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Area Deprivation Index and Oral Anticoagulation in New Onset Atrial Fibrillation

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ABSTRACT

Objective: Oral anticoagulation is a standard of care for thromboembolic stroke prevention in individuals with atrial fibrillation (AF). Social determinants of health have had limited investigation in AF and particularly in access to anticoagulation. We examined the relation between area deprivation index (ADI) and anticoagulation in individuals at risk of stroke due to AF.
Methods: We conducted a retrospective analysis of patients with incident, non-valvular AF from 2015-2020 receiving care at a large, regional health center. We extracted demographics, medications, and problem lists and used administrative coding to identify comorbid conditions and relevant covariates, and individual-level residential address to ascertain ADI. We examined the relation between ADI and receipt of prescribed oral anticoagulation (warfarin or direct-acting oral anticoagulant, or DOAC) at 90 days following AF diagnosis in multivariable-adjusted models.
Results: Following exclusions, the dataset included 20,210 individuals (age 74.5±10.9 years; 51% women; 94% white race). In multivariable-adjusted analyses, individuals in the highest quartile of ADI had a 16% lower likelihood of receiving anticoagulation prescription than those in the lowest ADI quartile (Odds Ratio [OR] 0.84; 95% Confidence Interval [CI], 0.75-0.95) at 90 days following AF diagnosis. In those receiving anticoagulation, individuals in the highest ADI quartile had a 24% lower likelihood of receiving a DOAC prescription as opposed to warfarin prescription than those in the lowest quartile (OR 0.76; 95% CI, 0.60-0.96) at 90 days following AF diagnosis.
Conclusions: We demonstrate the association of higher neighborhood deprivation as determined by ADI with decreased likelihood of (1) anticoagulation prescribing for stroke prevention in AF and (2) prescription of a DOAC when any oral anticoagulation is prescribed. Our results suggest neighborhood-based health inequities in the receipt of anticoagulation prescription for stroke prevention in AF in a large, regional health care system.

1. Introduction

Atrial fibrillation (AF) is an irregular heart rhythm associated with increased risk of thromboembolic stroke and multiple other cardiac and non-cardiac complications [1]. Oral anticoagulants such as warfarin and the more contemporary direct-acting oral anticoagulants (DOAC) are standard of care for stroke prevention in AF [2,3]. Social resources as represented by factors including income, education, and employment influence health outcomes. Specifically, data indicate an association between social deprivation and poorer health outcomes [4]. Additional data indicate that individuals with AF who have higher social deprivation have poorer health outcomes compared to those with lower social

Abbreviations: AF, Atrial Fibrillation; DOAC, Direct-acting oral anticoagulant; ADI, Area Deprivation Index.

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deprivation [5].

Neighborhood social characteristics and assets are a primary contributor to health care outcomes and cardiovascular risk [6,7]. Despite this, there has been limited investigation into how neighborhood social characteristics such as median family income, education level, and housing quality influence the implementation of anticoagulation. Area Deprivation Index (ADI) is a composite index that ranks neighborhoods based on social disadvantage [8,9]. Higher ADI indicates greater disadvantage, and factors that contribute to ADI include income, housing quality, education, and employment [9]. Therefore, ADI may provide insight into how neighborhood social characteristics relate to guideline-based metrics or standards of care.

We examined the relation of ADI to anticoagulation prescription in individuals with AF in a large, regional health care system. Our primary hypothesis was that individuals with AF living in neighborhoods with higher ADI (or greater disadvantage) would be less likely to receive oral anticoagulation prescription for stroke prevention compared to those residing in neighborhoods with lower ADI. Our secondary hypothesis was that among individuals prescribed oral anticoagulation, those who lived in neighborhoods with higher ADI would be more likely to receive warfarin rather than a more contemporary DOAC (i.e., apixaban, rivaroxaban, edoxaban, and dabigatran) than individuals living in neighborhoods with lower ADI.

2. Methods

The present study is a retrospective analysis conducted in a large, nonprofit, academic health care system delivering care throughout the central and western Pennsylvania region, the University of Pittsburgh Medical Center (UPMC). In 2020 UPMC had an annual operative revenue of $23 billion, a network of 40 hospitals, and approximately 5.5 million outpatient visits, and shares a common electronic health record which captures all individual contact with the health care system [10]. Individual-level records were used for extraction of relevant variables using the International Classification of Diseases (ICD) Ninth and Tenth Revision as well as Current Procedural Terminology. All ICD codes used in the analysis are summarized in **Supplementary Table 1**.

To conduct this analysis, we selected individuals who received an incident diagnosis of AF from January 1, 2015, through December 31, 2020. To verify the diagnosis as the incident or first occurrence of AF, we then selected those individuals who had contact with the health care system at least once during the 12 months prior to the first record of AF to verify absence of a prior diagnosis of the arrhythmia. We further selected those individuals with a minimum of 6 months of documented follow-up following diagnosis. We then identified and selected those individuals who would be designated as candidates for oral anticoagulation as determined by summation of stroke risk factors (i.e. the CHA_2DS_2-VASc [congestive heart failure, hypertension, age, diabetes, stroke/transient ischemic attack, vascular disease [history of myocardial infarction, peripheral vascular disease, or aortic atherosclerotic disease], and sex category] score $\geq$2) [11]. We excluded individuals with diagnoses of AF within 30 days of a cardiothoracic surgery, to avoid including post-operative AF; absence of a residential mailing address (such as P.O box or unknown address), which would thereby preclude determination of ADI; residence in an institutional setting (e.g., chronic care facility); and those prescribed oral anticoagulation within the 12 months prior to the recording of a diagnosis of AF, in order to diminish the possibility of such individuals being diagnosed with AF outside of our health care system.

To ascertain ADI, we used residential addresses as available in the electronic health record at the time of AF diagnosis. ADI is based on 17 social and economic variables obtained during the US census and is a well-defined and validated measure for neighborhood disadvantage which encompasses measures of employment, housing, education, and poverty [8,9]. Scores range from 1 to 100, with progressively increased scores indicating greater social deprivation. In this study, ADI was matched to patient addresses through the ZIP+4 Code via the US Postal Service Application Programming Interface.

The primary outcome for this analysis was receipt of oral anticoagulation prescription, either warfarin or DOAC, 90 days following diagnosis of AF, as determined by review of medication lists within the longitudinal electronic health record. Anticoagulant selection was distinguished as warfarin or DOAC. Our secondary outcome was determining the relation of ADI by quartile to the likelihood of receipt of warfarin or DOAC prescription in those individuals receiving any type of anticoagulation prescription. Age, sex, race (i.e., White, Black, and Other), and ethnicity (i.e., Hispanic/Latino) were derived from the electronic health record. Races defined as “other” included Asian, American Indian, Guam, and not specified. The clinical covariates for the CHA_2DS_2-VASc and diagnoses pertinent to the Elixhauser comorbidity index were also derived from the electronic health record [12,13]. This analysis was approved by the University of Pittsburgh Institutional Review Board with determination that the retrospective analysis of electronic health record data did not necessitate informed consent.

3. Statistical Analysis

We described continuous variables by their means and standard deviations and determined the distributions of categorial variables. We categorized ADI as quartiles based upon its distribution. Our primary analysis was the relation of ADI to receipt of oral anticoagulation within 90 days following diagnosis of AF, while the secondary analysis was the relation of ADI to receipt of a DOAC instead of warfarin. The relation between ADI and the primary and secondary outcomes was examined in logistic regression analyses in sequential multivariable-adjusted models with the lowest quartile (i.e., least deprivation) serving as the referent. Model 1 adjusted for age, sex, race and ethnicity. Model 2 included variables from model 1 as well as congestive heart failure, hypertension, diabetes, vascular disease, and stroke, and transient ischemic attack. Model 3 adjusted for all the variables included in model 2 as well as the diagnoses pertinent to the Elixhauser comorbidity index listed in **Supplementary Table 1**. We then completed sensitivity analysis to determine if individuals seen by a cardiologist during a 90 day follow up were more likely to receive oral anticoagulation prescription. We also examined the interaction between race and ADI. We used the Hosmer and Lemeshow test to assess the goodness of fit or our logistic regression models and correlation ecoefficiency and variance inflation to assess for multicollinearity. Analyses were completed using SAS version 9.4 (SAS Institute, Cary, NC), and an alpha value of .05 was used to determine statistical significance.

4. Results

The final dataset consisted of 20,210 individuals (age 74.5±10.9 years, 50.8% women, 94.3% white race) following exclusions, as shown by Fig. 1. Table 1 presents the baseline characteristics according to ADI, indicating that 76.4% of individuals had hypertension, 32.9% a history of coronary artery disease, and 64.0% hyperlipidemia. The median ADI was 60 (IQR 45, 75). Approximately 62.6% (12,647) of individuals received a prescription for anticoagulation by 90 days following AF diagnosis, while 37.4% (7,563) did not. Further, among the individuals who received any type of anticoagulation prescription after 90 days, 87.9% (11,066) received a DOAC, while 12.1% (1,521) received warfarin. There were no significant interactions between race and ADI. Further, follow up with a cardiologist during a 90 day follow up did not impact likelihood of receiving anticoagulation. Regarding multicollinearity, all variation inflation factors were less than 5, and none of the correlation ecoefficiency values were 0.5. For the goodness of fit, all values were greater than 0.05.

Table 2 presents the proportion of individuals within each ADI quartile receiving anticoagulation, as well as either warfarin or a DOAC. In the highest ADI quartile 61.5%; (95% CI, 60.1-62.8) of individuals

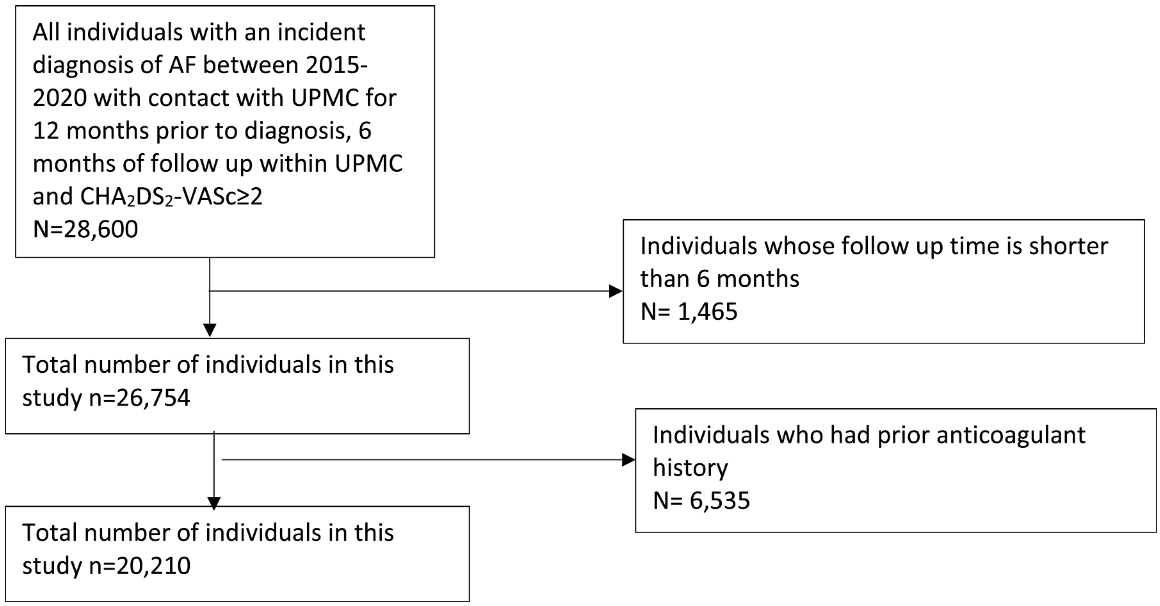

Fig. 1. Fig. 1 shows the total amount of individuals initially extracted from the dataset as well as the final number of individuals used in the analysis after all inclusion and exclusion criteria were applied. The CHA2DS2-VASc (Congestive Heart failure, Hypertension, Age, Diabetes, Previous Stroke/transient ischemic attack, Vascular disease, sex) Atrial Fibrillation (AF) University of Pittsburgh Medical Center (UPMC).

Table 1
Baseline Characteristics of Individuals by Area Deprivation Index Quartile

	TotalN=20210	Area Deprivation Index Quartile 1-25N=1605	Area Deprivation Index Quartile26-50N=5067	Area Deprivation Index Quartile 51-75N=8608	Area Deprivation Index Quartile 76-100N= 4930
Age, year	74.5 ± 10.9	75.3 ± 10.2	75.2 ± 10.4	74.7 ± 10.9	73.2 ± 11.7
Female	10270 (50.8%)	771 (48%)	2462 (48.6%)	4303 (50%)	2734 (55.5%)
Race					
White	19053 (94.3%)	1533 (95.5%)	4917 (97%)	8292 (96.3%)	4311 (87.4%)
Black	774 (3.8%)	18 (1.1%)	47 (0.9%)	165 (1.9%)	544 (11%)
Other	383 (1.9%)	54 (3.4%)	103 (2%)	151 (1.8%)	75 (1.5%)
Ethnicity					
Hispanic/Latino	73 (0.4%)	5 (0.3%)	17 (0.3%)	22 (0.3%)	29 (0.6%)
Not Hispanic/Latino	19269 (95.3%)	1529 (95.3%)	4819 (95.1%)	8230 (95.6%)	4691 (95.2%)
Other	868 (4.4%)	71 (4.4%)	231 (4.6%)	356 (4.1%)	210 (4.3%)
Body Mass Index	30.2 ± 7.3	28.5 ± 5.9	29.9 ± 6.7	30.3 ± 7.3	30.9 ± 8
Congestive Heart Failure	4447 (22%)	266 (16.6%)	972 (19.2%)	1875 (21.8%)	1334 (27.1%)
Hypertension History	15437 (76.4%)	1156 (72%)	3820 (75.4%)	6583 (76.5%)	3878 (78.7%)
Coronary Artery Disease History	6638 (32.9%)	434 (27%)	1553 (30.7%)	2929 (34%)	1722 (34.9%)
Stroke/Transient Ischemic Attack	2820 (14%)	222 (13.8%)	685 (13.5%)	1208 (14%)	705 (14.3%)
Hyperlipidemia History	12926 (64%)	1065 (66.4%)	3297 (65%)	5490 (63.8%)	3074 (62.4%)
Peripheral Vascular Disease History	1598 (7.9%)	106 (6.6%)	364 (7.2%)	658 (7.6%)	470 (9.5%)
Diabetes History	5745 (28.4%)	340 (21.2%)	1326 (26.2%)	2459 (28.6%)	1620 (32.9%)
Vascular disease history	1920 (9.5%)	115 (7.2%)	437 (8.6%)	841 (9.8%)	527 (10.7%)
Ischemic heart disease history	1791 (8.9%)	108 (6.7%)	386 (7.6%)	791 (9.2%)	506 (10.3%)

Mean ± Standard deviation for continuous variables, and N (%) for categorical variable

received any sort of anticoagulation, 12.7%; (95% CI, 11.5-13.9) received warfarin, and 87.3%; (95% CI, 86.1-88.5) received a DOAC. Conversely within the lowest ADI quartile, 65.3%; (95% CI, 63.0-67.6) of individuals received any sort of anticoagulation, 10.4%; (95% CI, 8.6-12.3) received warfarin, and 89.6%; (95% CI, 87.7-91.4) received a DOAC.

Table 3A presents the association between ADI and anticoagulation and Table 3B the association between receiving a DOAC (as opposed to warfarin) and ADI at 90 days after diagnosis of AF in multivariable-adjusted models. In the fully adjusted model (Model 3), individuals in the highest ADI quartile were 16% less likely (OR 0.84; 95% CI, 0.75-0.95) to receive anticoagulation than those in the lowest ADI quartile. Further, in the fully adjusted model, at 90 days after AF diagnosis, individuals in the highest ADI were 24% less likely (OR 0.76; 95% CI, 0.60-0.96) to receive a DOAC rather than warfarin compared to those in the lowest ADI quartile. The association between ADI and any anticoagulation or DOAC prescription is also visually represented in Fig. 2.

5. Discussion

We examined the association of ADI with anticoagulation in individuals with newly diagnosed AF receiving care in a large, regional health care system. We determined that those individuals residing in the highest quartile of area deprivation (i.e., having greater social

Table 2
Proportion of individuals prescribed oral Anticoagulation by Area Deprivation Index at 90 days following a diagnosis of atrial fibrillation.

Area Deprivation Index Quartile	Any anticoagulation (95% CI)	Warfarin (95% CI)	Direct oral anticoagulation(95% CI)
1-25 (N=1605)	65.3% (63.0 – 67.6)	10.4% (8.6 – 12.3)	89.6% (87.7 – 91.4)
26-50 (N=5067)	63.0% (61.7 – 64.3)	11.0% (9.9 – 12.0)	89.0% (88.0 – 90.1)
51-75 (N=8608)	62.5% (61.4 – 63.5)	12.7% (11.9 – 13.6)	87.3% (84.4 – 88.1)
76-100 (N=4930)	61.5% (60.1 – 62.8)	12.7% (11.5 – 13.9)	87.3% (86.1 – 88.5)

disadvantage) had a 16% decreased likelihood of receiving oral anticoagulation for stroke prevention compared to those in the lowest quartile. Additionally, in those who were prescribed anticoagulation, those residing in the highest ADI quartile had a 24% decreased likelihood of receiving a DOAC rather than warfarin compared to those residing in the lowest, or least disadvantaged, ADI quartile. Our results were not attenuated with adjustment for the variables included in the CHA_2DS_2-VASc and the broad range of comorbid conditions included in our multivariable-adjusted analyses.

Our findings are consistent with those from other studies identifying association between higher ADI and poorer patient outcomes [14–16]. The results reported here are also concordant with other data that indicate an association between social resources and patient outcomes [4,17]. Individuals living in neighborhoods with higher ADI may experience adverse environmental exposures and have increased risk factors for clinical adversity [18]. More specific to the mechanism of the association between ADI and anticoagulation prescription, our findings are consistent with prior data demonstrating associations between social disadvantage and access to care. Data suggest that housing instability and food insecurity are associated with not having access to a usual source of care and postponing essential medications and medical care [19,20]. The association that housing and food insecurity have with lower access to care is also present among individuals who have chronic diseases such as chronic lung and cardiovascular disease [21]. Data also suggest that living in a disadvantaged neighborhood is associated with being less likely to receive regular care from a health provider and less likely to receive guideline-based preventive screening for cholesterol and blood pressure [22]. Our findings extend and confirm prior studies identifying associations between social factors and treatment for AF including oral anticoagulation [23–27].

As stated, anticoagulation therapy is a foundation of AF treatment [2,3]. Over the last decade the use of DOACs has increased tremendously, and as of 2017 approximately 75% of anticoagulation therapy prescriptions are DOACs compared to about 20% of prescriptions being warfarin [28]. The rise in DOAC use is likely due to the improved safety profile and lower side effects associated with DOACs compared to warfarin [2]. As the paradigm for stroke prevention in patients with AF shifts, increasing the accessibility of anticoagulation therapy and especially to DOACs for all patients is essential to promoting pharmacoequity [29]. Given the impact of neighborhood factors on health outcomes, including social factors such as ADI in health services analyses can elucidate how neighborhood factors contribute to patient outcomes and access to care. Our study adds to the literature regarding how social disadvantage relates to patient outcomes and care access by showing an association between ADI and the likelihood of receiving anticoagulant prescription, and the association between ADI and the type of anticoagulant prescription that individuals with AF receive.

The mechanisms of our findings are likely to due to system- and provider-level causes. In regard to system-level causes, access to care and cost are major factors. The previously cited Danish study found an association between lower income, education, living alone, and

Table 3A
Association between Area Deprivation Index and Anticoagulation

	Model 1			Model 2			Model 3		
	Odds Ratio	Confidence interval	P value	Odds Ratio	Confidence interval	P value	Odds Ratio	Confidence interval	P value
Area Deprivation Index 1-25	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Area Deprivation Index 26-50	0.91	0.81-1.02	0.09	0.90	0.80 – 1.02	0.09	0.87	0.77-0.98	0.02
Area Deprivation Index 51-75	0.89	0.79-0.99	0.04	0.89	0.79 – 0.99	0.04	0.85	0.76-0.95	<0.01
Area Deprivation Index 76-100	0.87	0.77-0.98	0.02	0.87	0.77 – 0.98	0.02	0.84	0.75-0.95	<0.01

Table 3B
Association between Area Deprivation Index and Direct Oral Anticoagulant versus Warfarin

	Model 1			Model 2			Model 3		
	Odds Ratio	Confidence interval	P value	Odds Ratio	Confidence interval	P value	Odds Ratio	Confidence interval	P value
Area Deprivation Index 1-25	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Area Deprivation Index 26-50	0.94	0.75-1.17	0.6	0.94	0.75-1.18	0.6	0.90	0.71-1.13	0.35
Area Deprivation Index 51-75	0.78	0.63-0.97	0.02	0.79	0.64-0.98	0.03	0.78	0.63-0.97	0.03
Area Deprivation Index 76-100	0.77	0.61-0.96	0.02	0.77	0.63-0.99	0.04	0.76	0.60-0.96	0.02

The lowest ADI quartile (1-25) is the referent
Model 1 adjusted for age, race, and sex
Model 2 adjusted for variables in model 1 plus congestive heart failure, hypertension, diabetes, Stroke/Transient Ischemic Attack/thromboembolism history, vascular disease
Model 3 adjusted for variables in Model 2 plus diagnoses relevant to Elixhauser Comorbidity Index.

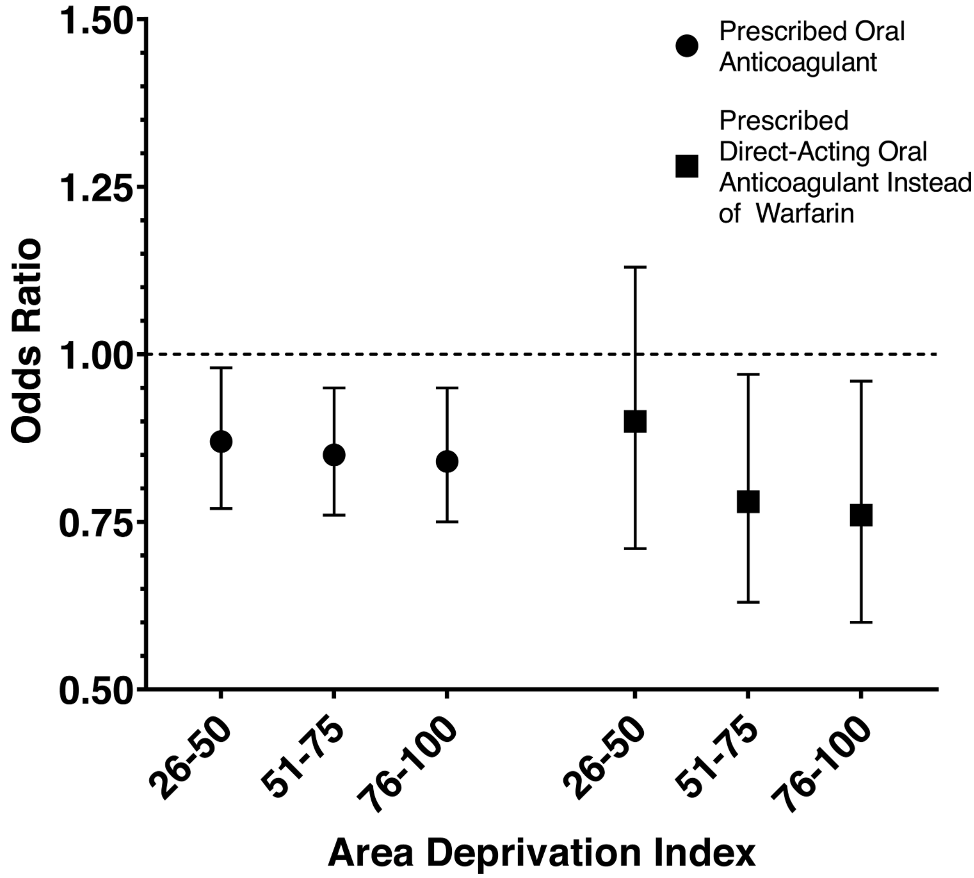

Fig. 2. Fig. 2 graphically presents the likelihood of (1) receipt of oral anticoagulation and (2) likelihood of receipt of Direct-Acting Oral Anticoagulant compared to Warfarin by quartile of Area Deprivation Index (ADI, where lowest ADI, or least deprived, serves as the referent).

decreased prescription of a DOAC for AF patients with a stroke [27]. Our results, showing that higher ADI (or greater disadvantage) is associated with decreased likelihood of receiving a DOAC compared to warfarin, consistently demonstrate that lower social resources and social support are associated with less likelihood of receiving a DOAC. Further, data indicate that among AF patients starting DOACs, higher insurance copayments are associated with lower adherence and greater likelihood of cessation [30]. The increased cost of DOACs may make copays financially challenging to individuals with higher ADI, who are expected to have lower economic resources.

With regard to provider-level causes, implicit bias may be another major factor which contributes to the findings described here. Provider bias was not measured in our study due to the retrospective study design and derivation of results from an electronic health record. However, considering provider bias is relevant given that implicit biases are associated with lower quality care [31]. Data also suggest that the race and socioeconomic status of patients impact physician perceptions [32]. Thus, the presence of implicit bias among providers may also explain why individuals living in neighborhoods with greater deprivation were less likely to receive oral anticoagulation, and when they did, less likely to receive a DOAC. We consider that the contribution of provider bias merits examination to elucidate our findings.

Our study has multiple strengths. First, the size of our cohort was reasonably large, increasing the statistical power of our results, and the use of a longitudinal electronic health record data allowed us to have complete capture of covariates for robust multivariable adjustment. ADI is a validated measure of neighborhood assets and its use here facilitated our examination of the association of a comprehensive measure of neighborhood disadvantage with anticoagulation. Our analysis further adjusted for multiple concomitant conditions as captured by the Elixhauser Comorbidity Index.

This study has multiple limitations. First, due to our use of administrative coding, we expect some degree of misclassification with regard to diagnosis of AF and other clinical diagnoses. However, we expect that misclassification was non-differential and would therefore bias our results towards the null, and the size of our cohort helped to mitigate the effects of administrative coding. Second, while ADI is a cumulative measure of deprivation, ADI may not reflect individual wealth. We were not able to include individual-level social factors in our analysis such as personal financial assets, educational attainment, and social support. Further while ADI is a composite measure, ADI does not encompass all the social determinants of health that play a role in our findings. Third, it is possible, albeit unlikely, that individuals in this dataset would have access to oral anticoagulation outside of the health care system in which the analysis was conducted. Fourth, our analysis was limited to patients cared for by a single, large health care system in Pennsylvania. However, we did not examine provider-level differences (e.g., rural versus metropolitan, years in practice, or proximity to disadvantaged neighborhoods) which may mediate the results observed here. We consider that such an analysis would be essential to identify the provider-level characteristics which inform ADI and provision of anticoagulation. We further note as an additional limitation that the vast majority of individuals in the study are of White race, thereby limiting the generalizability of our results may likewise be limited. Sixth, our data describe prescription of oral anticoagulation as reflected in the electronic health record, and do not provide evidence of initiation or longitudinal adherence. Additional research is essential to clarify how ADI relates to anticoagulation adherence. Finally, we cannot exclude residual confounding due to unmeasured factors which may contribute to the association between ADI and receipt of anticoagulation for stroke prevention in AF.

In conclusion, our analyses conducted in a large, regional health care system identified an association between ADI and likelihood of both receiving oral anticoagulation for stroke prevention in AF as well as the type of anticoagulant received. Our study identified that neighborhood-level social risk may influence access to AF care, and our results suggest the importance of considering ADI in studies examining delivery of anticoagulation. Further, our results demonstrate continued opportunities to promote health equity in disadvantaged populations with greater neighborhood social deprivation.

CRediT authorship contribution statement

Toluwa D. Omole: Writing – review & editing. **Jianuhi Zhu:** Software, Formal analysis, Investigation, Resources, Data curation, Writing – review & editing. **William Garrard:** Data curation, Writing – review & editing. **Floyd W. Thoma:** Data curation, Writing – review & editing. **Suresh Mulukutla:** Writing – review & editing. **Annie McDermott:** Writing – review & editing. **Brandon M. Herbert:** Visualization. **Utibe R. Essien:** Writing – review & editing. **Jared W. Magnani:** Conceptualization, Methodology, Investigation, Resources, Writing – original draft, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpc.2022.100346.

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