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ORIGINAL RESEARCH

Associations of Community and Individual Social Determinants of Health With Medication Adherence in Patients With Atrial Fibrillation: A Retrospective Cohort Study

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BACKGROUND: Despite guideline-recommended use of oral anticoagulation (OAC) for stroke prevention in atrial fibrillation (AF), OAC medication adherence among patients with AF in the United States ranges from 47% to 82%. To characterize potential causes of nonadherence, we analyzed associations between community and individual social risk factors and OAC adherence for stroke prevention in AF.

METHODS AND RESULTS: A retrospective cohort analysis of patients with AF was conducted using the IQVIA PharMetrics Plus claims data from January 2016 to June 2020, and 3-digit ZIP code-level social risk scores were calculated using American Community Survey and commercial data. Logistic regression models evaluated associations between community social determinants of health, community social risk scores for 5 domains (economic climate, food landscape, housing environment, transportation network, and health literacy), patient characteristics and comorbidities, and 2 adherence outcomes: persistence on OAC for 180 days and proportion of days covered ≥0.80 at 360 days. Of 28 779 patients with AF included in the study, 70.8% of patients were male, 94.6% were commercially insured, and the average patient age was 59.2 years. Multivariable regression found that greater health literacy risk was negatively associated with 180-day persistence (odds ratio [OR]=0.80 [95% CI, 0.76–0.83]) and 360-day proportion of days covered (OR, 0.81 [95% CI, 0.76–0.87]). Patient age and higher AF stroke risk score and AF bleeding risk scores were positively associated with both 180-day persistence and 360-day proportion of days covered.

CONCLUSIONS: Social risk domains, such as health literacy, may affect OAC adherence among patients with AF. Future studies should explore associations between social risk factors and nonadherence with greater geographic granularity.

Key Words: anticoagulants ■ atrial fibrillation ■ medication adherence ■ social determinants of health ■ social risk factors

The Centers for Disease Control and Prevention estimates that by 2030, 12.1 million people in the United States will have atrial fibrillation (AF).[1,2] AF is the primary diagnosis in >454 000[3] hospitalizations per year and contributes to ≈158 000 deaths annually.[4] The direct cost for AF treatment totals >$6.5 billion per year in the United State alone (2005 dollars).[5] A major contributor to these health outcomes and costs is the increased risk

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CLINICAL PERSPECTIVE

What Is New?

- Combining community-level social risk data with individual patient risk factors is a novel and a more comprehensive approach to evaluate exposure–outcome relationships in real-world studies.
- We found that elevated levels of health literacy risk at the community level were associated with lower odds of being persistent on a prescribed oral anticoagulant for atrial fibrillation at 90 and 180 days and of having a proportion of days covered of ≥0.8 after controlling for individual risk factors.

What Are the Clinical Implications?

- Incorporating community-level social risk data for patients will assist health care entities and providers in making more strategic decisions about population health initiatives.
- Future studies should utilize greater geographic specificity to identify opportunities for improving guideline-concordant anticoagulation related to social determinants of health for patients with atrial fibrillation and focus on health literacy.

Nonstandard Abbreviations and Acronyms

CHA_2DS_2-VASc	AF stroke risk score
DOAC	direct-acting oral anticoagulant
HAS-BLED	AF bleeding risk score
IRR	incidence-rate ratio
OAC	oral anticoagulant
PDC	proportion of days covered
SDoH	social determinants of health
ZIP-3	3-digit ZIP code prefix, denoting a broader geographic unit than the 5-digit ZIP code

of stroke in patients with AF, estimated at 4 to 5 times the risk of patients without AF.[6] Due to this increased stroke risk, the AF treatment guidelines created by the American College of Cardiology and the American Heart Association Task Force of Practice Guidelines and the Heart Rhythm Society recommend risk-stratified use of oral anticoagulants (OACs) for stroke prevention based on clinical evidence.[7] Despite these recommendations, a growing literature indicates that guideline-concordant anticoagulation in AF ranges from 50% to 70%.[8,9] Even when prescribed OACs, reported patient adherence varies from 47% to 82%,[10] and nonadherence has been associated with adverse patient outcomes such as stroke and mortality.[11]

Medication nonadherence is associated with worse patient health outcomes and increased health care costs.[12] While adherence is frequently perceived as an issue of forgetfulness, studies show that unintentional and intentional nonadherence may be predicted by medication beliefs, financial barriers, education, economic circumstances, and sociodemographic factors.[13–15] More broadly, social determinants of health (SDoH) are defined as the "conditions in the environments where people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks."[16] SDoH associated with adverse health outcomes may also be associated with medication nonadherence.[17] Incremental increases in the number of an individual's social risk factors have been found to increase stroke risk in adults <75 years of age.[18] Social risk factors (eg, housing insecurity, food insecurity, and health illiteracy) are defined as "specific adverse social conditions that are associated with poor health"[19] and are associated with poorer medication adherence for people living with HIV and diabetes.[20–24] Specific to the AF population, Essien and colleagues found that in multiple patient populations, Black patients were less likely to be initially prescribed an OAC compared with White patients, as well as less likely to be prescribed a direct-acting OAC.[25–27] This finding illustrates the disadvantage experienced by some patient populations and highlights the importance of understanding the role of SDoH and social risk factors in patient access to medications.

Despite growing evidence of associations between SDoH, social risk factors, and health outcomes, little published research has examined association of community-level and patient-level SDoH and social risk factors with medication adherence in patients with AF prescribed anticoagulants to mitigate stroke risk. To address these gaps, we combined deidentified payer claims data with community-level social risk scores (ie, economic climate, food landscape, housing environment, transportation network, and health literacy) and community contextual data to assess how SDoH and social risk factors impact medication adherence in AF. We hypothesized that select community-level and patient-level SDoH and social risk factors will be associated with lower adherence and persistence to OAC in patients with AF compared with patients with lower levels of community-level and patient-level social risk, as measured by multiple factors, including novel social risk scores. A secondary aim of this study included assessing the association between select community characteristics and the time from AF diagnosis to OAC prescription.

METHODS

The IntegReview Institutional Review Board determined that this research was exempt from the regulatory requirements of the federal Common Rule because no protected health information was used. We followed Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines.[28] The authors declare that all supporting data are available within the article (and its online supplementary files). The authors had full access to the data in the study and take responsibility for its integrity and the data analysis.

Data Sources

This study utilized multiple sources of secondary data to address the research objectives. First, IQVIA PharMetrics Plus data with claims from January 2016 to June 2020 served as the primary source for identifying the patient populations and outcome measures. IQVIA PharMetrics Plus is a health plan claims database comprising fully adjudicated medical and pharmacy claims for >210 million unique enrollees since 2006. Data contributors to the database are largely commercial health plans. It is representative of the commercially insured US national population (payers and plans are not identifiable in the data). It contains a longitudinal view of inpatient and outpatient services, prescription and office/outpatient administered drugs, costs, and detailed enrollment information. All data are compliant with the Health Insurance Portability and Accountability Act (HIPAA) to protect patient privacy. IQVIA data elements included inpatient and outpatient claims, diagnoses, and procedures based on *International Classification of Diseases, Tenth Revision, Clinical Modification* (*ICD-10-CM*) and retail and mail order pharmacy claims. To meet HIPAA's standards, the most granular data available to the study authors for patient's address in IQVIA was at the level of 3-digit ZIP code (ZIP-3).

Second, community-level social risk scores were derived from the US Census Bureau's American Community Survey data, commercial data from Dun & Bradstreet, infrastructure data from Homeland Infrastructure Foundation-Level Data, the US Environmental Protection Agency's Area Health Resources File, and US Department of Agriculture guidelines on household food budgets.[29–32] Additional US Census Bureau data were also utilized to provide community characteristics at the ZIP-3 level. Socially Determined's social risk scores were created from the aforementioned data sources for 5 distinct domains (economic climate, food landscape, housing environment, transportation network, and health literacy) to measure the environment around individuals. These social risk scores were included to explore their associations with the outcomes of interest. Table S1 provides a list of the variables collected, data source, and level of collection (eg, individual or ZIP-3).

Study Design and Patient Population

A retrospective cohort design was used to assess associations between community-level and patient-level SDoH and OAC medication adherence in patients with AF. Patients were included if they were ≥18 years old and had a new primary or secondary diagnosis of AF (*ICD-10-CM* code of I480, I481, I482, I4891; Table S2) and a prescription for an OAC (apixaban, dabigatran, edoxaban, rivaroxaban, or warfarin; Table S3) between January 1, 2017, and June 30, 2019. The first date patients were diagnosed with AF during the study window served as the index diagnosis date. In addition, patients were required to have continuous insurance eligibility 12 months before the diagnosis index date. A lookback period of 12 months was used to ensure that only patients with newly diagnosed AF were included. Patients were excluded if they were <18 years of age; had a prescription claim for an OAC or an *ICD-10* code for AF in the 12 months before the index diagnosis date; did not fill the index prescription within 360 days; were pregnant; had a diagnosis of valvular disease, cardiac inflammation; or hip or knee replacement within 6 weeks before the index diagnosis date. Finally, patients without a valid ZIP-3 or, due to HIPAA standards, who lived in a ZIP-3 with a total population of <20 000, were also excluded from the analysis.

Pharmacy claims for an OAC were assessed at and following index diagnosis to determine an index prescription date. The index prescription date could range from the same date as the index diagnosis to June 30, 2019, and the index prescription must be within 360 days of the index diagnosis. OAC adherence was measured at the drug class level (direct-acting OACs or vitamin K antagonists).

Exposure Variables

Community Level

Community data from the US Census Bureau's American Community Survey, Dun & Bradstreet, infrastructure data from Homeland Infrastructure Foundation-Level Data, US Environmental Protection Agency's Area Health Resources File, and US Department of Agriculture guidelines on household food budgets are incorporated into 5 composite variables reflecting domains of social risk: economic climate, food landscape, housing environment, transportation network, and health literacy. Socially Determined's proprietary community risk scores are designed to assess the factors in peoples' lives that shape the way

they use the health care system and the health care outcomes they achieve by providing insight into the communities in which patients reside.[33] The social risk scores are calculated at a specific geospatial unit represented as a hexagon, where each hexagon is 200 or 400 m in diameter, depending on population density. For this research, the risk scores and other contextual data points were aggregated from the hexagon to the ZIP-3 level to align with the geographic availability of the patient-level data.

The risk scores for each social risk domain (economic climate, food landscape, housing environment, transportation network, and health literacy) are calculated using multiple data elements. The data elements include population age, population sex, marital status, household income, housing costs, household size and composition, the locations of healthy and unhealthy food options, the rate of Supplementary Nutrition Assistance Program utilization, household food costs, vehicle ownership and access, housing costs, climate measures, ratios of owners and renters, the locations of a variety of health resources (including providers, hospitals, and pharmacies), use of public transit, educational attainment, time in the United States, citizenship, racial and ethnic composition, and language spoken at home. The US Census Bureau data provided additional data points at the ZIP-3 level that are not directly included in the risk scores, but that could be included in models. These contextual data points include area population density, area insurance coverage rates, area saturation of medical providers/hospitals (number of medical providers per 1000 population), and area saturation of pharmacies (number per 1000 population).

In order to calculate the risk scores, Socially Determined starts by taking unique community data elements such as area home renting and area household size/composition and grouping them into engineered features (eg, household crowding). These engineered features are further grouped to determine what features are most influential for a domain (Figure S1). The influencers are built from data elements and engineered features using multiple mathematical and statistical techniques, including integration, complementary cumulative distribution functions, cubic spline approximations, normalization, quantile transforms, and differentiation. The risk score is calculated for each domain using linear combination, then risk scores are binned based on an evaluation of the entire population of hexagons in the United States to create an approximately normal distribution. The scores for each domain range from 1 to 5, where 1 is little to no risk, 2 is low risk, 3 is moderate risk, 4 is high risk, and 5 is severe risk (Table S1). An example of how a risk score is created with variables and engineered features has been provided in Figure S1. For example, the data elements included in the Health Literacy community risk score can be categorized into 3 major influencers—demographics, education, and culture. One of the primary influencers to the health literacy risk score is area-level demographics. In this case, demographics reflect the distributions of age, sex, and marital status in the ZIP-3. Nationwide maps of ZIP-3 level population density, health literacy risk, and housing environment risk have been provided in Figures S2 through S4.

Individual Level

Individual variables captured from IQVIA included sex, age, geographic region, insurance type, index diagnosis location, history of health care utilization, comorbidities, and additional information about the prescription claim (formulary status). Estimated AF stroke risk (CHA_2DS_2-VASc) and AF bleeding risk (HAS-BLED) scores were constructed using diagnosis and procedure codes included in the data set (Table S1).[34,35] The International Normalized Ratio was missing for many patients with prior warfarin treatment, so a modified HAS-BLED score was calculated with a range of 0 to 8. Race is not reported in IQVIA PharMetrics Plus claims data.

Outcome Variables

To evaluate how SDoH and social risk factors relate to medication adherence on OACs, 2 adherence measures were examined: the proportion of patients persistent on OAC for 180 days and the proportion of patients with proportion of days covered (PDC) ≥0.80 at 360 days. PDC ≥0.80 will be referenced as "high PDC," and PDC <0.80 will be referenced as "low PDC."

Persistence was calculated as the number of days for which a patient has claims for an OAC prescription, beginning on the index prescription date. Discontinuation of the index OAC was defined as no evidence of index anticoagulant use for 30 days from the last day of the days' supply of the last filled prescription. PDC was calculated as the total prescription days' supply over a fixed timeframe (ie, 90, 180, and 360 days). Secondary end points were persistence at 90 and 360 days, PDC at 180 days, and time between index diagnosis and receipt of an OAC index prescription. Medication adherence was calculated from the time of first outpatient oral anticoagulation prescription (OAC prescription index date), and a medication switch was defined as a prescription for a new OAC medication (different from the index prescription class) within a time period of 1.5 times the day supply from the index prescription date. For example, a patient with a 30-day prescription for their index OAC medication would be defined as switching if they received a prescription for an OAC of a different class within 45 days (Table S4).

To ensure sufficient follow-up time for adherence calculations, patients were required to have either 6 months or 12 months of continuous insurance eligibility after the OAC prescription index date for 180-day and 360-day measures, respectively. Patients were followed up to 12 months, to health plan disenrollment/death or discontinuation of the OAC, whichever occurred first.

Statistical Analysis

Sociodemographic characteristics and medical history for the analytic sample were stratified by level of adherence according to the PDC calculated at 360 days (<0.80 versus ≥0.80). Bivariable logistic regression analyses were performed to establish unadjusted associations between community- and individual-level characteristics and the primary end points.

Hierarchical linear modeling was considered to account for the clustering of risk scores and community contextual information at the ZIP-3 level. Intraclass correlation coefficients were assessed for hierarchical logit models regressing medication adherence on each risk score. In addition, odds ratios (ORs) were compared between hierarchical and nonhierarchical models. Intraclass correlation coefficients were small (intraclass correlation coefficient=0.015–0.016) and ORs were nearly identical between the 2 sets of regressions. Therefore, the nonhierarchical model is presented.

ORs and 95% CIs were estimated using multivariable logistic regression analyses assessing associations between individual comorbidities and SDoH, community-level SDoH, and medication adherence in patients with AF. Models were adjusted for sociodemographic characteristics, comorbidities, health care utilization history, and community SDoH at the ZIP-3 area.

Variable selection for multivariable models proceeded using backward selection after elimination of redundant community-level indicators (indicators that were part of risk score calculations). Patient sociodemographic characteristics (sex and age) were included in all models. Risk scores and additional covariates were added to models as a set and then removed in an automated iterative process if $P>0.15$. The cutoff value of 0.15 was chosen based on common practice.[36] Time to index prescription was modeled continuously with time measured in days. Backward selection negative binomial regressions were run to assess associations between community- and patient-level social risk and covariates and days elapsed from index diagnosis date to the date the index prescription was received. A negative binomial regression model was selected because all patients were required to have the outcome (anticoagulant prescription within 360 days). Thus, no patients were right-censored. Incidence rate ratios (IRRs) were reported for these models.

A sensitivity analysis was performed using Pharmacy Quality Alliance's criterion for OAC PDC: individuals 18 years and older who fill at least 2 prescriptions for an OAC on 2 unique dates of service at least 180 days apart during the treatment period and who received >60 days' supply of the medication during the treatment period.[37]

Statistical analyses were performed using STATA/MP version 16.1[38] and the *statsmodels* module in Python 3,[39] with statistical significance set at $P<0.05$.

RESULTS

Baseline Characteristics

Among 495 547 patients with a diagnosis of AF, 28 779 patients with AF met the inclusion criteria with 6 months continuous enrollment after index OAC prescription, and 22 572 met the criteria with 12 months continuous enrollment after index OAC prescription (Figure 1). Baseline characteristics are represented in Table 1 by nonadherent patients (360-day low PDC), adherent patients (360-day high PDC), and total patients. The adherence to OAC of patients with AF for 180-day and 360-day was 56.7% (n=16 323/28 779) and 42.6% (n=9614/22 572), respectively. The majority of patients were male (70.8%), and the average patient age was 59.2±9.3 years. All 4 regions of the country were represented, with the largest percentage of patients residing in the South (44.9%). The average CHA_2DS_2-VASc score was 2.1±1.5, and the average HAS-BLED score was 1.4±1.1. Most patients were commercially insured (94.6%) and were prescribed a direct-acting OAC (93.2%). At the area level, 88.7% (824/929) of US ZIP-3s were represented in the analytic data set, and these community contextual characteristics for the ZIP-3s are presented in Table 2.

Outcomes

Bivariable Logistic Regression Results

Community/ZIP-3 Level

Bivariable logistic regression analyses were performed for all individual and community level characteristics for 180-day persistence and 360-day PDC (Figures S5 and S6). Bivariable analysis of the full set of community-level covariates revealed several significant associations. For 360-day PDC, the proportion of elderly (age 70 years or older) people (OR, 1.20 [95% CI, 1.09–1.32]) and married people (OR, 1.07 [95% CI, 1.02–1.12]) in the ZIP-3 area were positively associated with adherence, and the proportion of residents who were Black, Asian, and minority races (OR, 0.96 [95% CI, 0.94–0.97]), Hispanic (OR, 0.93 [0.91–0.95]),

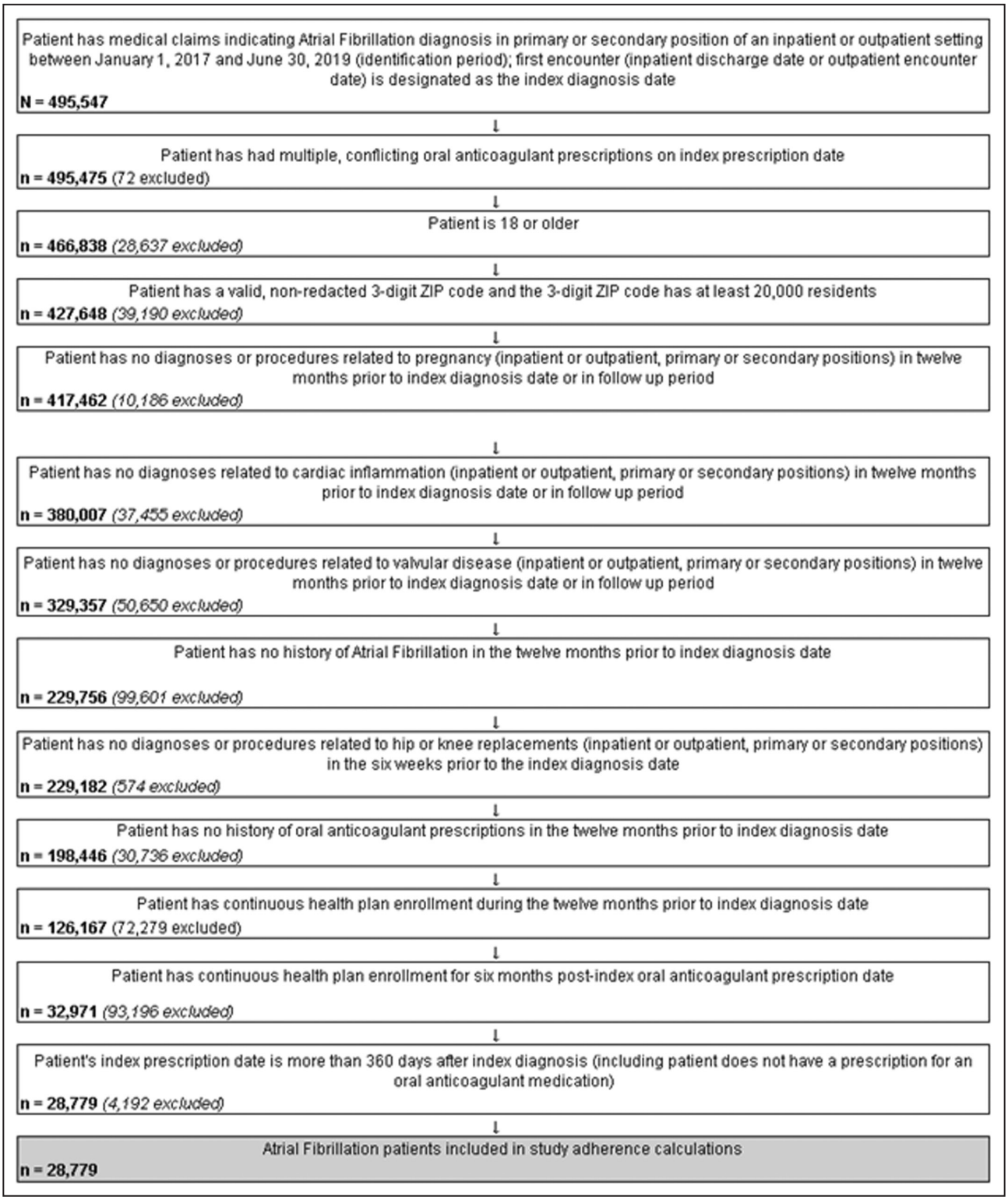

Figure 1. Patient selection criteria.

recent immigrants (OR, 0.80 [0.69–0.92]), non-English-speaking (OR, 0.90 [95% CI, 0.86–0.96]), had less than a high school diploma (OR, 0.80 [95% CI, 0.75–0.86]), rented their homes (OR, 0.97 [95% CI, 0.94–1.00]), lived below the Federal Poverty Line (OR, 0.81 [95% CI, 0.75–0.87]), or did not have health insurance (OR, 0.75

Table 1. Baseline Descriptive Characteristics of Patients With Atrial Fibrillation

	Atrial fibrillation index diagnosis sample					
	Low PDC at 360 d* n=12 958		High PDC at 360 d n=9614		Overall n=28 779	
Variable	Mean/N (%)	95% CI	Mean/N (%)	95% CI	Mean/N (%)	95% CI
Average age, y	57.68	(57.52–57.85)	61.05	(60.88–61.22)	59.22	(59.12–59.33)
Age, y, categories						
18–54	3967 (30.64)	(29.85–31.45)	1751 (18.16)	(17.39–18.95)	7123 (24.77)	(24.27–25.28)
55–64	6670 (51.36)	(50.49–52.23)	5237 (54.44)	(53.43–55.45)	15 236 (52.87)	(52.28–53.45)
65–74	1780 (13.75)	(13.16–14.36)	1947 (20.26)	(19.46–21.08)	4912 (17.05)	(16.61–17.49)
75+	541 (4.24)	(3.91–4.61)	679 (7.14)	(6.64–7.68)	1508 (5.31)	(5.06–5.58)
Sex						
Male	9503 (73.29)	(72.52–74.06)	6545 (68.00)	(67.05–68.94)	20 369 (70.70)	(70.16–71.23)
Female	3455 (26.71)	(25.94–27.48)	3069 (32.00)	(31.06–32.95)	8410 (29.30)	(28.77–29.84)
Geographic region						
Northeast	2212 (16.32)	(15.68–16.97)	1823 (18.13)	(17.36–18.92)	5192 (17.27)	(16.84–17.72)
Midwest	2974 (23.39)	(22.66–24.14)	2392 (25.45)	(24.58–26.34)	6762 (23.98)	(23.48–24.48)
South	6090 (47.05)	(46.19–47.92)	4002 (41.56)	(40.57–42.56)	12 928 (44.93)	(44.35–45.51)
West	1682 (13.24)	(12.66–13.84)	1397 (14.87)	(14.16–15.60)	3897 (13.82)	(13.42–14.23)
CHA_2DS_2-VASc score	1.85	(1.82–1.87)	2.29	(2.26–2.32)	2.06	(2.04–2.08)
CHA_2DS_2-VASc <2	6053 (46.61)	(45.74–47.48)	3006 (31.24)	(30.31–32.19)	11 350 (39.38)	(38.82–39.96)
CHA_2DS_2-VASc ≥2	6905 (53.39)	(52.52–54.26)	6608 (68.76)	(67.81–69.69)	17 429 (60.62)	(60.04–61.18)
HAS-BLED score	1.30	(1.28–1.32)	2.00	(1.50–1.54)	1.41	(1.40–1.42)
HAS-BLED <2	8387 (64.76)	(63.92–65.58)	5447 (56.53)	(55.53–57.53)	17 430 (60.55)	(59.98–61.12)
HAS-BLED=2	2847 (21.85)	(21.14–22.57)	2590 (26.94)	(26.05–27.85)	6971 (24.12)	(23.63–24.63)
HAS-BLED ≥3	1724 (13.40)	(12.81–14.00)	1577 (16.53)	(15.79–17.29)	4378 (15.32)	(14.90–15.75)
Comorbid conditions						
Cerebrovascular disease	3345 (25.90)	(25.15–26.67)	2777 (28.86)	(27.95–29.78)	7975 (27.76)	(27.24–28.28)
Congestive heart failure	1737 (13.47)	(12.88–14.07)	1502 (15.66)	(14.94–16.41)	4280 (14.92)	(14.51–15.34)
Coronary artery disease	2955 (22.93)	(22.20–23.67)	2404 (25.01)	(24.14–25.90)	6994 (24.38)	(23.88–24.89)
Hemodialysis	91 (0.68)	(0.55–0.84)	38 (0.39)	(0.29–0.54)	199 (0.68)	(0.59–0.78)
History of bleeding	1219 (9.44)	(8.95–9.97)	845 (8.82)	(8.27–9.41)	2720 (9.49)	(9.15–9.84)
History of estrogen therapy	76 (0.59)	(0.47–0.74)	50 (0.52)	(0.39–0.69)	166 (0.58)	(0.50–0.68)
Liver disease	386 (2.96)	(2.68–3.27)	313 (3.30)	(2.96–3.68)	911 (3.17)	(2.97–3.38)
Myocardial infarction	1038 (8.02)	(7.56–8.50)	791 (8.24)	(7.70–8.81)	2386 (8.30)	(7.98–8.63)
Renal disease	1655 (12.82)	(12.25–13.41)	1244 (13.00)	(12.34–13.70)	3859 (8.30)	(13.05–13.85)
Thrombocytopenia	330 (2.52)	(2.27–2.81)	247 (2.59)	(2.29–2.93)	772 (8.30)	(2.50–2.88)
Tobacco use/smoking	1653 (12.76)	(12.19–13.35)	1039 (10.77)	(10.16–11.42)	3526 (8.30)	(11.86–12.63)
Trauma/surgery	3302 (25.42)	(24.67–26.19)	2248 (23.39)	(22.55–24.26)	7217 (8.30)	(24.56–25.57)
Anticoagulant						
DOAC	11 932 (92.10)	(91.62–92.56)	9078 (94.41)	(93.92–94.85)	26 823 (93.20)	(92.90–93.49)
VKA	1026 (7.90)	(7.44–8.38)	536 (5.59)	(5.15–6.08)	1956 (6.80)	(6.51–7.10)
Payer type at time of index diagnosis						
Commercial†	12 343 (97.38)	(97.09–97.64)	8956 (95.44)	(95.00–95.84)	27 236 (96.75)	(96.53–96.95)
PPO‡	10 325 (81.46)	(80.77–82.13)	7406 (78.92)	(78.08–79.73)	22 623 (80.37)	(79.90–80.83)
HMO‡	1566 (12.36)	(11.79–12.94)	1354 (14.43)	(13.73–15.15)	3670 (13.05)	(12.66–13.45)
Point of service‡	567 (4.47)	(4.13–4.85)	430 (4.58)	(4.18–5.02)	1337 (4.73)	(4.49–4.98)

(*Continued*)

Table 1. Continued

	Atrial fibrillation index diagnosis sample					
	Low PDC at 360 d* n=12 958		High PDC at 360 d n=9614		Overall n=28 779	
Variable	Mean/N (%)	95% CI	Mean/N (%)	95% CI	Mean/N (%)	95% CI
Indemnity‡	217 (1.71)	(1.50–1.95)	194 (2.07)	(1.80–2.38)	521 (1.85)	(1.70–2.02)
Formulary	12 549 (96.99)	(96.68–97.28)	9340 (97.54)	(97.20–97.83)	27 906 (97.30)	(97.11–97.49)
Outpatient visits	10.2	(9.94–10.47)	10.5	(10.22–10.75)	10.51	(10.34–10.69)
0–3 visits	4085 (31.49)	(30.68–32.30)	2663 (27.70)	(26.80–28.61)	8468 (29.39)	(28.86–29.93)
4–7 visits	3314 (25.54)	(24.79–26.31)	2506 (26.04)	(25.17–26.94)	7400 (25.69)	(25.18–26.20)
8–13 visits	2558 (19.80)	(19.12–20.51)	2069 (21.56)	(20.74–22.40)	5917 (20.60)	(20.13–21.08)
14 or more visits	3001 (23.17)	(22.45–23.91)	2376 (24.70)	(23.84–25.58)	6994 (24.32)	(23.82–24.82)

DOAC indicates direct-acting oral anticoagulant; HAS-BLED, atrial fibrillation bleeding risk score; HMO, health maintenance organization; PDC, proportion of days covered; PPO, preferred provider organization; and VKA, vitamin K antagonist.

*PDC 360 days is a binary variable reflecting adherence (proportion of days covered) at 360 days. Low PDC is <0.8, and high PDC is ≥0.80. 6207 people are missing on the PDC 360-day outcome due to disenrolling from the study before the end of the 360-day window.

†Commercial payer type includes self-insured.

‡628 patients are missing insurance type information.

[95% CI, 0.71–0.80]) were negatively associated with having a high PDC at 360 days. In addition, saturation of medical providers per 1000 ZIP-3 residents was negatively associated with medication adherence (OR, 0.97 [95% CI, 0.94–1.00]). Almost identical bivariable associations were observed for 180-day persistence as for 360-day PDC, shown in Figure S6.

The risk scores for food landscape and health literacy were inversely associated with both 360-day PDC and 180-day persistence. For a 1-point higher food landscape risk, an individual had 6% lower odds of having a high PDC (95% CI, 0.89–0.99) than of someone residing in an area with a lower food landscape risk score. For a 1-point higher health literacy risk score, an individual's odds of having a high PDC was 15% lower (OR, 0.85 [95% CI, 0.81–0.88]). For 180-day persistence, for a 1-point higher food landscape risk score in an individual's ZIP-3 area, an individual had 5% lower odds of having a high PDC (OR, 0.95 [95% CI, 0.91–1.00]) than someone with a lower food landscape risk score. For a 1-point higher health literacy risk score, an individual's odds of having a high PDC was reduced by 14% (OR, 0.86 [95% CI, 0.82–0.89]). Economic climate risk, housing environment risk, and transportation network risk were not significantly associated with persistence or PDC.

Individual Characteristics

Bivariable regressions of individual-level characteristics on 360-day PDC and 180-day persistence revealed significant positive associations between patient sociodemographic characteristics (age and sex), patient CHA_2DS_2-VASc and HAS-BLED scores, patient comorbid conditions (cerebrovascular disease, congestive heart failure, and coronary artery disease), having nonpreferred provider organization insurance, and number of outpatient visits in the prior year and adherence/persistence. Significant negative associations with adherence were observed between region (living in the South compared with the Northeast), comorbid conditions (history of bleeding, tobacco use, and trauma/surgery), and being on a vitamin K antagonist. Plots of these associations are presented in Figures S5 and S6.

Multiple Logistic Regression Results

One Hundred and Eighty-Day Persistence

Of 28 779 patients in the analytic sample, 15 385 (53.5%) were persistent on medication at 180 days. Backward selection logistic regression indicated that housing environment risk was positively associated with medication persistence at 180 days (OR, 1.10 [95% CI, 1.04–1.16]) and health literacy risk was negatively associated with 180-day persistence (OR, 0.80 [95% CI, 0.76–0.83]). ZIP-3 characteristics associated with greater odds of 180-day persistence included elderly composition (OR, 1.29 [95% CI, 1.17–1.42]), medical provider saturation (OR, 0.93 [95% CI, 0.89–0.97]), and population density (greater density was associated with higher odds of persistence). Patient age, CHA_2DS_2-VASc and HAS-BLED scores, and multiple comorbid conditions were also associated with 180-day persistence (Figure 2, Table 3).

PDC at 360 Days

Backward selection logistic regression indicated that housing environment risk was positively associated with medication PDC at 360 days (OR, 1.10 [95% CI, 1.03–1.17]) and health literacy risk was negatively

Table 2. Baseline Community Contextual Data* (N=28 779)

Variable	Mean/%	(95% CI)	Min.	Max.
Risk scores†				
Economic climate risk score	3.0	(3.00–3.01)	1.4	4.7
Food landscape risk score	2.8	(2.76–2.77)	1.0	4.1
Housing environment risk score	2.7	(2.69–2.70)	1.2	4.8
Transportation network risk score	1.9	(1.91–1.92)	1.0	4.3
Health literacy risk score	2.9	(2.87–2.88)	1.2	4.9
Community characteristics‡				
Area population	664 175	(657 848–670 501)	27 369	3 195 460
Female	50.77	(50.76–50.78)	43	57
Age ≥70 y	11.11	(11.08–11.15)	2	25
Married	51.15	(51.09–51.21)	17	63
Prop. Black, Asian, and minority races	23.35	(23.18–23.52)	2	84
Prop. Hispanic	12.39	(12.25–12.53)	0	92
Prop. noncitizens	4.69	(4.64–4.74)	0	31
Prop. recent immigrants	2.20	(2.17–2.22)	0	15
Prop. speak a language other than English at home	3.42	(3.37–3.48)	0	44
Prop. less than HS diploma/GED	10.90	(10.85–10.94)	3	35
Average income, per person	20132.46	(20082.56–20182.36)	10067.30	49932.80
Prop. below federal poverty line	9.15	(9.11–9.19)	2	31
Household size	2.64	(2.64–2.64)	2	4
Monthly housing costs	1076.64	(1073.75–1079.54)	444.25	2218.96
Prop. renting	32.49	(32.40–32.59)	12	83
Household food costs	453.57	(453.17–453.97)	331.44	675.34
Prop. SNAP utilization	11.70	(11.66–11.75)	2	36
Household vehicle access	93.06	(93.00–93.11)	23	98
Prop. commute on public transit	2.87	(2.80–2.93)	0	67
Prop. uninsured	8.40	(8.35–8.45)	1	30
Area saturation medical provider, per 1000	1.86	(1.85–1.87)	0.33	9.59
Area saturation pharmacies, per 1000	0.21	(0.21–0.22)	0.03	0.56
Area population density	1101	(1064.18–1137.15)	1	101 227
Population density–quartiles	Ppl./sq. mile			
1	1–108			
2	108–251			
3	254–1140			
4	1140–101 227			

GED indicates general education development; HS, high school; Prop, proportion; and SNAP, supplemental nutrition assistance program.

*824 ZIP-3 areas are represented in the data set.

†Social determinants of health risk scores are continuous variables on a 1–5 scale, where 1=little to no risk, 2=low risk, 3=moderate risk, 4=high risk, and 5=severe risk.

‡Community characteristics are measured at the 3-digit ZIP code (ZIP-3) level. Proportional community-level characteristics represent the prevalence of the named characteristic ("female," "married," etc.) among residents of the ZIP-3. Other community measures represent median or mean values for the area, as denoted in the table variable label.

associated with 360-day PDC (OR, 0.81 [95% CI, 0.76–0.87]). ZIP-3 characteristics associated with greater odds of 360-day PDC included elderly composition (OR, 1.32 [95% CI, 1.17–1.49]), medical provider saturation (OR, 0.92 [95% CI, 0.88–0.97]), and population density—living in areas with 254 to 1140 people per square mile and 1140 to 101 227 people per square mile was associated with higher odds of persistence than living in an area with 1 to 108 people per square mile (respectively, OR, 1.11 [95% CI, 1.00–1.23]; OR, 1.20 [95% CI, 1.07–1.35]). Patient age, CHA_2DS_2-VASc and HAS-BLED scores, and multiple comorbid

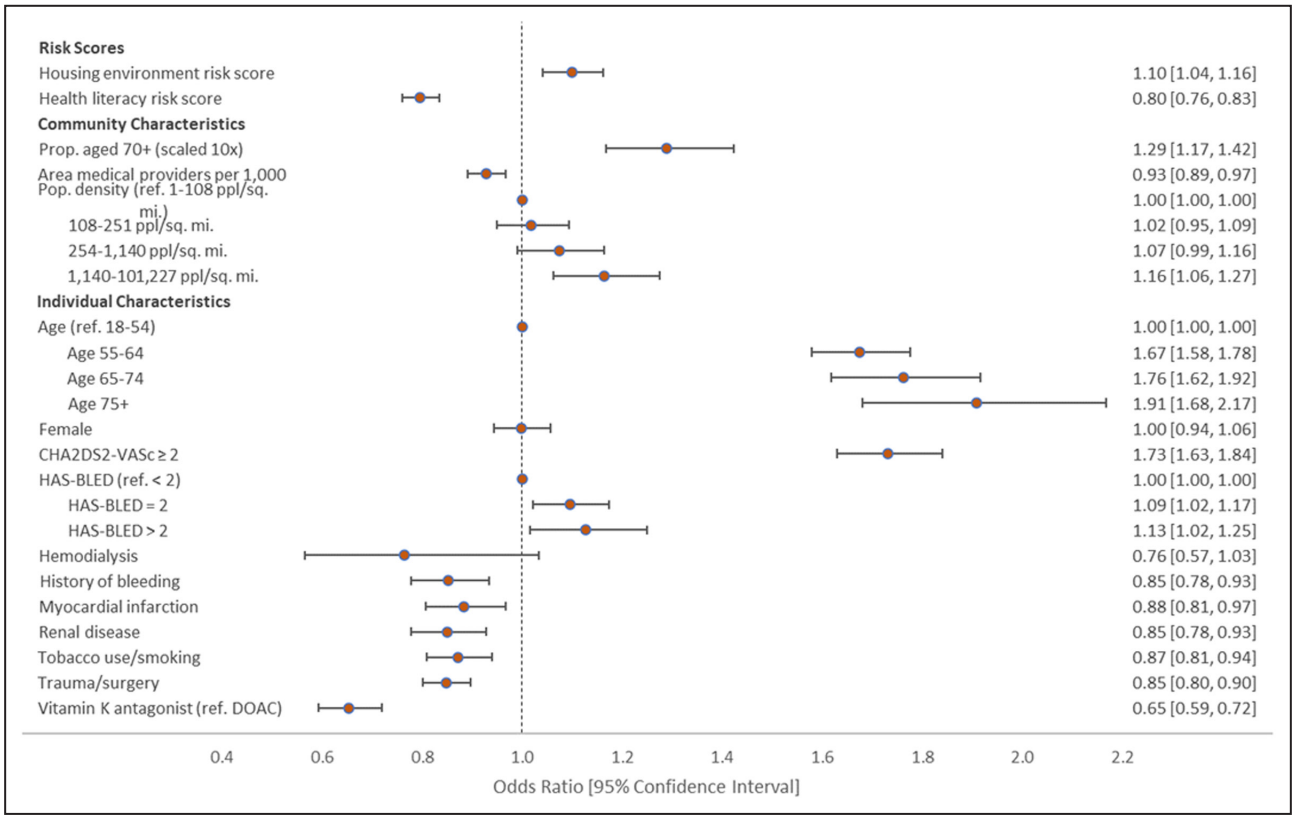

Figure 2. Associations between community- and patient-level characteristics and persistence on index anticoagulant at 180 days (multivariable regression).
Risk scores are continuous variables on a 1–5 scale, where 1=little to no risk, 2=low risk, 3=moderate risk, 4=high risk, and 5=severe risk. Community characteristics are measured at the 3-digit ZIP code (ZIP-3) level. Proportional community-level measures are scaled by a factor of 10. For example, a 1-unit increase in "Prop. aged 70 and older" is equivalent to a 10% increase in the prevalence of residents aged ≥70 years in the ZIP-3 area. Other measures represent median or mean values. DOAC indicates direct-acting oral anticoagulant; and HAS-BLED, atrial fibrillation bleeding risk score.

conditions were also associated with PDC at 360 days (Figure 3, Table 4).

Time Elapsed From Index Diagnosis Date to Index Prescription Date

No social risk scores were associated with days elapsed between the index diagnosis date and index prescription date. At the community (ZIP-3) level, proportion of Hispanic residents was negatively associated with time to index prescription (IRR, 0.98 [95% CI, 0.97–1.00]). Region of patient residence was associated with the outcome such that patients in the South and West took longer to pick up their prescriptions than patients in the Northeast (IRR, 1.12 [95% CI, 1.06–1.18]; IRR, 1.12 [95% CI, 0.04–0.20], respectively). CHA_2DS_2-VASc score was negatively associated with time to pick up an index prescription (IRR, 0.72 [95% CI, 0.68–0.76]). Co-presence of coronary artery disease (IRR, 0.87 [95% CI, 0.78–0.98]), cerebrovascular disease (IRR, 1.12 [95% CI, 1.00–1.25]), or tobacco use (IRR, 0.92 [95% CI, 0.87–0.98]) with AF was negatively associated with time to index prescription. A history of estrogen therapy (IRR, 1.39 [95% CI, 1.07–1.80]) or trauma/surgery (IRR, 1.06 [95% CI, 1.01–1.11]), or having more than 13 outpatient visits in the previous year (IRR, 1.14 [95% CI, 1.08–1.21]) were positively associated with time to index prescription. Results are summarized in Table 5.

Sensitivity and Subgroup Analyses

A sensitivity analysis using Pharmacy Quality Alliance's criterion for OAC PDC revealed significant associations between transportation network risk (OR, 0.79 [95% CI, 0.65–0.95]), housing environment risk (OR, 1.22 [95% CI, 1.03–1.44]), and health literacy risk (OR, 0.75 [95% CI, 0.63–0.90]) and PDC-360. Patient age (ages 55–64: OR, 1.33 [95% CI, 1.14–1.55]; ages 65–74: OR, 1.72 [95% CI, 1.39–2.12]; ages 75+: OR, 1.90 [95% CI, 1.35–2.68]), sex (OR, 1.19 [95% CI, 1.02–1.38]), Midwest region (OR, 1.27 [95% CI, 1.02–1.58]), and having 8–13 outpatient visits in the previous year (OR, 1.24 [95% CI, 1.04–1.50]) were all positively associated with high

Table 3. Backward Selection Logistic Regression of 180-Day Persistence on Social Risk and Community and Individual Characteristics (N=28 151)

	Odds ratio	(95% CI)	*P* value
Social risk scores*, 1=low risk, 5=severe risk			
Housing environment risk score	1.10	(1.04–1.16)	0.001
Health literacy risk score	0.80	(0.76–0.83)	<0.001
Community characteristics†			
Prop. aged 70 and older, scaled 10×	1.29	(1.17–1.42)	<0.001
Area medical provider saturation, per 1000	0.93	(0.89–0.97)	<0.001
Population density, ref.=1–108 ppL/mi^2			
108–251 ppL/mi^2	1.02	(0.95–1.09)	0.612
254–1140 ppL/mi^2	1.07	(0.99–1.16)	0.083
1140–101 227 ppL/mi^2	1.16	(1.06–1.27)	0.001
Individual characteristics			
Age, y, ref.=18–54			
55–64	1.67	(1.58–1.78)	<0.001
65–74	1.76	(1.62–1.92)	<0.001
75 and older	1.91	(1.68–2.17)	<0.001
Female	1.00	(0.94–1.06)	0.941
CHA_2DS_2-VASc ≥2	1.73	(1.63–1.84)	<0.001
HAS-BLED, ref. ≤2			
HAS-BLED=2	1.09	(1.02–1.17)	0.011
HAS-BLED >2	1.13	(1.02–1.25)	0.025
Hemodialysis	0.76	(0.57–1.03)	0.081
History of bleeding	0.85	(0.78–0.93)	0.001
Myocardial infarction	0.88	(0.81–0.97)	0.007
Renal disease	0.85	(0.78–0.93)	<0.001
Tobacco use/smoking	0.87	(0.81–0.94)	<0.001
Trauma/surgery	0.85	(0.80–0.90)	<0.001
Vitamin K antagonist, ref.=DOAC	0.65	(0.59–0.72)	<0.001

DOAC indicates direct-acting oral anticoagulant.

*Risk Scores are continuous variables on a 1–5 scale, where 1=little to no risk, 2=low risk, 3=moderate risk, 4=high risk, and 5=severe risk.

†Community characteristics are measured at the 3-digit ZIP code (ZIP-3) level. Proportional community-level measures are scaled by a factor of 10. For example, a 1-unit increase in "Prop. Hispanic" is equivalent to a 10% increase in the prevalence of Hispanic residents in the ZIP-3 area. Other measures represent median or mean values for the area, as denoted in the table variable label. 824 ZIP-3 areas are represented in the data.

adherence. A plot summarizing these associations is presented in Figure S7.

Multiple regression analyses regressed 90-day, 180-day, and 360-day binary persistence measures, 180-day, and 360-day PDC, and days elapsed between index diagnosis date and index prescription date on social risk scores and selected community- and patient-level indicators (Data S1, Table S5, Table 3, Table S6, Table S7, Table 4, and Table 5, respectively). For all persistence and PDC measures, housing environment risk showed positive associations with the outcome (elevated housing risk was associated with higher odds of adherence) and health literacy risk showed negative associations (elevated health literacy risk was associated with lower odds of adherence). No significant associations were revealed between risk scores and time elapsed between index diagnosis date and index prescription date.

DISCUSSION

In this national retrospective cohort study of patients diagnosed with AF, we evaluated associations between SDoH, multiple domains of social risk, and medication adherence as measured by persistence and PDC. We found that elevated levels of health literacy risk were associated with lower odds of being persistent on a prescribed anticoagulant at 90 and 180 days and of having a high PDC, and higher levels of housing environment risk were associated with higher odds of adherence. That is, patients residing in ZIP-3 areas with higher area-level housing environment risk are more likely to be persistent on medication at 90 and 180 days and to have a high PDC compared with patients living in ZIP-3 areas with lower housing environment risk scores. Although this finding related to housing risk is counterintuitive, it may be a result of the

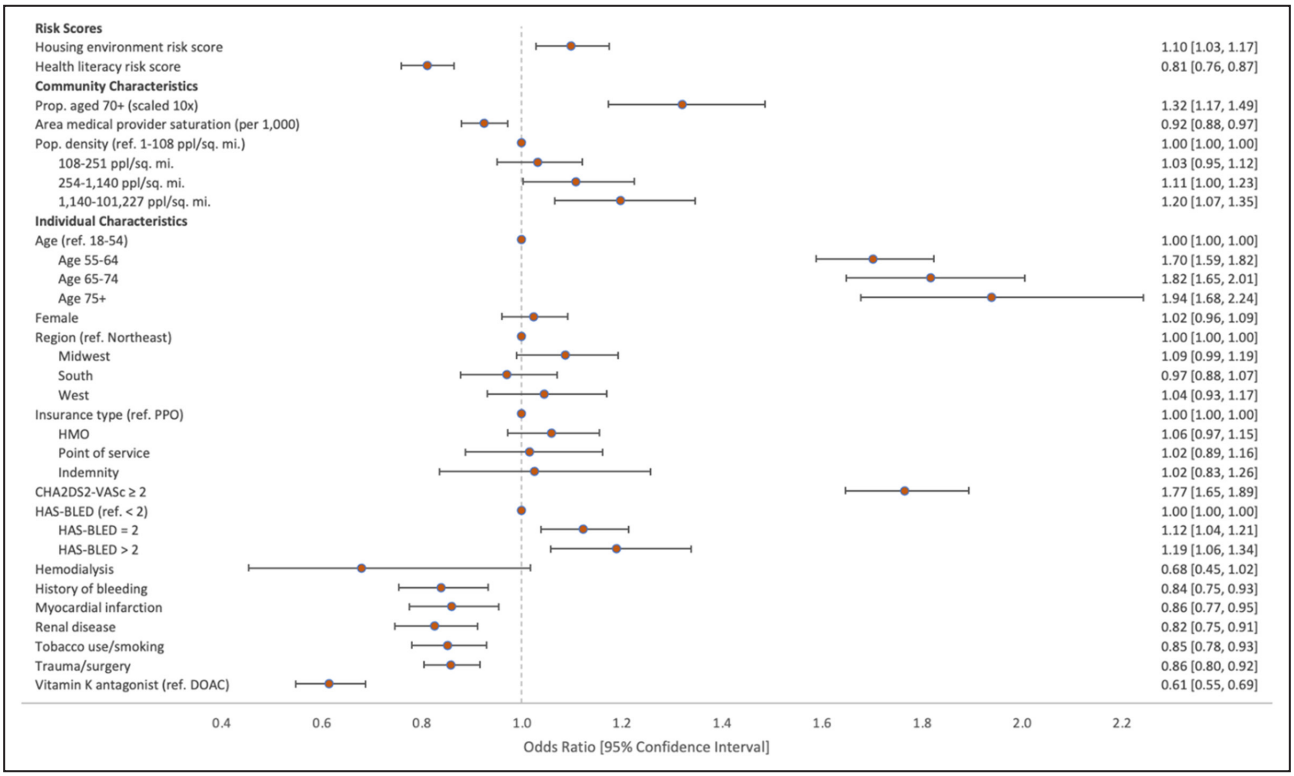

Figure 3. Associations between community- and patient-level characteristics and PDC at 360 days (multivariable regression).

Risk scores are continuous variables on a 1–5 scale, where 1=little to no risk, 2=low risk, 3=moderate risk, 4=high risk, and 5=severe risk. Community characteristics are measured at the 3-digit ZIP code (ZIP-3) level. Proportional community-level measures are scaled by a factor of 10. For example, a 1-unit increase in "Prop. aged 70 and older" is equivalent to a 10% increase in the prevalence of residents aged ≥70 years in the ZIP-3 area. Other measures represent median or mean values. DOAC indicates direct-acting oral anticoagulant; HAS-BLED, atrial fibrillation bleeding risk score; HMO, health maintenance organization; PDC, proportion of days covered; and PPO, preferred provider organization.

very high proportion (94.6%) of commercially insured patients in the sample. Since continuous insurance enrollment over the study period was a study inclusion criterion, individuals in the sample may represent a subset of the general population for whom housing risk is not a salient factor for prescription access, regardless of overall level of housing risk in their area.

A comparison of bivariable and multiple regression results indicates that some initial associations between social risk and adherence were mediated by covariates in full models. For example, food landscape risk was negatively associated with both high PDC and persistence in bivariable models, but became a nonsignificant predictor in full models, with intermediate models revealing that the inclusion of any one of health literacy risk, patient age, or patient region of residence mitigated the association to nonsignificance. These findings suggest commonality in the way that health literacy and food landscape are associated with an individual's ability to consistently access a prescribed medication. Alternatively, both risk domains reflect underlying social challenges that impact residents of a given area. Conversely, housing environment risk is not significantly associated with either outcome in bivariable models but is positively associated with both in full multiple regression. This may be due to a suppression effect, which occurs when the direct and indirect associations of a variable with an outcome are in opposing directions. In the case of housing, it appears that when individual-level characteristics are accounted for, housing risk is associated with an increased likelihood of being adherent on a prescribed OAC, despite not being significantly associated with adherence in the absence of these characteristics.

This study contributes to a growing literature examining links between SDoH, social risk factors, and medication adherence and extends the usual set of predictors examined to include community-level attributes reflecting possible socioecological barriers to adherence. Although many studies have examined associations between patient sociodemographic characteristics and adherence,[10,11] few have interrogated area-level SDoH and social risk factors that may have an impact on the financial or physical ability of a patient

Table 4. Associations Between Patient- and Community-Level Characteristics and Proportion Days Covered ≥0.8 over 360-Day Study Window (N=22059)

	Odds ratio	(95% CI)	*P* value
Social risk scores*, 1=low risk, 5=severe risk			
Housing environment risk score	1.10	(1.03–1.17)	0.005
Health literacy risk score	0.81	(0.76–0.87)	<0.001
Community characteristics†			
Prop. aged ≥70 y, scaled 10x	1.32	(1.17–1.49)	<0.001
Area medical provider saturation, per 1000	0.92	(0.88–0.97)	0.002
Population density, ref.=1–108 ppL/mi^2			
108–251 ppL/mi^2	1.03	(0.95–1.12)	0.445
254–1140 ppL/mi^2	1.11	(1.00–1.23)	0.044
1140–101 227 ppL/mi^2	1.20	(1.07–1.35)	0.002
Individual characteristics			
Age, y, ref.=18–54			
55–64	1.70	(1.59–1.82)	<0.001
65–74	1.82	(1.65–2.01)	<0.001
75+	1.94	(1.68–2.24)	<0.001
Female	1.02	(0.96–1.09)	0.469
Region, ref.=Northeast			
Midwest	1.09	(0.99–1.19)	0.081
South	0.97	(0.88–1.07)	0.541
West	1.04	(0.93–1.17)	0.460
Insurance type, ref.=PPO‡			
HMO	1.06	(0.97–1.15)	0.186
Point of service	1.02	(0.89–1.16)	0.820
Indemnity	1.02	(0.83–1.26)	0.815
CHA_2DS_2-VASc ≥2	1.77	(1.65–1.89)	<0.001
HAS-BLED, ref. ≤2			
HAS-BLED=2	1.12	(1.04–1.21)	0.004
HAS-BLED >2	1.19	(1.06–1.34)	0.004
Hemodialysis	0.68	(0.45–1.02)	0.060
History of bleeding	0.84	(0.75–0.93)	0.001
Myocardial infarction	0.86	(0.77–0.95)	0.004
Renal disease	0.82	(0.75–0.91)	<0.001
Tobacco use/smoking	0.85	(0.78–0.93)	<0.001
Trauma/surgery	0.86	(0.80–0.92)	<0.001
Vitamin K antagonist, ref.=DOAC	0.61	(0.55–0.69)	<0.001

DOAC indicates direct-acting oral anticoagulant; HAS-BLED, atrial fibrillation bleeding risk score; HMO, health maintenance organization; and PPO, preferred provider organization.

*Risk Scores are continuous variables on a 1–5 scale, where 1=Little to no risk, 2=Low risk, 3=Moderate risk, 4=High risk, and 5=Severe risk.

†Community Characteristics are measured at the 3-digit ZIP code (ZIP-3) level. Proportional community-level measures are scaled by a factor of 10. For example, a 1-unit increase in "Prop. Hispanic" is equivalent to a 10% increase in the prevalence of Hispanic residents in the ZIP-3 area. Other measures represent median or mean values for the area, as denoted in the table variable label. 824 ZIP-3 areas are represented in the data.

‡628 patients are missing insurance type information. Point of service plans are based on a managed care model in which patients exchange choice (must see in-network providers) for lower costs. Indemnity refers to a "fee for service" plan that allows patients to be seen by any provider but with only a set portion of costs covered.

with AF to access a prescribed medication. Of articles that studied SDoH, several focused on HIV, a context where medication adherence is particularly important and where food instability has been found to be reliably linked to medication.[20–24] However, our study did not find an association between food landscape risk and adherence, perhaps because characterizing food insecurity at the ZIP-3 level compresses too much heterogeneity into a single measure for an association to be detectable.

In a systematic review and meta-analysis of 29 articles examining SDoH and medication adherence,

Table 5. Associations Between Patient- and Community-Level Characteristics and Time to Index Prescription* over 360-Day Study Window (N=28 151)

	Incidence-rate ratio	(95% CI)	*P* value
Community characteristics†			
Prop. Hispanic, scaled 10×	0.98	(0.97–1.00)	0.028
Individual characteristics			
Female	0.99	(0.94–1.03)	0.575
Age, y, ref.=18–54			
55–64	1.00	(0.95–1.04)	0.858
65–74	1.00	(0.93–1.07)	0.931
75+	1.02	(0.92–1.13)	0.649
Region, ref.=Northeast			
Midwest	1.06	(0.99–1.12)	0.084
South	1.12	(1.06–1.18)	<0.001
West	1.12	(1.04–1.20)	0.003
CHA_2DS_2-VASc ≥2	0.72	(0.68–0.76)	<0.001
HAS-BLED, ref. ≤2			
HAS-BLED =2	0.96	(0.91–1.01)	0.112
HAS-BLED >2	1.04	(0.97–1.11)	0.316
Coronary artery disease	0.87	(0.78–0.98)	0.022
Cerebrovascular disease	1.12	(1.00–1.25)	0.043
History of bleeding	1.06	(0.99–1.14)	0.114
History of estrogen therapy	1.39	(1.07–1.80)	0.012
Myocardial infarction	0.94	(0.86–1.02)	0.146
Tobacco use/smoking	0.92	(0.87–0.98)	0.007
Trauma/surgery	1.06	(1.01–1.11)	0.018
Vitamin K antagonist, ref.=DOAC	1.07	(0.99–1.16)	0.082
Outpatient visits year prior, ref.=0–3			
4–7 visits	0.98	(0.93–1.03)	0.381
8–13 visits	1.01	(0.95–1.07)	0.784
14–365 visits	1.14	(1.08–1.21)	<0.001

DOAC indicates direct-acting oral anticoagulant; and HAS-BLED, atrial fibrillation bleeding risk score.

*Outcome (time to index Rx) is a continuous variable measured in days.

†Community characteristics are measured at the 3-digit ZIP code (ZIP-3) level. Proportional community-level measures are scaled by a factor of 10. For example, a 1-unit increase in "Prop. Hispanic" is equivalent to a 10% increase in the prevalence of Hispanic residents in the ZIP-3 area. 824 ZIP-3 areas are represented in the data.

Wilder and colleagues found that food insecurity and housing instability were negatively associated with medication adherence, in contrast to this study's finding that elevated housing environment risk is associated with increased odds of adherence.[17] There are a couple of possible reasons for the discrepancy. First, the housing risk measure captures area-level housing environment (eg, prevalence of renting, household size, housing costs relative to income at the 3-digit ZIP code level) rather than individual-level housing instability, reflecting a socioecological rather than individual-level framing of social risk. Second, the Wilder review was not constrained to studies of populations of patients with AF and included multiple studies of medication adherence in patients with HIV, which may not be comparable to the current study.

This study's finding that health literacy risk is associated with lower odds of medication adherence is consistent with the limited available literature on this topic.[17] Wilder and colleagues found that higher health literacy was associated with improved medication adherence, though the study population was not AF-specific. In a small (n=30) qualitative study by Mansukhani, patients with AF completed questionnaires regarding their reasons for nonadherence to OACs. The authors found that fear of bleeding or other side effects and concerns about medication cost were the most frequently cited reasons for not refilling a prescription, representing an opportunity to better communicate the benefits and risks of OAC.[15]

This study found that higher CHA_2DS_2-VASc and HAS-BLED scores were associated with increased odds of medication adherence among patients with AF.

In contrast, renal disease, a history of bleeding, myocardial infarction, and trauma or surgery were associated with lower adherence. This is consistent with prior studies and could reflect a perceived increased risk of bleeding by those patients.[11,40] In addition, smoking/tobacco use was associated with lower medication adherence, similar to studies in other therapeutic areas.[41]

This study highlights many opportunities to further study SDoH and social risk factors in medication adherence and patient outcomes. A deeper understanding of pathways linking SDoH, social risk factors, and adherence will enable effective programming by health systems, biopharmaceutical companies, and other stakeholders to improve adherence by targeting specific barriers. Identifying health literacy as a geography-graded barrier to adherence in each region, for instance, would enable the development of public education programs and provider–patient partnerships to address observed gaps, which could be further targeted through local data collection efforts guided by an understanding of the SDoH and social risk landscape. Integrating SDoH and social risk factors into medication adherence research is a vital step to creating a full picture of the resources needed to optimize adherence for diverse patient populations and address health inequities. More broadly, characterizing the relationships between SDoH, social risk factors, disease states, and health outcomes will assist the health care community in better understanding patient challenges and creating patient-centric solutions to address them.

Limitations

The inferential power of this retrospective observational cohort study is limited to the identification of statistical associations between SDoH, social risk, and medication adherence, because it is not possible to identify causal relationships with the available data and study design. The social risk scores used in our analysis have not been validated in a peer-reviewed publication. Use of ZIP-3-level data limits the scope of the analysis to relatively large geographic units. Because social risk is engendered at the local level, often within neighborhoods, regressions at this analytic scale may fail to capture relationships among the independent and dependent variables that would be observed using finer-grained risk data. Limited patient-level demographic information was available, which further limited our models' explanatory power.

Medication adherence is a complex construct influenced by multiple factors at both the individual and community levels. Although we adjusted for as many of these factors as possible, residual confounding by factors such as race and patient perceptions (ie, fear of bleeding) may impact results.[15,25–27] In 3 studies of anticoagulation initiation and use in AF, Essien and colleagues found that socioeconomic factors accounted for race differences in anticoagulant use and that, among Medicare patients, rates of anticoagulant initiation were lower for Black patients and women than for non-Black and male counterparts.[25–27] However, data on either patient race or proportion of Black residents in the ZIP-3 area were unavailable in the present study, preventing the authors from evaluating differences in associations between social risk and adherence by race. Given that SDoH represent vehicles by which structural racism impacts individual health, this is an important topic for future health equity research. Incorporating patient voice would also strengthen this study: Adherence is an individual-level measure of patient behavior, and only patients can describe proximate motivators of their decisions. Also, many factors lead to medication discontinuation, including adverse effects and development of new contraindications. Using claims data to measure adherence does not guarantee that a patient was taking the medicine as directed. Although examining community- and individual-level characteristics of patients and their environments enables identification of important factors impacting decision-making, patient reports of perceptions, beliefs, and barriers would provide additional valuable insights into mechanisms by which SDoH and social risk impact outcomes.

Our sample was largely (94.6%) commercially insured, suggesting it may not be representative of the US patient population with AF. We also required that patients be continuously enrolled on their insurance plan for 12 months before the index diagnosis date, so we are capturing a relatively stable, potentially high-resource group of patients for whom social risk factors may be less salient than for lower-resourced Americans. Thus, we may have attrition bias present with more resourced and healthier patients remaining throughout the measurement timeframe. Lastly, this study had a large sample size, so the clinical significance and implications of the statistical associations found should be weighed carefully. These limitations should be addressed in future research.

CONCLUSIONS

Our study found community SDoH and social risks are contributors to OAC adherence in AF after controlling for individual characteristics. Despite measurement limitations, this study points to a new potential avenue of research for understanding guideline-nonconcordant medication adherence rates and suggests pathways by which adherence may be improved for some groups. It also uses novel multifactorial measures of social risk, which reduce large amounts of data to manageable constructs while maintaining domain specificity

to reflect multiple sources of risk experienced by patients. Future research should further explore ways in which patients' ability to access medical resources is impacted by their community or neighborhood setting using both finer-grained geographic data and patient-provided data on perceived barriers.

ARTICLE INFORMATION

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Supplemental Material

Data S1
Tables S1–S7
Figures S1–S7

REFERENCES

1. Miyasaka Y, Barnes ME, Gersh BJ, Cha SS, Bailey KR, Abhayaratna WP, Seward JB, Tsang TS. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. *Circulation.* 2006;114:119–125. doi: 10.1161/CIRCULATIONAHA.105.595140
2. Colilla S, Crow A, Petkun W, Singer DE, Simon T, Liu X. Estimates of current and future incidence and prevalence of atrial fibrillation in the U.S. adult population. *Am J Cardiol.* 2013;112:1142–1147. doi: 10.1016/j.amjcard.2013.05.063
3. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Chang AR, Cheng S, Das SR, et al. Heart disease and stroke statistics-2019 update: a report from the American Heart Association. *Circulation.* 2019;139:e56–e528.
4. Atrial Fibrillation. Centers for Disease Control. Accessed May 13, 2021. https://www.cdc.gov/heartdisease/atrial_fibrillation.htm.
5. Coyne KS, Paramore C, Grandy S, Mercader M, Reynolds M, Zimetbaum P. Assessing the direct costs of treating nonvalvular atrial fibrillation in the United States. *Value Health.* 2006;9:348–356. doi: 10.1111/j.1524-4733.2006.00124.x
6. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham study. *Stroke.* 1991;22:983–988. doi: 10.1161/01.STR.22.8.983
7. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *Circulation.* 2014;130:e199–e267. doi: 10.1161/CIR.0000000000000041
8. Barnett AS, Kim S, Fonarow GC, Thomas LE, Reiffel JA, Allen LA, Freeman JV, Naccarelli G, Mahaffey KW, Go AS, et al. Treatment of atrial fibrillation and concordance with the American Heart Association/American College of Cardiology/Heart Rhythm Society guidelines: findings from ORBIT-AF (Outcomes Registry for Better Informed Treatment of Atrial Fibrillation). *Circ Arrhythm Electrophysiol.* 2017;10:e005051. doi: 10.1161/CIRCEP.117.005051
9. Hsu JC, Maddox TM, Kennedy KF, Katz DF, Marzec LN, Lubitz SA, Gehi AK, Turakhia MP, Marcus GM. Oral anticoagulant therapy prescription in patients with atrial fibrillation across the spectrum of stroke risk: insights from the NCDR PINNACLE registry. *JAMA Cardiol.* 2016;1:55–62. doi: 10.1001/jamacardio.2015.0374
10. Salmasi S, Loewen PS, Tandun R, Andrade JG, De Vera MA. Adherence to oral anticoagulants among patients with atrial fibrillation: a systematic review and meta-analysis of observational studies. *BMJ Open.* 2020;10:e034778. doi: 10.1136/bmjopen-2019-034778
11. Borne RT, O'Donnell C, Turakhia MP, Varosy PD, Jackevicius CA, Marzec LN, Masoudi FA, Hess PL, Maddox TM, Ho PM. Adherence and outcomes to direct oral anticoagulants among patients with atrial fibrillation: findings from the Veterans Health Administration. *BMC Cardiovasc Disord.* 2017;17:236. doi: 10.1186/s12872-017-0671-6
12. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med.* 2005;353:487–497. doi: 10.1056/NEJMra050100
13. Berkowitz SA, Seligman HK, Choudhry NK. Treat or eat: food insecurity, cost-related medication underuse, and unmet needs. *Am J Med.* 2014;127:303–310.e3. doi: 10.1016/j.amjmed.2014.01.002
14. Gadkari AS, McHorney CA. Unintentional non-adherence to chronic prescription medications: how unintentional is it really? *BMC Health Serv Res.* 2012;12:98. doi: 10.1186/1472-6963-12-98
15. Mansukhani SG, MacLean EA, Manzey LL, Possidente CJ, Cappelleri JC, Deal LS. Development of a new patient-reported medication adherence instrument: concerns influencing medication adherence. *Patient Prefer Adherence.* 2021;15:1991–2007. doi: 10.2147/PPA.S318030
16. Social Determinants of Health. Healthy People 2030. Office of Disease Prevention and Health Promotion. Accessed January 10, 2022. https://health.gov/healthypeople/objectives-and-data/social-determinants-health.
17. Wilder ME, Kulie P, Jensen C, Levett P, Blanchard J, Dominguez LW, Portela M, Srivastava A, Li Y, McCarthy ML. The impact of social determinants of health on medication adherence: a systematic review and meta-analysis. *J Gen Intern Med.* 2021;36:1359–1370. doi: 10.1007/s11606-020-06447-0
18. Reshetnyak E, Ntamatungiro M, Pinheiro LC, Howard VJ, Carson AP, Martin KD, Safford MM. Impact of multiple social determinants of health on incident stroke. *Stroke.* 2020;51:2445–2453. doi: 10.1161/STROKEAHA.120.028530
19. Alderwick H, Gottlieb LM. Meanings and misunderstandings: a social determinants of health lexicon for health care systems. *Milbank Q.* 2019;97:407–419. doi: 10.1111/1468-0009.12390
20. Chen Y, Kalichman SC. Synergistic effects of food insecurity and drug use on medication adherence among people living with HIV infection. *J Behav Med.* 2015;38:397–406. doi: 10.1007/s10865-014-9612-3
21. Kalichman SC, Pope H, White D, Cherry C, Amaral CM, Swetzes C, Flanagan J, Kalichman MO. Association between health literacy and HIV treatment adherence: further evidence from objectively measured medication adherence. *J Int Assoc Physicians AIDS Care (Chic).* 2008;7:317–323. doi: 10.1177/1545109708328130
22. Pellowski JA, Kalichman SC, Cherry S, Conway-Washington C, Cherry C, Grebler T, Krug L. The daily relationship between aspects of food insecurity and medication adherence among people living with HIV with recent experiences of hunger. *Ann Behav Med.* 2016;50:844–853. doi: 10.1007/s12160-016-9812-x
23. Surratt HL, O'Grady CL, Levi-Minzi MA, Kurtz SP. Medication adherence challenges among HIV positive substance abusers: the role of food and housing insecurity. *AIDS Care.* 2015;27:307–314. doi: 10.1080/09540121.2014.967656
24. Weiser SD, Tuller DM, Frongillo EA, Senkungu J, Mukiibi N, Bangsberg DR. Food insecurity as a barrier to sustained antiretroviral therapy adherence in Uganda. *PLoS One.* 2010;5:e10340. doi: 10.1371/journal.pone.0010340
25. Essien UR, Holmes DN, Jackson LR II, Fonarow GC, Mahaffey KW, Reiffel JA, Steinberg BA, Allen LA, Chan PS, Freeman JV, et al. Association of race/ethnicity with oral anticoagulant use in patients with atrial fibrillation: findings from the Outcomes Registry for Better

Informed Treatment of Atrial Fibrillation II. *JAMA Cardiol.* 2018;3:1174–1182. doi: 10.1001/jamacardio.2018.3945
26. Essien UR, Kim N, Magnani JW, Good CB, Litam TMA, Hausmann LRM, Mor MK, Gellad WF, Fine MJ. Association of race and ethnicity and anticoagulation in patients with atrial fibrillation dually enrolled in VA and Medicare: effects of Medicare part D on prescribing disparities. *Circ Cardiovasc Qual Outcomes.* 2021;15:e008389. doi: 10.1161/CIRCOUTCOMES.121.008389
27. Essien UR, Magnani JW, Chen N, Gellad WF, Fine MJ, Hernandez I. Race/ethnicity and sex-related differences in direct oral anticoagulant initiation in newly diagnosed atrial fibrillation: a retrospective study of Medicare data. *J Natl Med Assoc.* 2020;112:103–108. doi: 10.1016/j.jnma.2019.10.003
28. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol.* 2008;61:344–349. doi: 10.1016/j.jclinepi.2007.11.008
29. American Community Survey (ACS). United States Census Bureau. Accessed December 8, 2021. https://www.census.gov/programs-surveys/acs.html.
30. USDA Food Plans: Cost of Food. 2021. Food and Nutrition Service. U.S. Department of Agriculture. Accessed December 8, 2021. https://www.fns.usda.gov/cnpp/usda-food-plans-cost-food-reports
31. HIFLD Data Catalog. Homeland Infrastructure Foundation-Level Data. U.S. Department of Homeland Security, Washington, D.C. 2021. Accessed December 8, 2021. https://gii.dhs.gov/hifld/
32. About the Data. Health Resources & Services Administration. 2021 Accessed December 8, 2021. https://data.hrsa.gov/data/about.
33. A Strategic Approach to Address the Social Determinants of Health Effectively. Socially Determined, Washington, D.C. 2021. Accessed December 16, 2021. https://www.sociallydetermined.com/resources/strategic-approach-to-sdoh
34. Lip GYH, Nieuwlaat R, Pisters R, Lane DA, Crijns HJGM. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest.* 2010;137:263–272. doi: 10.1378/chest.09-1584
35. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. *Chest J.* 2010;138:1093–1100. doi: 10.1378/chest.10-0134
36. Bursac Z, Gauss CH, Williams DK, Hosmer DW. Purposeful selection of variables in logistic regression. *Source Code Biol Med.* 2008;3:17. doi: 10.1186/1751-0473-3-17
37. McHorney CA, Crivera C, Laliberté F, Nelson WW, Germain G, Bookhart B, Martin S, Schein J, Lefebvre P, Deitelzweig S. Adherence to non-vitamin-K-antagonist oral anticoagulant medications based on the Pharmacy Quality Alliance measure. *Curr Med Res Opin.* 2015;31:2167–2173. doi: 10.1185/03007995.2015.1096242
38. StataCorp. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC; 2019. Accessed March 15, 2022. https://www.stata.com/
39. Seabold S and Perktold J. *Statsmodels: Econometric and Statistical Modeling with Python*. Proc. of the 9th Python in Science Conf (SCIPY 2010), Austin, TX. 2010.
40. Hernandez I, He M, Chen N, Brooks MM, Saba S, Gellad WF. Trajectories of oral anticoagulation adherence among Medicare beneficiaries newly diagnosed with atrial fibrillation. *J Am Heart Assoc.* 2019;8:e011427. doi: 10.1161/JAHA.118.011427
41. Jin J, Sklar GE, Min Sen OV, Chuen LS. Factors affecting therapeutic compliance: a review from the patient's perspective. *Ther Clin Risk Manag.* 2008;4:269–286. doi: 10.2147/TCRM.S1458

Supplemental Material

Data S1.

Supplemental Results

90-Day Persistence. Backward selection logistic regression indicated that housing environment risk was positively associated with medication persistence at 90 days (OR = 1.07, 95% CI: 1.01 - 1.13) whereas health literacy risk was negatively associated with 90-day persistence (OR = 0.84, 95% CI: 0.80 - 0.89). ZIP-3 characteristics associated with greater odds of 90-day persistence included proportion of the area population 70 or older (OR = 1.17, 95% CI: 1.06 - 1.30), medical provider saturation (OR = 0.94, 95% CI: 0.90 - 0.98), and population density (greater density was associated with higher odds of persistence). Patient age, CHA2DS2-VASc and HAS-BLED scores, and multiple comorbid conditions were also associated with 90-day persistence. See Table S4 for full regression results.

360-Day Persistence. Backward selection logistic regression indicated that housing environment risk was positively associated with medication persistence at 360 days (OR = 1.07, 95% CI: 1.00 - 1.14) and health literacy risk was negatively associated with 360-day persistence (OR = 0.85, 95% CI: 0.80 - 0.90). ZIP-3 characteristics associated with greater odds of 360-day persistence included elderly composition (OR = 1.26, 95% CI: 1.13 - 1.41), medical provider saturation (OR = 0.95, 95% CI: 0.90 - 1.00), and population density—living in an area with 1,140-101,227 people per square mile was associated with higher odds of persistence than living in an area with 1-108 people per square mile (OR = 1.16, 95% CI: 1.04 - 1.29). Patient age, CHA2DS2-VASc and HAS-BLED scores, and multiple comorbid conditions were also associated with 360-day persistence. See Table S5 for full regression results.

PDC at 180 Days. Backward selection logistic regression indicated that housing environment risk was positively associated with high PDC at 180 days (OR = 1.09, 95% CI: 1.03 - 1.15) and health literacy risk was negatively associated with high PDC at 180 days (OR = 0.81, 95% CI: 0.77 - 0.86). ZIP-3 characteristics associated with greater odds of high PDC at 180 days included elderly composition (OR = 1.29, 95% CI: 1.16 - 1.43), medical provider saturation (OR = 0.93, 95% CI: 0.89 - 0.97), and population density—living in areas with 254-1,140 people per square mile and 1,140-101,227 people per square mile was associated with higher odds of high PDC than living in an area with 1-108 people per square mile (respectively, OR = 1.09, 95% CI: 1.00 - 1.19; OR = 1.18, 95% CI: 1.07 - 1.31). Patient age, CHA2DS2-VASc and HAS-BLED scores, and multiple comorbid conditions were also associated with high PDC at 180 days. See Table S6 for full regression results.

Table S1. Community and Individual-level characteristics.

Variables of Interest	Level	Source
Demographic	Individual	IQVIA
Comorbidity	Individual	IQVIA
CHA_2DS_2-VASc (Congestive heart failure=1 point, Hypertension=1 point, Age ≥75 years=2 points, Diabetes Mellitus=1 point, prior Stroke or TIA or thromboembolism=2 points, Vascular disease (e.g. peripheral artery disease, myocardial infarction, aortic plaque)=1 point, Age 65–74 years=1 point, Sex category (i.e. female sex)=1 point)	Individual	IQVIA-calculation with ICD-10 codes
HAS-BLED (Uncontrolled Hypertension=1 point, Abnormal renal function=1 point and/or Abnormal liver function=1 point, prior Stroke=1 point, prior Major Bleeding or Predisposition to Bleeding=1 point, Labile INR (not included), Elderly: Age > 65 years=1 point, Prior Alcohol or Drug Usage History=1 point, Medication Usage Predisposing to Bleeding: (Antiplatelet agents, NSAIDs)=1 point)	Individual	IQVIA-calculation with ICD-10 codes
Diagnosis Date	Individual	IQVIA
Patient Adherence (Proportion of Days Covered), and Persistence	Individual	IQVIA
Anticoagulant Prescription, Refill, Switching, and Discontinuation dates	Individual	IQVIA
Community Social Risk Scores Economic Climate (A measure of the economic conditions in a community that affect the ability of residents to obtain appropriate healthcare)	ZIP-3	Socially Determined
Community Social Risk Score Food Landscape (A measure of the conditions that affect the ability of the residents in a community to get proper nutrition)	ZIP-3	Socially Determined
Community Social Risk Score Housing Environment (A measure of housing-related standard of living)	ZIP-3	Socially Determined
Community Social Risk Score Transportation Network (A measure of the adequacy of the	ZIP-3	Socially Determined

transportation network to facilitate the populace accessing proper healthcare)		
Community Social Risk Score Health Literacy (A measure of the potential that the community has a high percentage of residents that may struggle to understand and navigate the healthcare system)	ZIP-3	Socially Determined
Population density	ZIP-3	ACS 5-year estimates (2019)
Area racial composition	ZIP-3	ACS 5-year estimate (2019)
Population age	ZIP-3	ACS 5-year estimate (2019)
Population sex	ZIP-3	ACS 5-year estimate (2019)
Marital status	ZIP-3	ACS 5-year estimate (2019)
Area insurance coverage rate	ZIP-3	ACS 5-year estimate (2019)
Area home renting	ZIP-3	ACS 5-year estimate (2019)
Area household size and composition	ZIP-3	ACS 5-year estimate (2019)
Area income characteristics	ZIP-3	ACS 5-year estimate (2019)
Area educational attainment	ZIP-3	ACS 5-year estimate (2019)
Area household utilization of SNAP	ZIP-3	ACS 5-year estimate (2019)
Household vehicle access	ZIP-3	ACS 5-year estimate (2019)
Household food costs	ZIP-3	ACS 5-year estimate (2019)
Monthly housing costs	ZIP-3	ACS 5-year estimate (2019)
Use of public transportation for commuting to work	ZIP-3	ACS 5-year estimate (2019)
Language spoken at home	ZIP-3	ACS 5-year estimate (2019)
Citizenship	ZIP-3	ACS 5-year estimate (2019)
Time in U.S.	ZIP-3	ACS 5-year estimate (2019)
Area saturation of medical providers/hospitals (# medical providers per 10,000)	ZIP-3	ACS 5-year estimate (2019)
Area saturation of pharmacies (# per 10,000).	ZIP-3	ACS 5-year estimate (2019)

Table S2. ICD-10 Codes associated with study medical conditions.

ICD-10 Code	Description	Condition
I480	Paroxysmal atrial fibrillation	Atrial Fibrillation
I481	Persistent atrial fibrillation	Atrial Fibrillation
I482	Chronic atrial fibrillation	Atrial Fibrillation
I4891	Unspecified atrial fibrillation	Atrial Fibrillation

Table S3. Outpatient oral anticoagulant medications.

Drug Name	Brand Name(s)	First 6 digits of GPI code	Route	USC Code
Apixaban	Eliquis	83370010XXXXXX	Oral	11190 - Anticoagulants, Other
Rivaroxaban	Xarelto	83370060XXXXXX	Oral	11190 - Anticoagulants, Other
Dabigatran	Pradaxa	83337030XXXXXX	Oral	11151 – Direct Thrombin Inhibitors
Edoxaban	Savaysa	83370030XXXXXX	Oral	11190 - Anticoagulants, Other
Warfarin	Coumadin, Jantoven	83200030XXXXXX	Oral	11110 – Vitamin K Antagonists

Table S4. Drug cohort Definitions.

Low-molecular-weight heparin) LMWH monotherapy	Patient had LMWH for greater than or equal to 14 days after the index diagnosis date and did not have another anticoagulant during the period between the index diagnosis date and 14 days after LMWH initiation; LMWH outpatient prescription fill date is designated as start date for anticoagulant.
LMWH bridging therapy	Patient has a claim for LMWH within 14 days before or after OAC initiation and LMWH duration of less than or equal to 14 days.
Oral vitamin k antagonist (VKA)	Patient had outpatient oral VKA prescription after index diagnosis date without an outpatient claim for any other anticoagulant (except for LMWH as a bridging therapy); first oral VKA outpatient prescription fill date is designated as OAC prescription index date. (Cohort includes oral VKA patients with and without LMWH bridging therapy.)
DOAC	Patient had outpatient DOAC prescription after index diagnosis date without an outpatient claim for any other anticoagulant (except for LMWH as a bridging therapy); first DOAC outpatient prescription fill date is designated as OAC prescription index date. (Cohort includes DOAC patients with and without LMWH bridging therapy.)

Table S5. Backward Selection Logistic Regression of 90-Day Persistence on Social Risk and Community and Individual Characteristics[*] (N=28,151).

		Odds Ratio	[95% Conf. Interval]		P-value
Social Risk Scores[†] (1=Low risk, 5=Severe risk)					
	Housing environment risk score	1.07	1.01	1.13	0.030
	Health literacy risk score	0.84	0.80	0.89	<0.001
Community Characteristics[‡]					
	Prop. aged 70+, scaled 10x	1.17	1.06	1.30	0.003
	Area medical provider saturation (per 1,000)	0.94	0.90	0.98	0.003
	Population density (ref. = 1-108 ppl/mi^2)				
	108-251 ppl/mi^2	1.03	0.95	1.11	0.477
	254-1,140 ppl/mi^2	1.14	1.05	1.25	0.003
	1,140-101,227 ppl/mi^2	1.20	1.09	1.33	<0.001
Individual Characteristics					
	Age (ref. = 18-54)				
	55-64	1.56	1.47	1.66	<0.001
	65-74	1.56	1.42	1.71	<0.001
	75+	1.57	1.36	1.81	<0.001
	Female	0.97	0.91	1.03	0.305
	Insurance type (ref. = PPO)[§]				
	HMO	0.95	0.88	1.03	0.229
	Point of service	1.10	0.97	1.25	0.131
	Indemnity	0.93	0.76	1.12	0.436
	CHA_2DS_2-VASc (ref. = < 2)	1.58	1.49	1.69	<0.001
	HAS-BLED (ref. = < 2)				
	HAS-BLED = 2	1.11	1.03	1.20	0.005
	HAS-BLED > 2	1.14	1.02	1.29	0.027
	Hemodialysis	0.68	0.50	0.91	0.011
	History of bleeding	0.91	0.83	1.00	0.056
	Liver disease	1.17	1.00	1.37	0.054
	Renal disease	0.87	0.79	0.96	0.005
	Tobacco use/smoking	0.88	0.81	0.95	0.001
	Trauma/surgery	0.81	0.76	0.86	<0.001

	Vitamin K antagonist (ref. = DOAC)	0.74	0.67	0.81	<0.001

Notes:

*Outcome (persist_90) is a binary variable coded (0,1) with '1' indicating medication persistence of at least 90 days.

[†]Risk Scores are continuous variables on a 1-5 scale, where 1 = Little to no risk, 2 = Low risk, 3 = Moderate risk, 4 = High risk, and 5 = Severe risk.

[‡]Community Characteristics are measured at the 3-digit ZIP code (ZIP-3) level. Most Community Characteristics are measured as scaled proportions representing the area prevalence of the named characteristic ('female,' 'married,' etc.) multiplied by ten. Other measures represent median or mean values for the area, as denoted in the table variable label. 824 ZIP-3 areas are represented in the data.

[§]628 patients are missing insurance type information. Point of service plans are based on a managed care model in which patients exchange choice (must see in-network providers) for lower costs. Indemnity refers to a 'fee for service' plan that allows patients to be seen by any provider but with only a set portion of costs covered.

Table S6. Backward Selection Logistic Regression of 360-Day Persistence on Social Risk and Community and Individual Characteristics[*] (N=28,151).

		Odds Ratio	[95% Conf. Interval]		P-value
Social Risk Scores[†] (1=Low risk, 5=Severe risk)					
	Housing risk score	1.07	1.00	1.14	0.045
	Health literacy risk score	0.85	0.80	0.90	<0.001
Community Characteristics[‡]					
	Prop. aged 70+ (scaled 10x)	1.26	1.13	1.41	<0.001
	Area medical provider saturation (per 1,000)	0.95	0.90	1.00	0.031
	Population density (ref. = 1-108 ppl/mi^2)				
	108-251 ppl/mi^2	1.06	0.98	1.15	0.139
	254-1,140 ppl/mi^2	1.07	0.98	1.18	0.139
	1,140-101,227 ppl/mi^2	1.16	1.04	1.29	0.008
Individual Characteristics					
	Age (ref. = 18-54)				
	55-64	1.62	1.51	1.73	<0.001
	65-74	1.63	1.48	1.78	<0.001
	75+	1.92	1.68	2.19	<0.001
	Female	1.00	0.94	1.06	0.964
	Region (ref. = Northeast)				
	Midwest	1.07	0.98	1.17	0.126
	South	0.93	0.85	1.02	0.143
	West	1.07	0.96	1.19	0.225
	Insurance type (ref. = PPO)[§]				
	HMO	1.08	0.99	1.17	0.078
	Point of service	0.95	0.84	1.07	0.404
	Indemnity	1.03	0.85	1.24	0.792
	CHA_2DS_2-VASc (ref. = < 2)	1.57	1.47	1.68	<0.001
	HAS-BLED (ref. = < 2)				
	HAS-BLED = 2	1.14	1.06	1.23	<0.001
	HAS-BLED > 2	1.18	1.06	1.32	0.002
	Hemodialysis	0.57	0.38	0.84	0.004
	History of bleeding	0.83	0.75	0.92	<0.001

	Myocardial infarction	0.86	0.78	0.95	0.004
	Renal disease	0.79	0.72	0.87	<0.001
	Tobacco use/smoking	0.83	0.77	0.90	<0.001
	Trauma/surgery	0.85	0.80	0.90	<0.001
	Vitamin K antagonist (ref. = DOAC)	0.65	0.59	0.73	<0.001

Notes:

*Outcome (persist_360) is a binary variable coded (0,1) with '1' indicating medication persistence of at least 360 days.

†Risk Scores are continuous variables on a 1-5 scale, where 1 = Little to no risk, 2 = Low risk, 3 = Moderate risk, 4 = High risk, and 5 = Severe risk.

‡Community Characteristics are measured at the 3-digit ZIP code (ZIP-3) level. Proportional community-level measures are scaled by a factor of 10. For example, a one-unit increase in 'Prop. Hispanic' is equivalent to a 10% increase in the prevalence of Hispanic residents in the ZIP-3 area. Other measures represent median or mean values for the area, as denoted in the table variable label. 824 ZIP-3 areas are represented in the data.

§628 patients are missing insurance type information. Point of service plans are based on a managed care model in which patients exchange choice (must see in-network providers) for lower costs. Indemnity refers to a 'fee for service' plan that allows patients to be seen by any provider but with only a set portion of costs covered.

Table S7. Backward Selection Logistic Regression of 180-Day Proportion Days Covered > 0.8 on Social Risk and Community and Individual Characteristics[*] (N=28,151).

		Odds Ratio	[95% Conf. Interval]		P-value
Social Risk Scores[†] (1=Low risk, 5=Severe risk)					
	Housing risk score	1.09	1.03	1.15	0.005
	Health literacy risk score	0.81	0.77	0.86	<0.001
Community Characteristics[‡]					
	Prop. aged 70+ (scaled 10x)	1.29	1.16	1.43	<0.001
	Area medical provider saturation (per 1,000)	0.93	0.89	0.97	0.001
	Population density (ref. = 1-108 ppl/mi^2)				
	108-251 ppl/mi^2	1.05	0.97	1.12	0.230
	254-1,140 ppl/mi^2	1.09	1.00	1.19	0.046
	1,140-101,227 ppl/mi^2	1.18	1.07	1.31	0.001
Individual Characteristics					
	Age (ref. = 18-54)				
	55-64	1.67	1.58	1.77	<0.001
	65-74	1.73	1.58	1.88	<0.001
	75+	1.82	1.59	2.08	<0.001
	Female	1.00	0.94	1.06	0.938
	Region (ref. = Northeast)				
	Midwest	1.06	0.98	1.15	0.155
	South	1.01	0.93	1.11	0.782
	West	1.04	0.94	1.15	0.440
	Insurance type (ref. = PPO)[§]				
	HMO	0.97	0.90	1.05	0.457
	Point of service	1.12	1.00	1.26	0.057
	Indemnity	1.03	0.86	1.24	0.747
	CHA_2DS_2-VASc (ref. = < 2)	1.70	1.60	1.81	<0.001
	HAS-BLED (ref. = < 2)				
	HAS-BLED = 2	1.09	1.02	1.17	0.015
	HAS-BLED > 2	1.12	1.01	1.25	0.031
	Hemodialysis	0.68	0.51	0.92	0.013
	History of bleeding	0.85	0.78	0.93	0.001
	Myocardial infarction	0.89	0.82	0.98	0.016
	Renal disease	0.88	0.80	0.96	0.004
	Tobacco use/smoking	0.89	0.83	0.96	0.003
	Trauma/surgery	0.84	0.79	0.89	<0.001

	Vitamin K antagonist (ref. = DOAC)	0.67	0.61	0.74	<0.001
	Outpatient visits year prior (ref. = 0-3)				
	4-7 visits	1.03	0.97	1.10	0.354
	8-13 visits	1.00	0.93	1.07	0.930
	14-365 visits	1.06	0.99	1.14	0.120

Notes:

*Outcome (high_pdc180) is a binary variable coded (0,1), with '1' indicating medication adherence of > 0.8 at 180 days.

†Risk Scores are continuous variables on a 1-5 scale, where 1 = Little to no risk, 2 = Low risk, 3 = Moderate risk, 4 = High risk, and 5 = Severe risk.

‡Community Characteristics are measured at the 3-digit ZIP code (ZIP-3) level. Proportional community-level measures are scaled by a factor of 10. For example, a one-unit increase in 'Prop. Hispanic' is equivalent to a 10% increase in the prevalence of Hispanic residents in the ZIP-3 area. Other measures represent median or mean values for the area, as denoted in the table variable label. 824 ZIP-3 areas are represented in the data.

§628 patients are missing insurance type information. Point of service plans are based on a managed care model in which patients exchange choice (must see in-network providers) for lower costs. Indemnity refers to a 'fee for service' plan that allows patients to be seen by any provider but with only a set portion of costs covered.

Figure S1. Risk Score Construction Methodology.

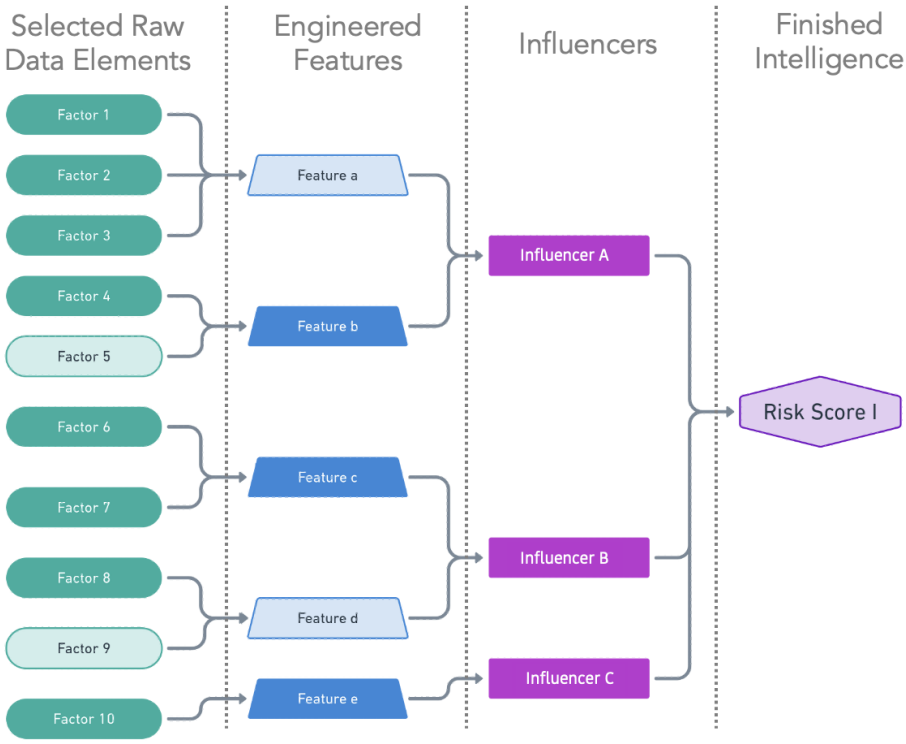
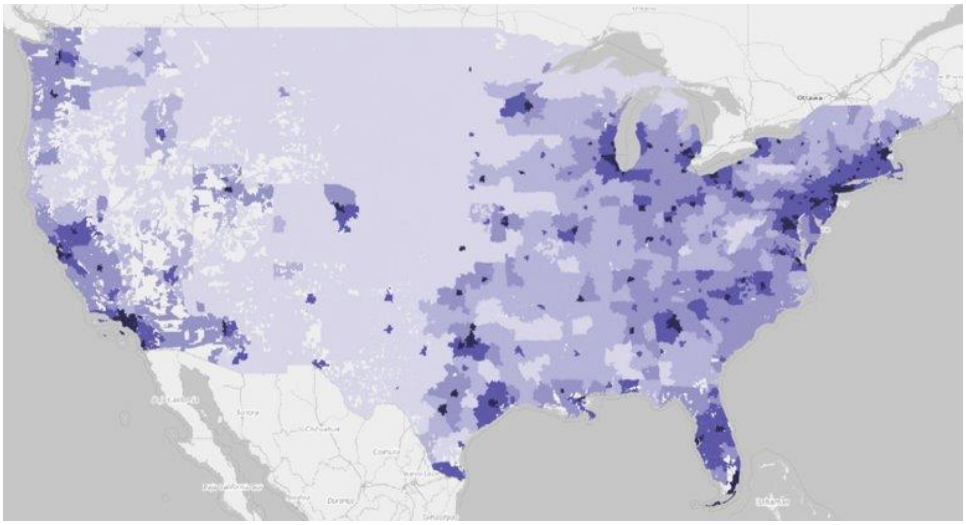
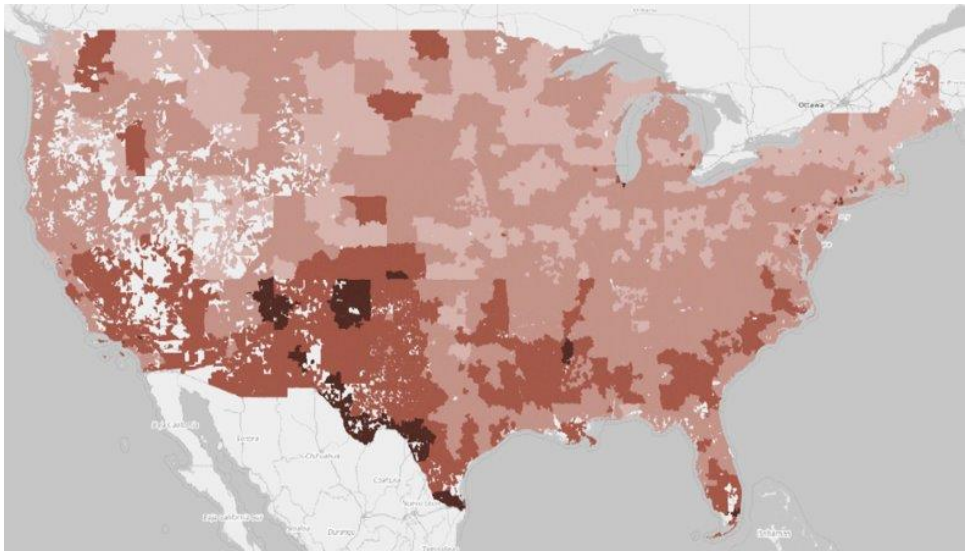


Figure S2. Population Density Map (ZIP-3 Level).



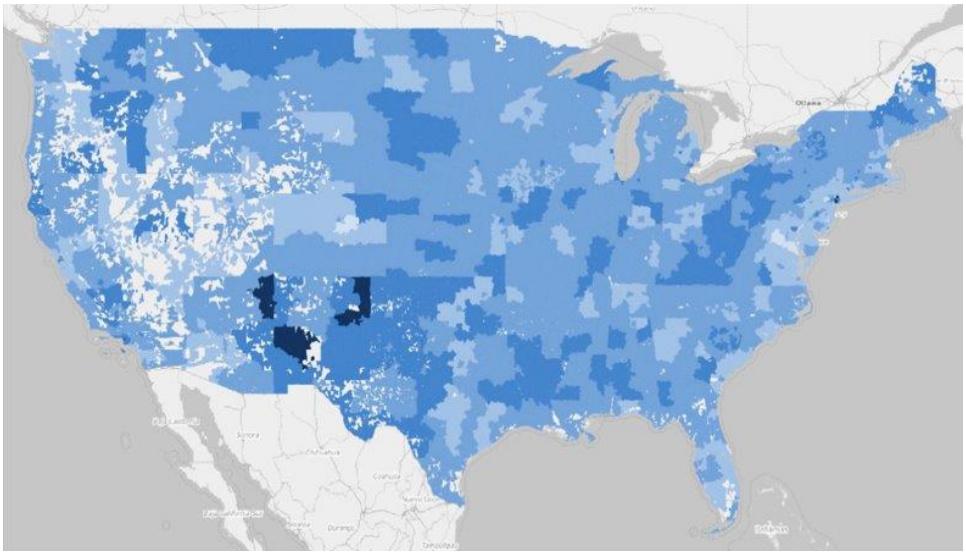
Darker areas indicate greater population density.

Figure S3. Community Health Literacy Risk Distribution (ZIP-3 Level).



Darker areas indicate higher health literacy risk.

Figure S4. Community Housing Landscape Risk Distribution (ZIP-3 Level).



Darker areas indicate higher housing landscape risk.

Figure S5. Bivariate Associations Between Community- and Individual-Level Characteristics and Medication Persistence at 180 Days.

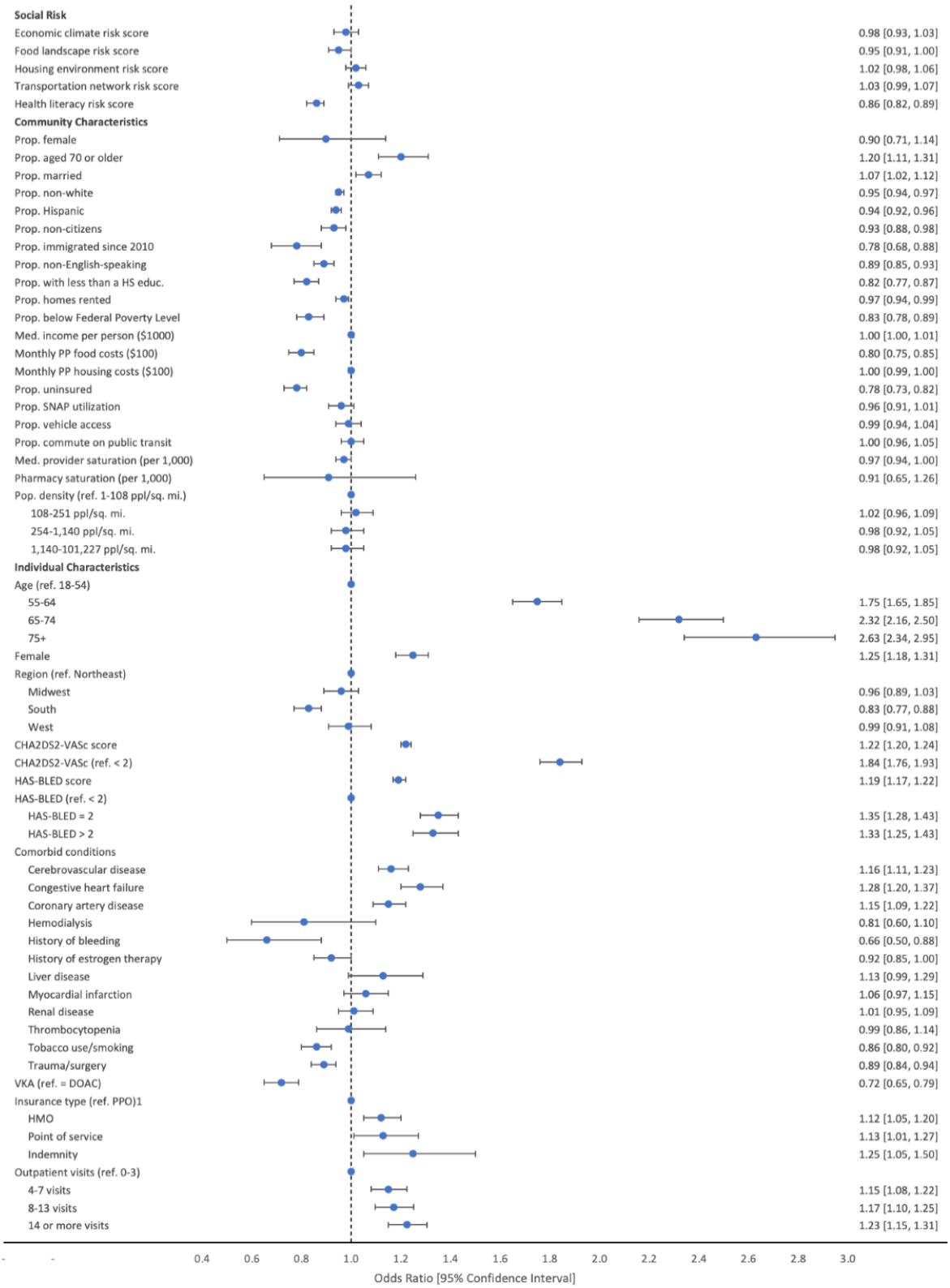


Figure S6. Bivariate Associations between Community- and Individual-Level Characteristics and Proportion Days Covered (PDC) >= 0.8 at 360 Days.

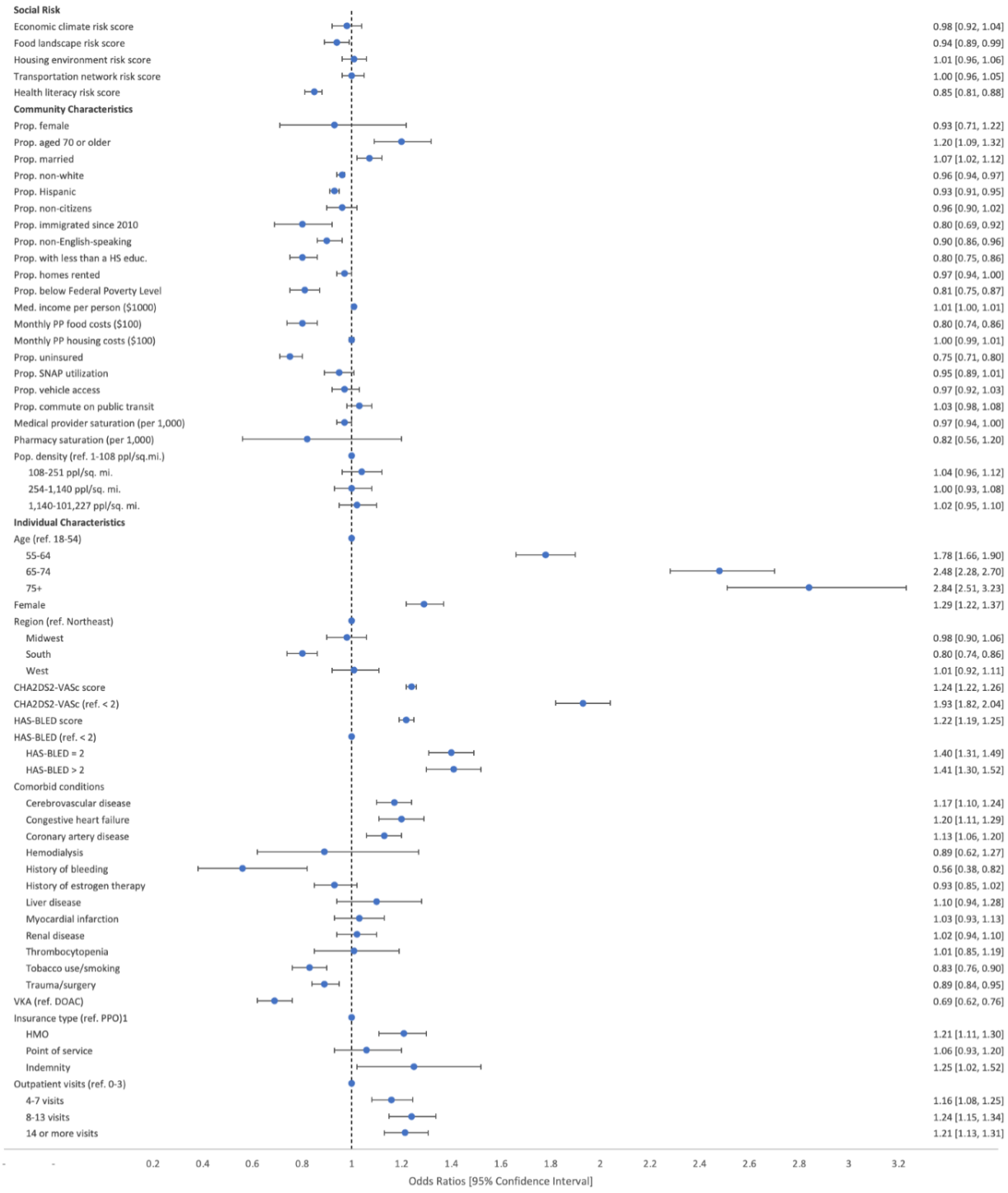
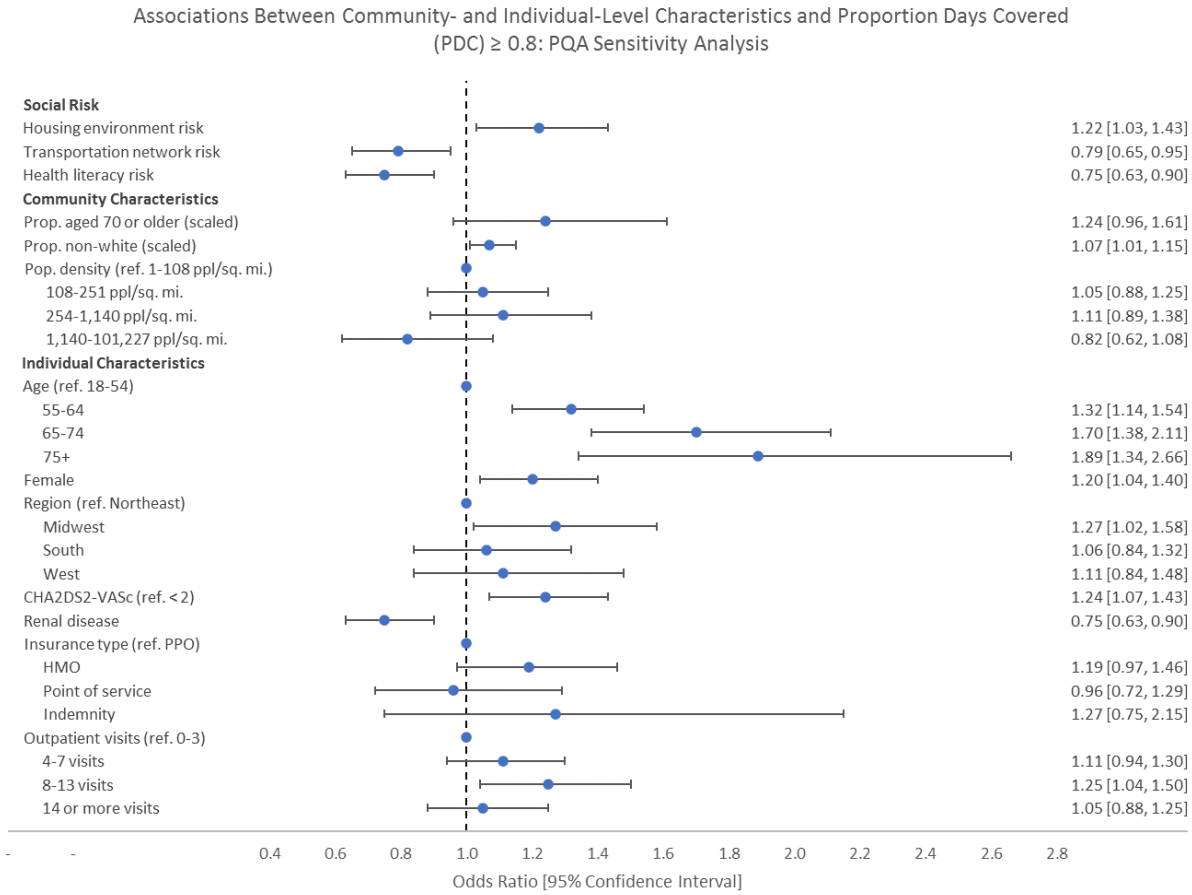


Figure S7. Associations Between Community- and Individual-Level Characteristics and Proportion Days



Covered (PDC) >= 0.8: PQA Sensitivity Analysis