Ischemic stroke is one of the most devastating consequences of atrial fibrillation (AF). Oral anticoagulation for stroke risk reduction in those at moderate to high risk is a cornerstone of AF management. Direct oral anticoagulants (DOACs) were first approved in the US in 2010 and have since supplanted warfarin as the first-line oral anticoagulant for AF in most cases.1 A major advantage of DOAC therapy, beyond its improved effectiveness and safety over warfarin, is the ease of dosing without the need for laboratory monitoring as well as fewer drug and food interactions. However, among the initial barriers to effective uptake of DOACs were the higher costs of these newer drugs. Furthermore, racial and ethnic differences in the initiation of DOAC therapy have been previously described.2-5

In this issue of JAMA Network Open, Reynolds et al6 sought to extend this literature, examining racial and ethnic differences in the initiation of DOACs vs warfarin among Medicare beneficiaries with AF and no evidence of valvular heart disease. The authors identified 950,698 episodes of oral anticoagulant initiation in this cohort from 2010 to 2019. After adjustment for individual demographic and clinical covariates, as well as county-level social vulnerability, they found that Black and Hispanic individuals were less likely than White individuals to initiate DOACs for most of the study period. These differences were most significant in earlier years and narrowed over time, as DOAC use increased across all racial and ethnic groups. The authors also found that these differences took longer to diminish among individuals living in areas with the highest social vulnerability.

The presence of racial and ethnic differences in thromboembolic risk reduction for individuals with AF is well established.7 In analyses of racial and ethnic differences in treatment with warfarin, Black and Hispanic individuals with AF were less likely than White individuals to be prescribed warfarin and spent less time in the therapeutic range (ie, international normalized ratio of 2.0-3.0).7 After the introduction of DOACs, similar differences persisted. In recent observational studies, individuals with AF from underrepresented racial and ethnic groups remained less likely to begin use of any form of oral anticoagulation compared with their White counterparts and less likely to begin use of DOACs in particular.3,4 These racial and ethnic differences in AF management regrettably mirror the disparities in AF outcomes. Although the incidence of AF is higher in White individuals, the rates of stroke and death are higher in Black and Hispanic individuals with AF, even among those receiving oral anticoagulation.5,8

The findings by Reynolds et al6 are broadly consistent with these prior studies, but their work has several strengths that make it a unique contribution to the literature. Because AF is most common in older adults and most Medicare beneficiaries are eligible for the insurance based on age, the chosen study population was advantageous for examining national trends in DOAC use in the US. Additional strengths of this design include a large sample size and minimal variability of insurance coverage, which plays an important role in medication access in the US. This study is one of the first to explicitly demonstrate that the racial and ethnic differences in DOAC prescriptions have narrowed over time. This finding complements previously observed trends suggesting similar rates of change over time in DOAC use across race and ethnicity, albeit from different starting points.4,5 The authors also examined specific DOAC agents, finding no major differences in the DOAC prescribed across racial and ethnic groups. Nonetheless, the study was limited in its inclusion of only Black, White, and Hispanic individuals. Other underrepresented racial and ethnic groups have to date been minimally...
studied in the AF literature, although evidence supports similar undertreatment with oral anticoagulation in these groups, including among Asian, American Indian, and Alaska Native individuals.4,9,10

Another important addition of this analysis was its assessment of socioeconomic factors, which play a key role in the management of AF, including oral anticoagulant initiation and adherence.11 Because large administrative databases, such as Medicare claims data, generally lack detailed socioeconomic variables, geographically aggregated data are commonly used as surrogates for individual-level social determinants of health. In this study, the authors incorporated the Centers for Disease Control and Prevention’s Social Vulnerability Index (SVI) and its 4 components (ie, socioeconomic status, household composition and disability, racial and ethnic minority status and language, and housing and transportation).12 Seemingly in contrast to prior studies2-4 in which socioeconomic factors appear to mediate some of the observed racial and ethnic differences, adding the SVI to the multivariable models in this analysis made the racial and ethnic differences more apparent. Of note, the amplification of these differences in the most socially vulnerable quartile was driven by White individuals in these areas having greater uptake of DOACs compared with White individuals from less vulnerable areas. Meanwhile, the patterns of DOAC prescription for Black and Hispanic individuals appeared similar at the extreme quartiles of social vulnerability. These findings raise questions about what may be driving the differences among White individuals and whether social vulnerability is the most appropriate measure of social determinants of health in this context. Compared with neighborhood-level measures, such as the Area Deprivation Index, the county-level version of the SVI used in this study may be a less reliable surrogate for individual-level social factors.

Altogether, in the context of other research in which adjustment for socioeconomic factors has not been sufficient to explain observed racial and ethnic differences in AF management, this study demonstrates that the mechanisms driving these differences are complex (Figure). Traditional socioeconomic factors, such as income, educational level, rurality, and insurance status, are easily measured and are associated with race and ethnicity as well as oral anticoagulant use.13 Additional factors that have emerged as influencing oral anticoagulation use but remain understudied include homelessness, health literacy, primary language spoken, health care discrimination, and racism, all of

Figure. Determinants of Racial and Ethnic Disparities in Direct Oral Anticoagulant Prescribing

This figure represents a conceptual model for the multifaceted drivers of racial and ethnic disparities in direct oral anticoagulant prescribing including at the structural and health system, patient, clinician, and clinical encounter levels.
which are particularly relevant when considering racial and ethnic differences in care. Other potential drivers of unequal AF management that are more difficult to measure include clinician implicit bias, cultural differences among individuals in weighing risks vs benefits of anticoagulation, medical mistrust, and quality of shared decision-making in relation to cultural concordance of physician-patient relationships. Further exploration of these themes would require qualitative or mixed-methods research, which, although challenging to conduct on large scales, is critical to move the field of pharmacoequity in AF forward.13

Important questions remain that were beyond the scope of this study. It is reassuring that among those who are prescribed oral anticoagulation, the gaps in DOAC initiation across race and ethnicity appear to have narrowed. However, we are far from concluding that racial and ethnic differences in AF management are no longer present. For example, this study does not address overall rates of oral anticoagulant initiation for eligible individuals with AF, racial and ethnic differences in adherence to oral anticoagulant therapy, or long-term safety and efficacy outcomes on oral anticoagulation. Furthermore, the lag in leveling of the playing field for DOAC initiation should raise concern for the equitable implementation of other stroke risk reduction strategies among those with AF. There is a growing body of literature on the use of percutaneous left atrial appendage occlusion as an alternative to oral anticoagulation for those at high bleeding risk, and this research has shown lower use of these procedures among individuals from underrepresented racial and ethnic groups, with worse outcomes in Black individuals specifically.14 Similarly, higher AF burden is associated with increased stroke risk, but rhythm control strategies, including catheter ablation, are applied less often to individuals from underrepresented racial and ethnic groups.15

The study by Reynolds et al6 is further evidence that it takes years to overcome widespread racial and ethnic differences in AF management and reminds us there is still work left to do to better understand the determinants of disparities in stroke risk reduction for individuals with AF. At the research level, it will be imperative for ongoing and future clinical trials of novel anticoagulants, such as factor XI inhibitors, to ensure adequate racial and ethnic representation to help mitigate these prescribing differences upfront. At the policy level, eliminating cost-related barriers to medication access through policies such as the Inflation Reduction Act may reduce disparities in treatment. Lastly, at the patient and clinician levels, additional research examining aspects of care, such as shared decision-making, can guide efforts toward targeted interventions to promote equitable medication initiation and adherence and improve long-term outcomes for the increasing population of individuals with AF.
REFERENCES


