.¹⁰ Observation continued until an outcome or censoring occurred; censoring occurred when a participant died of non-CHD causes, no longer had Medicare fee-for-service coverage, dropped out of the REGARDS study, or reached December 31, 2016. We used Poisson regression to estimate absolute adjusted rates of CHD events. We used Cox proportional hazards models to estimate unadjusted and adjusted hazard ratios.^{34–36} Using Schoenfeld residuals, we determined that the assumption of proportional hazards was met. We included in multivariate models those covariates that had a bivariate association with fragmentation ($p < 0.10$), except for gender, race, and region, which were automatically included to account for the sampling frame. If two variables had bivariate *p* values < 0.10 , but

one was embedded in the definition of another (e.g., use of antihypertensive medication was embedded in the definition of hypertension), we only adjusted for the broader variable to avoid collinearity.

We conducted a formal test of interaction between fragmentation and self-rated health category (excellent, very good or good, fair or poor) and stratified models if the interaction term was statistically significant. We used three groupings of self-rated health in order to detect any differences across subgroups, while maximizing statistical power.

We conducted six separate sensitivity analyses. First, we used the same covariates as in the base case analysis with multiple imputation to handle missing covariates.³⁷ The most frequently missing variable was C-reactive protein (missing for 6%); 85% of the sample was included in the complete case analysis. Second, we restricted the analysis to those ≥ 65 years old at baseline, excluding those who aged into Medicare over the study period. Third, we changed the time period for outcomes from 3 to 6 months immediately following each exposure period. Fourth, we used all unique covariates (not including variables embedded in the definitions of other variables), instead of selecting covariates based on bivariate *p* values, with a complete case approach. Fifth, we used all unique covariates, with multiple imputation to handle missing covariate values. Sixth, we stratified the sample into 5 self-rated health groups instead of 3.

Analyses were conducted with SAS (version 9.4, Cary, NC) and Stata (version 14, StataCorp, College Station, TX). Multivariate *p* values < 0.05 were considered statistically significant.

RESULTS

Sample Characteristics

Of the REGARDS study participants, 10,566 met the inclusion criteria (Appendix 3). The mean age of participants was 70 years (Table 1, Appendix 4). More than half of participants (57%) were women, and 34% were African-American. Two-thirds (66%) had very good or good self-rated health. By design, one-fourth (25%) had high fragmentation. Differences in participant characteristics between those with high vs. low fragmentation in the first year of observation are shown in Table 1. Participant characteristics stratified by self-rated health are shown in Appendix 5.

Ambulatory Utilization

Those with high fragmentation had an average of 10.7 visits across 6.3 providers, an average of 29% of visits with the most frequently seen provider, and an average fragmentation score of 0.91; by contrast, those with low fragmentation had an average of 8.8 visits across 3.5 providers, an average of 58% of visits with the most frequently seen provider, and an average fragmentation score of 0.63 (Table 2, $p < 0.001$ for each comparison).

Table 1 Baseline Characteristics, Overall and Stratified by Fragmentation Score in the First Year of Observation

Characteristic	Overall (N=10,556)	Low fragmentation during first year of observation (N=7889)	High fragmentation during first year of observation (N=2667)	p value
Demographic characteristics				
Age, years, mean (SD)	70.3 (5.9)	70.4 (5.9)	69.9 (5.8)	<0.001
Gender, female, N (%)	6007 (57)	4453 (56)	1554 (58)	0.10
Race, white, N (%)	6968 (66)	5013 (64)	1955 (73)	<0.001
Marital status, married, N (%)	6195 (59)	4548 (58)	1647 (62)	<0.001
Education, college graduate, N (%)	3850 (36)	2723 (35)	1127 (42)	<0.001
Annual household income, <\$35,000, N (%)	4541 (43)	3540 (45)	1001 (38)	<0.001
Geographic region, N (%)				
Stroke belt ^a	3876 (37)	2858 (36)	1018 (38)	0.04
Stroke buckle ^b	2434 (23)	1865 (24)	569 (21)	
Neither stroke belt nor stroke buckle	4246 (40)	3166 (40)	1080 (40)	
Residence in urban area, N (%)	7210 (76)	5376 (76)	1834 (77)	0.78
Medical conditions ^c				
Hypertension, N (%)	6331 (60)	4866 (62)	1465 (55)	<0.001
Hyperlipidemia, N (%)	5966 (59)	4524 (59)	1442 (56)	0.01
Diabetes, N (%)	2030 (20)	1576 (21)	454 (18)	<0.001
Atrial fibrillation, N (%)	774 (7)	547 (7)	227 (9)	0.01
Stroke, N (%)	609 (6)	470 (6)	139 (5)	0.15
Medications				
Number of medications, median (IQR)	5 (3, 8)	5 (3, 8)	6 (3, 9)	<0.001
Anti-hypertensive medication, N (%)	5471 (54)	4219 (55)	1252 (48)	<0.001
Insulin use, N (%)	476 (5)	354 (5)	122 (5)	0.87
Statin use, N (%)	3151 (30)	2356 (30)	795 (30)	0.96
Health behaviors				
Current smoker, N (%)	1130 (11)	890 (11)	240 (9)	<0.001
Alcohol use, none, N (%)	6629 (64)	5050 (65)	1579 (60)	<0.001
Exercise frequency, 0 times per week, N (%)	3560 (34)	2675 (34)	885 (34)	0.72
Psychosocial variables				
Cares for a family member with a chronic illness or disability, N (%)	1300 (12)	980 (12)	320 (12)	0.56
Lack of social support, N (%)	429 (4)	302 (4)	127 (5)	0.04
Depressive symptoms, N (%)	588 (6)	439 (6)	149 (6)	0.97
Physiological variables				
Body mass index, kg/m ² , mean (SD)	28.8 (5.8)	28.9 (5.9)	28.6 (5.7)	0.01
Systolic blood pressure, mmHg, mean (SD)	128.5 (16.3)	129.0 (16.4)	127.1 (15.9)	<0.001
Total cholesterol, mg/dL, mean (SD)	193.5 (38.9)	194.0 (39.3)	192.1 (37.7)	0.03
Low-density lipoprotein cholesterol, mg/dL, mean (SD)	114.4 (33.9)	115.1 (34.3)	112.5 (32.4)	<0.001
High-density lipoprotein cholesterol, mg/dL, mean (SD)	52.7 (16.4)	52.4 (16.3)	53.6 (16.7)	0.002
Glucose, mg/dL, mean (SD)	102.6 (32.3)	103.1 (33.0)	101.1 (30.2)	0.01
Estimated glomerular filtration rate, mL/min/1.73 m ² , mean (SD)	81.9 (18.3)	81.8 (18.5)	82.2 (17.7)	0.34
Urinary albumin-to-creatinine ratio, mg/g, median (IQR)	7.6 (4.8, 15.8)	7.7 (4.9, 16.1)	7.4 (4.7, 14.6)	0.02
C-reactive protein, mg/L, median (IQR)	2.1 (0.9, 4.8)	2.2 (1.0, 4.8)	2.0 (0.9, 4.6)	0.05
Self-rated health				
Self-rated general health (SF-1), N (%)				
Excellent	1959 (19)	1423 (18)	536 (20)	0.11
Very good	3428 (32)	2564 (33)	864 (32)	
Good	3606 (34)	2721 (34)	885 (33)	
Fair	1315 (12)	986 (12)	329 (12)	
Poor	248 (2)	195 (2)	53 (2)	

Missing data: education (N=5), hypertension (N=27), hyperlipidemia (N=382), diabetes (N=370), atrial fibrillation (N=203), body mass index (N=557), number of medications (N=8), smoking status (N=38), alcohol use (N=187), social support (N=248), urinary albumin-to-creatinine ratio (N=443), and C-reactive protein (N=616). Percentages may not sum to 100 due to rounding. See [Appendix 3](#) for a longer version of this table with all categories of each variable shown

IQR interquartile range, SF short-form survey³¹

^aStroke Belt = North Carolina, South Carolina, Georgia, Tennessee, Mississippi, Alabama, Louisiana, and Arkansas (except for 153 coastal counties that constitute the Stroke Buckle)¹⁵

^bStroke Buckle = 153 coastal counties in North Carolina, South Carolina, and Georgia^{15,38}

^cSee "METHODS" section for detailed definitions of variables

Within each self-rated health group, those with high fragmentation had more visits, more providers, a lower proportion of visits with the most frequently seen provider, and higher fragmentation scores than those with low fragmentation ($p < 0.001$ for each comparison).

CHD Events

Participants were followed up for up to 11.8 years (median 5.5 years) (Table 3). Overall, 569 participants (5.4%) experienced an acute incident CHD event, equivalent to an

Table 2 Ambulatory Utilization During the First Year of Observation, Overall and Stratified by Fragmentation Score and by Self-Rated Health

	Overall			Self-rated health								
	Total	Low rBBI (< 0.85)	High rBBI (≥ 0.85)	Excellent			Very good or good			Fair or poor		
				Total	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)
N (%)	10,556 (100)	7889 (75)	2667 (25)	1959 (100)	1423 (73)	536 (27)	7034 (100)	5285 (75)	1749 (25)	1563 (100)	1181 (76)	382 (24)
Visits, mean (SD)	9.3 (6.1)	8.8 (5.8)	10.7 (6.9)	7.5 (4.5)	7.3 (4.4)	8.1 (4.7)	9.3 (6.0)	8.7 (5.5)	10.9 (7.0)	11.9 (7.5)	11.2 (7.3)	13.8 (7.9)
Providers, mean (SD)	4.2 (2.3)	3.5 (1.7)	6.3 (2.4)	3.9 (1.8)	3.2 (1.4)	5.5 (1.8)	4.2 (2.2)	3.5 (1.6)	6.3 (2.4)	4.8 (2.7)	3.9 (2.1)	7.4 (2.8)
Percent of visits with the most frequently seen provider, mean, (SD)	51 (20)	58 (18)	29 (7)	50 (19)	58 (17)	30 (7)	51 (20)	58 (18)	29 (7)	51 (21)	58 (19)	28 (7)
Fragmentation score, rBBI (SD)	0.70 (0.23)	0.63 (0.22)	0.91 (0.04)	0.72 (0.22)	0.64 (0.21)	0.92 (0.05)	0.70 (0.23)	0.63 (0.22)	0.91 (0.04)	0.68 (0.24)	0.61 (0.23)	0.90 (0.04)

Key: rBBI = reversed Bice-Boxerman Index (BBI), equivalent to $1 - \text{BBI}$, 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
SD standard deviation

unadjusted rate of 8.8 events per 1000 person-years. Those with worse self-rated health at baseline had more CHD events: 4.0% of those with excellent self-rated health, 5.4% of those with very good/good self-rated health, and 6.9% of those with fair/poor self-rated health had a CHD event ($p = 0.001$). Adjusted incidence rates are shown in Figure 1.

Overall, the adjusted hazard ratio (HR) for the association between fragmentation and CHD events was 1.14 (95% confidence interval (CI) 0.92, 1.39) (Table 4, Appendix 6). However, there was an interaction between fragmentation and self-

rated health (Wald test: $p < 0.01$). Among those with excellent self-rated health, there was no association between fragmentation and CHD events (adjusted HR 0.91; 95% CI 0.53, 1.57; $p = 0.74$). Among those with very good or good self-rated health, high fragmentation was associated with an increased hazard of CHD events (adjusted HR 1.35; 95% CI 1.06, 1.73; $p = 0.01$), compared to low fragmentation. Among those with fair or poor self-rated health, high fragmentation was associated with a trend toward a decreased hazard of CHD events (adjusted HR 0.54; 95% CI 0.29, 1.01; $p = 0.052$).

Table 3 Incident Rates of Acute Coronary Heart Disease Event, Stratified by Self-Rated General Health and by Fragmentation Status

	Overall	Self-rated general health		
		Excellent	Very good or good	Fair or poor
Sample sizes and observation time				
N (%)	10,556 (100)	1959 (19)	7034 (66)	1563 (15)
Range of observation time	4 days to 11.8 years	4 days to 11.8 years	7 days to 11.8 years	7 days to 11.8 years
Median observation time, years (IQR)	5.5 (2.8, 9.1)	6.4 (3.2, 9.9)	5.7 (3.0, 9.3)	4.0 (2.0, 7.5)
Event counts and rates				
Total				
Observed number of events (% persons)	569 (5.4%)	78 (4.0%)	383 (5.4%)	108 (6.9%)
Observed number of person-years	63,130	12,712	42,761	7656
Unadjusted rate per 1000 person-years	9.0	6.1	8.9	14.1
Adjusted rate per 1000 person-years	9.1	6.6	9.0	14.2
Low fragmentation				
Observed number of events (% persons)	430 (5.5%)	65 (4.6%)	279 (5.3%)	86 (7.3%)
Observed number of person-years	43,363	8459	29,484	5419
Unadjusted rate per 1000 person-years	8.7	6.3	8.2	15.3
Adjusted rate per 1000 person-years	8.7	6.8	8.0	16.1
High fragmentation				
Observed number of events (% persons)	139 (5.2%)	13 (2.4%)	104 (6.0%)	22 (5.8%)
Observed number of person-years	19,767	4253	13,277	2237
Unadjusted rate per 1000 person-years	9.7	5.9	10.6	11.2
Adjusted rate per 1000 person-years	10.0	6.3	11.1	9.1

Adjusted rates were derived from Poisson models that adjusted for age, gender, race, marital status, educational attainment, income, region, hypertension, hyperlipidemia, diabetes, body mass index, albumin-to-creatinine ratio, C-reactive protein, number of medications, smoking, alcohol use, and lack of social support. Fragmentation status is a time-varying exposure based on the reversed Bice-Boxerman Index (low < 0.85 , high ≥ 0.85). See "METHODS" for more details

Figure 1 Absolute adjusted rates of incident coronary heart disease (CHD) events, stratified by healthcare fragmentation status and self-rated general health. Adjusted rates were derived from Poisson models that adjusted for age, gender, race, marital status, educational attainment, income, region, hypertension, hyperlipidemia, diabetes, body mass index, albumin-to-creatinine ratio, C-reactive protein, number of medications, smoking, alcohol use, and lack of social support. Fragmentation status is a time-varying exposure based on the reversed Bice-Boxerman Index (low <0.85, high $\geq$ 0.85). See “METHODS” for more details.

Results persisted in the sensitivity analyses that used the base case set of covariates with multiple imputation, the 6-month outcome period, all covariates with a complete case approach, and all covariates with a multiple imputation approach (Appendix 7). In the sensitivity analysis that excluded participants < 65 years old at baseline, the results for excellent and very good/good self-rated health persisted, and the results for fair/poor self-rated health reached statistical significance (adjusted HR 0.42; 95% CI 0.20, 0.91). In the sensitivity analysis stratifying self-rated health into 5 groups, confidence intervals were wider and high fragmentation was associated with a decreased hazard of CHD events in the fair self-rated health group (adjusted HR 0.43; 95% CI 0.20, 0.92, Appendix 8).

DISCUSSION

In this 12-year study of 10,556 Medicare beneficiaries from the REGARDS cohort, the association between fragmented ambulatory care and incident CHD events varied with health status. Among those with very good or good self-rated health, having highly fragmented care was associated with an increased adjusted hazard of a CHD event in the 3 months following the exposure. Among those with fair or poor self-rated health, having highly fragmented care was associated with a decreased adjusted hazard a CHD event over the same time period. Among those with excellent self-rated health, there was no association between fragmentation and CHD events. The ambulatory care patterns underlying high vs. low

Table 4 Association Between Healthcare Fragmentation and Incident Coronary Heart Disease (CHD) Events, Overall and Stratified by Self-Rated General Health (N=10,556)

	Overall	Self-rated general health		
		Excellent	Very good or good	Fair or poor
Hazard ratios (95% confidence intervals) comparing high fragmentation to low fragmentation ^a				
Unadjusted	1.06 (0.89, 1.26)	0.93 (0.58, 1.50)	1.21 (0.98, 1.49)	0.71 (0.46, 1.12)
Model 1 ^b	1.09 (0.90, 1.32)	0.92 (0.55, 1.52)	1.26 (1.00, 1.58)	0.60 (0.35, 1.02)
Model 2 ^c	1.10 (0.90, 1.34)	1.00 (0.59, 1.68)	1.27 (1.00, 1.62)	0.52 (0.28, 0.95)
Model 3 ^d	1.14 (0.92, 1.39)	0.91 (0.53, 1.57)	1.35 (1.06, 1.73)	0.54 (0.29, 1.01)

^aResults 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. High fragmentation is defined as a score of $\geq$ 0.85 on a reversed Bice-Boxerman Index

^bModel 1 adjusts for demographic characteristics (age, gender, race, marital status, educational attainment, income, and region)

^cModel 2 adjusts for the variables in model 1 plus medical conditions (hypertension, hyperlipidemia, diabetes) and physiological variables (body mass index, albumin-to-creatinine ratio, C-reactive protein)

^dModel 3 adjusts for the variables in model 2 plus medications (number of medications), health behaviors (smoking, alcohol use), and psychosocial variables (lack of social support). Model 3 is a fully adjusted model using a complete case analysis. See Appendix 6 for a full display of this model, including the effect sizes and statistical significance of the covariates

fragmentation were clinically and statistically different from each other: those with high fragmentation had an average of 11 visits to 6 providers per year, with the most frequently seen provider accounting for 29% of the visits, whereas those with low fragmentation had an average of 9 visits to 4 providers per year, with the most frequently seen provider accounting for 58% of visits.

These results are concordant with our previous study of Medicare beneficiaries in New York State, which found that healthcare fragmentation was not associated with hospitalizations among those with 0 chronic conditions, was associated with an increased hazard of hospitalization among those with 1–4 chronic conditions, and was associated with a decreased hazard of hospitalization among those with ≥ 5 chronic conditions.¹² Other studies of fragmentation have adjusted for burden of illness (rather than stratify), precluding additional comparisons.^{6,7,10}

The exact mechanisms by which fragmentation could increase or decrease cardiac risk, depending on health status, are not clear. On the one hand, sicker patients may require more providers,¹ and providers may make more of an effort to coordinate care for sick patients,³⁹ thereby ameliorating the risk of gaps in communication. Sicker patients may also have access to more ancillary providers like care managers, who may facilitate care coordination.⁴⁰ On the other hand, for patients with a moderate burden of illness, more fragmented care may lead to worse control of cardiac risk factors, through less aggressive management of those risk factors or discontinuation of beneficial medications.^{41–44} Multiple providers may also unknowingly prescribe drugs that interact, exacerbating cardiac risk factors.^{45–47} More work is needed to distinguish between beneficial and deleterious care fragmentation.

Strengths of this study include the national sampling frame, large sample size, long time horizon, homogeneity of insurance benefits across study participants through Medicare, use of a previously validated measure of fragmentation, treatment of fragmentation as a time-varying exposure, adjudicated CHD events, and adjustment for clinically detailed potential confounders.

This study has several limitations. First, it is observational; we cannot rule out residual confounding or infer causation. Second, we did not have data on cardiac risk factor control over time, so we cannot directly test the hypothesized mechanisms above. Third, this study did not measure communication between providers, so the presence of fragmentation cannot be interpreted as the definite absence of communication. Fourth, self-rated health was measured at baseline and may change over time. However, self-rated health at baseline was a significant predictor of CHD events. Fifth, we were not able to account for whether physicians were in the same practice; if physicians practicing together had access to the same medical records, buffering potential harm from fragmentation, this would have biased our study toward the null.

In conclusion, among Medicare beneficiaries with very good or good self-rated health (which was two-thirds of the

sample), highly fragmented ambulatory care was associated with an independent increase in the short-term risk of an incident CHD event. More research is needed to determine exactly how fragmentation contributed to this risk and to determine whether interventions are needed to reduce unnecessary fragmentation of care.

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Access to Data: Dr. Kern, Ms. Rajan, and Ms. Ringel had full access to the study data and take responsibility for the integrity of the analysis.

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Compliance with Ethical Standards:

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