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Original article

Investigation of selection bias in the association of race with prevalent atrial fibrillation in a national cohort study: REasons for Geographic And Racial Differences in Stroke (REGARDS)

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ABSTRACT

Purpose: Atrial fibrillation (AF) is diagnosed more commonly in whites than blacks in the United States. In epidemiologic studies, selection bias could induce a noncausal positive association of white race with prevalent AF if voluntary enrollment was influenced by both race and AF status. We investigated whether nonrandom enrollment biased the association of race with prevalent self-reported AF in the US-based REasons for Geographic And Racial Differences in Stroke Study (REGARDS).
Methods: REGARDS had a two-stage enrollment process, allowing us to compare 30,183 fully enrolled REGARDS participants with 12,828 people who completed the first-stage telephone survey but did not complete the second-stage in-home visit to finalize their REGARDS enrollment (telephone-only participants).
Results: REGARDS enrollment was higher among whites (77.1%) than among blacks (62.3%) but did not differ by self-reported AF status. The prevalence of AF was 8.45% in whites and 5.86% in blacks adjusted for age, sex, income, education, and perceived general health. The adjusted white/black prevalence ratio of self-reported AF was 1.43 (95% CI, 1.32–1.56) among REGARDS participants and 1.38 (1.22–1.55) among telephone-only participants.
Conclusions: These findings suggest that selection bias is not a viable explanation for the higher prevalence of self-reported AF among whites in population studies such as REGARDS.

Introduction

Atrial fibrillation (AF) is the most commonly diagnosed cardiac arrhythmia, becomes increasingly common with age, and carries increased risks for heart failure, stroke, cognitive decline, hospitalization, and death [1]. Unlike most cardiovascular conditions, which occur more commonly in blacks than in whites in the United States, AF is diagnosed more commonly in whites than in blacks [2–5]. This occurs in a variety of settings including integrated health systems [6–8] and population-based or community-based epidemiologic studies [9–14]. AF occurring more in whites is considered paradoxical because blacks have higher prevalence of many risk factors for AF including hypertension, diabetes, obesity, chronic kidney disease, heart failure, and cigarette smoking [14,15]. Some evidence suggests that higher occurrence of AF in whites may have a biological basis, for example, whites tend to have larger left atria than blacks [16], and among blacks, AF risk is associated with genetically defined European ancestry [17]. However, the association of white race with higher occurrence of AF could also potentially reflect biases arising from racial differences in data collection (information bias) or racial differences in study participation (selection bias).

Information bias could induce a noncausal positive association of white race with AF if whites were more frequently or more carefully examined for AF, leading to more complete detection and

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diagnosis of AF among whites [4]. However, information bias is unlikely to explain the association of white race with AF in studies conducted in integrated health systems or in population-based or community-based epidemiologic studies. In integrated health systems, information bias is unlikely because health system enrollees would all have, at least in principle, equal access to the same clinical care and diagnostic services [6–8]. Evidence from the Veterans Health Administration suggests these resources are not disproportionately accessed by whites compared to blacks [7]. In epidemiologic studies, information bias may occur when AF is determined by self-report, if whites are more likely than blacks to correctly recall and report their physician diagnosis of AF [18]. This could occur if, for example, whites had higher health literacy or better relationships with their physicians than blacks. However, other data collection methods to determine AF status in epidemiologic studies are standardized for all study participants, including electrocardiography, medical record review, and health insurance database linkage. These methods also yield higher AF prevalence among whites, making information bias an unlikely explanation [9–14].

Selection bias could induce a noncausal positive association of white race with AF, if selection of participants into studies was a function of race and, simultaneously, a function of AF status. As described in the causal inference literature, two factors that each separately strongly influence selection of participants into research studies will tend to be associated among study participants, even if they are not associated in the underlying population from which participants were selected [19–21]. For example, if whites were more likely than blacks to agree to participate in a study, and independently, people with prevalent AF were less likely than people without prevalent AF to agree to participate in that same study, then the association of white race with prevalent AF observed among the study participants could be biased in a positive direction.

In studies conducted in integrated health systems, selection bias is unlikely because individuals eligible for enrollment in the health system would decide whether to enroll without regard to their own AF status [6–8]. For example, evidence from the Kaiser system indicates that history of hypertension and diabetes among enrollees is fairly similar to that of nonenrollees, which suggests that other chronic diseases like AF would be unlikely to influence enrollment [22]. Health system enrollment decisions among eligible individuals could differ by race due to racial differences in trusting health care or doctors. However, Kaiser data also show that whites are not over-represented among enrollees compared to blacks, relative to the underlying population [22,23]. This makes selection bias an unlikely explanation for the association of white race with AF observed in integrated health systems.

However, selection bias *is* a concern in population-based or community-based epidemiologic studies with voluntary enrollment, because whites tend to enroll in such studies more readily than blacks [24,25], *and* people free of chronic diseases tend to enroll more readily than people with a history of chronic diseases [25,26]. If study participation was nonrandom with respect to race, and simultaneously, nonrandom with respect to chronic disease status, the observed associations of race with chronic conditions, including prevalent AF, could be biased among enrolled participants [19–21]. Because voluntary epidemiologic studies play an important role in identifying associations of social, psychosocial, and behavioral factors with AF, this potential selection bias warrants investigation.

The purpose of the present study was to investigate whether nonrandom study enrollment biased the association of white race with prevalent self-reported AF observed at baseline among participants in a population-based epidemiologic study in the United States, REasons for Geographic And Racial Difference in Stroke (REGARDS) [27]. As previously reported, baseline prevalence of self-reported physician diagnosis of AF in REGARDS participants was significantly higher in whites than in blacks [10]. To determine whether nonrandom study enrollment influenced this observed racial difference in prevalence, ideally, we would compare the distributions of race and prevalent self-reported AF in REGARDS participants versus the underlying population of people eligible to participate in REGARDS. However, race and AF status are not available from the underlying population, rendering a direct comparison impossible. Instead, we compared REGARDS participants with a group of people who were invited to join REGARDS and initially agreed to participate and reported their race and medical history by telephone, but who ultimately did not participate in REGARDS. During REGARDS enrollment, In-home assessments were required to be performed on Monday through Thursday mornings, to allow fasting blood samples to be collected and shipped to the central laboratory during weekdays. Owing to these scheduling constraints and perhaps other reasons, not all who completed the telephone survey were able to complete the in-home component of the study. As such, those who failed to complete the required in-home study visit never finalized their enrollment in REGARDS. These people are referred to hereafter as "telephone-only participants." In contrast, those who completed the in-home study visit are referred to as "REGARDS participants." We considered REGARDS participants a more-selected group and telephone-only participants a less-selected group, relative to the underlying population. We compared the distributions of race and prevalent self-reported AF in REGARDS participants versus telephone-only participants to investigate selection bias due to nonrandom study enrollment after completion of the telephone survey.

Materials and methods

Study design, setting, and participants

This is a cross-sectional analysis of baseline data from REGARDS. From 2003 to 2007, REGARDS enrolled black and white men and women aged 45 years and older from all 48 contiguous Unites States using a two-stage baseline data collection design [27]. A nationwide list stratified by age, sex, race, and geographic region was obtained from a commercially available source (Gensys, Inc.). Potentially eligible households were contacted first by letter then by phone. When a household was contacted by phone, household members were enumerated, and one eligible member of the household was selected to participate in the study. In the first stage, an eligible participant completed the telephone survey in which they answered questions about their demographic characteristics and medical history. In the second stage, after the telephone survey, a participant finalized enrollment in REGARDS by completing the in-home visit, which included various physical measurements and additional questionnaires. Telephone-only participants completed the first stage but not the second stage. Institutional review boards of the collaborating institutions approved the REGARDS study protocol. Verbal informed consent was obtained during the telephone survey and written informed consent during the in-home visit. Analyzing differences in the characteristics of in-home visit completers versus telephone-only participants was anticipated when the REGARDS study was designed [27].

Data collection

In the telephone survey, participants self-reported their demographic characteristics including age, sex, race, annual household income, and education; their perceived general health; and