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# Let's Not Repeat History's Mistakes: Two Cautions to Scientists on the Use of Race in Alzheimer's Disease and Alzheimer's Disease Related Dementias Research

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## Abstract

Alzheimer's disease and Alzheimer's disease related dementias (AD/ADRD) research has advanced gene and biomarker technologies to aid identification of individuals at risk for dementia. This innovation is a lynchpin in development of disease-modifying therapies. The emerging science could transform outcomes for patients and families. However, current limitations in the racial representation and inclusion of racial diversity in research limits the relevance of these technologies: AD/ADRD research cohorts used to define biomarker cutoffs are mostly White, despite clinical and epidemiologic research that shows Black populations are among those experiencing the greatest burdens of AD/ADRD. White cohorts alone are insufficient to characterize heterogeneity in disease and in life experiences that can alter AD/ADRD's courses. The National Institute on Aging (NIA) has called for increased racial diversity in AD/ADRD research. While scientists are working to implement NIA's plan to build more diverse research cohorts, they are also seeking out opportunities to consider race in AD/ADRD research. Recently, scientists have posed two ways of including race in AD/ADRD research: ancestry-based verification of race and race-based adjustment of biomarker test results. Both warrant careful examination for how they are impacting AD/ADRD science with respect to specific study objectives and the broader mission of the field. If these research methods are not grounded in pursuit of equity and justice, biases they introduce into AD/ADRD science could perpetuate, or even worsen, disparities in AD/ADRD research and care.

### Keywords

Alzheimer's disease; biomarkers; genetics; preclinical Alzheimer's; racism; scientific discoveries

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CONFLICT OF INTEREST

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## INTRODUCTION

Addressing underrepresentation in Alzheimer's disease and related dementias (AD/ADRD) research is a major goal of the National Institute on Aging's (NIA's) strategic plan, which increased funding to improve racial representativeness and participation in research samples [1]. The impetus for this plan emerged from recognition that AD/ADRD research samples are disproportionately comprised of White individuals. Thus, the discoveries made with data from those samples may not be applicable to Black populations, which are among those who experience the greatest burdens of AD/ADRD [2–5]. Research shows Black populations meet clinical criteria for AD dementia at higher rates, are less likely to be diagnosed, are diagnosed at later stages of the disease, receive lower quality of care, and have worse mortality rates than their White counterparts [6, 7].

Success of the NIA's plan will require more individuals from minoritized social groups—those made subordinate in status to a group that controls more social resources—to be part of AD/ADRD research. The participation of Black Americans and other minoritized populations that follows is expected to strengthen AD/ADRD science.

Characteristics of research samples reflect who is most likely to benefit from discoveries made using those samples. Scientific advances that hinge on racial representativeness of research samples include more generalizable study results, effective therapies, and expanded benefits of research innovations. When the characteristics of research participants reflect the diversity in culture and other conditions of AD/ADRD patient populations, it facilitates successful translation of findings and inferences into real-world use. The discoveries emerging from diverse research samples, including biomarker-based diagnosis and disease-modifying treatments, would be built to reduce the burden of disease and improve quality of life for all individuals living with AD/ADRD and their families.

As they undertake efforts to build socioculturally diverse research cohorts, AD/ADRD scientists are simultaneously carrying out the national plan to transform the clinical syndromes associated with AD/ADRD to biologically defined and treatable diseases [8]. Because of advances in biomarkers, it is currently possible to identify cognitively unimpaired individuals who are showing early pathological markers of AD, including amyloid, tau, and neurodegeneration [9–11]. Biomarkers are expanding opportunities to develop disease-modifying therapies, which will rely on methods of early diagnosis.

While they are independent initiatives, the NIA's two goals are being carried out by a shared workforce of investigators with shared resources. Actions taken in pursuit of one may influence outcomes of the other. Without careful interrogation and conscious course setting for these initiatives, the field could inadvertently repeat history's biases. The field's emphasis on race in tandem with edict to advance a biological framework for a disease, for which Black Americans are among the most burdened, could lay the foundation for inadvertent racism. Steps are needed to address structural racism in research practices and assure structural racism is not built into new discoveries [12].

Structural racism—also known as institutional racism or systemic racism—is racism that is embedded as normal practice within society, organizations, or communities. Structural

racism can take the form of stereotypes, harmful beliefs, and discriminatory practices that create systematic exclusion or disadvantage based on race, which is broadly recognized as a social construction [13]. Researchers can perpetuate systemic biases by what scientific inquiries are prioritized, how studies are designed and conducted, and how results are interpreted [14]. Biased practices in research can spill over to influence clinical care as these practices can accompany discoveries as they are translated from research into routine care.

Recently, researchers have used race in AD/ADRD research in two ways that warrant careful examination: ancestry-based verification of race and race-based adjustment of biomarker test results. They are impacting AD/ADRD science in terms of specific study objectives and the broader mission of the field. In the future, the practices used in research will inform clinical care for individuals with AD/ADRD and their families. If research practices are not grounded in pursuit of equity and justice, biases they introduce into the conduct of AD/ADRD science could perpetuate, or even worsen, disparities in AD/ADRD research and care.

## THE SCIENCE: ANCESTRY TESTING

Like in other fields, genetics is a leading focus of AD/ADRD researchers. The heritability of late onset AD dementia is high, estimated to be between 60% and 80% [15]. The strong genetic contribution presents an opportunity to determine pathophysiological processes and further scientific knowledge about AD/ADRD biomarkers. In turn, what is learned from genetic studies may help identify therapeutic targets.

Analysis of an individual's genome can also reveal details about that person's ancestry because of genetic recombination, which is affected by migration, survivorship, and other population-levels factors. Researchers are examining genetic patterns associated with AD/ADRD in ancestry groups with the hope of finding causal genetic polymorphisms that are associated with differences in disease risk [16]. This approach has been shown to have scientific value in studying neurodegenerative diseases. Studies among Ashkenazi Jewish populations, for example, aided discovery of mutations in the leucinerich repeat kinase 2 (LRRK2) gene, which are the most common genetic determinant of Parkinson's disease identified to date [17].

## THE CONCERN: ANCESTRY-BASED VERIFICATION OF RACE

In contrast to revealing data about a person's ancestry or genetic patterns associated with disease, some researchers are combining data on genetic ancestry with self-report questions about racial identity in order to "validate" research participants' races [18,19]. Scientists wish to use this information to document diversity in research samples; however, the practice is problematic.

History has shown genetic attributions of social group differences can stoke stereotyping and prejudice [20]. The relationship between genetic ancestry and race is complex and often fraught [21, 22]. People tend to use what they know about a person's genetic make-up to over attribute the individual's characteristics and behaviors. A specific form of this genetic essentialism is racial essentialism, which is belief in a genetic or biological

essence that defines members of a racial category. Racial essentialism is a cognitive bias, a misattribution, that conflates the ideas of race and ancestry. This appears in the scientific literature as researchers sometimes use genetic ancestry data interchangeably with self-report questions about racial identity [23, 24], likely because the convergence between ancestry data and self-report can be high, upwards to 95% [21].

Like genetic data, self-report questions about racial identity may add value to AD/ADRD research. They are commonly used in AD/ADRD research to document sociocultural representation in federally-funded research [25]. Despite the seemingly utilitarian purpose, these questions can be complex for research participants and researchers. The concept of race has a sorted history in medicine [26], and research communities operate within the constraints imposed by this history [27]. Inclusion of self-reported race in research is also complicated by commercial and regulatory imperatives, media representations, and definition ambiguity [27]. Because of these contextual factors, analysis of self-reported race data can present opportunities to identify societal factors that contribute to population-level differences in health and disease [28].

Inquiries using self-reported race data may, along with other studies, help explicate social and structural factors that influence AD/ADRD outcomes [29,30]. Research shows Black populations are less likely to be diagnosed, are diagnosed at later stages of the disease, and receive lower quality of care than their White counterparts [6, 7]. Analysis of self-reported race data may help identify correlates that aid in explicating barriers to appropriate care, which would be useful to know in order to inform interventions to mitigate these problems.

## THE SLIPPERY SLOPE: RACIAL ESSENTIALISM

The evaluation of the validity of a person's self-reported race using genetic ancestry, be that for purposes of attribution, verification, prediction, or prognostication, is problematic.

How individuals identify their race is not fixed and can depend on many factors [31]. Individuals may privilege one aspect of their racial identity over another for purposes of, for example, conforming or distancing in social relationships. The emotional valence of relationships and family secrets influence how people identify their racial identities, whether intentionally or unintentionally. These considerations exemplify how racial identity is a social construct, dependent on social factors.

In contrast, genetic ancestry is typically determined by a test. Interpretation of the results of that test are based on statistical samples. Subgroups are identified in these samples that are more versus less genetically similar. Individuals with ancestry from multiple subgroups are described as "admixed." Most individuals are admixed. The compositions of admixtures, even within one self-identified ethnic group, vary significantly [23, 32–35]. The vast majority of diversity in the human genome reflects individual uniqueness [36].

While perhaps each construct—genetic ancestry and self-reported race—can independently add valuable information to scientific studies, their juxtaposition is problematic when one is used to substantiate the other. When ancestry test results are positioned as evaluative of an aspect of a person's identity, an implied goal is to confirm a person's stated race

with a biologic measure. This objective, however, is erroneous. Race and ancestry are often correlated but independent constructs.

Methods, like the flawed equating of race and ancestry data, may be being used differentially in Black, Indigenous, and people of color (BIPOC) and other minoritized groups. Researcher choices, like inaccurate interpretation of results, research goals of confirming or disputing Blackness, and choice to use a method, can undermine research participants' trust and be counterproductive to efforts aimed at increasing sociocultural diversity in AD/ADRD research [1]. Other researcher decisions, like respecting participant life experiences and community ties, can strengthen participant trust.

Disseminating results of research that arise from flawed methods can also inadvertently undermine diversity and equity work in AD/ADRD research. The misuse of self-report data and genetic data can stoke worries among stakeholders. Results that misconstrue race (a social construct) as a biologic phenomenon can exacerbate racism and stigma as they risk perpetuating inaccurate and harmful ideas of biological difference. Lines of research notably at risk to this kind of hazard include work on AD/ADRD mechanisms and on structural and social determinants of AD/ADRD disparities.

Researcher decisions can impact clinical care. The language, ideas, and techniques used by AD/ADRD researchers accompany their discoveries through translation from research to care.

## THE SCIENCE: AD/ADRD BIOMARKER TESTING

Biomarkers, a measurable substance in the body that indicates disease or its risk, are accelerating AD/ADRD science. They are allowing identification of pathology before the onset of clinical impairment and thereby helping to usher in disease-modifying treatments that could slow the onset of impairments [9]. For example, testing for the Apolipoprotein (*APOE*) *ε*4 allele that is associated with higher risk for AD dementia is already impacting routine care [37], and blood-based biomarkers, which can detect amyloid, p-tau, and other relevant proteins, have recently created an ease of access to testing that is expected to bring early diagnosis and treatment of AD/ADRD closer to fruition [38].

## THE CONCERN: RACE-ADJUSTMENTS IN CLINICAL GUIDELINES FOR AD/ADRD BIOMARKER USE

In 2019, the first study was published that reported differences detected on PET scan and cerebrospinal fluid (CSF) concentrations of $A\beta_{42}$, t-tau, and p-tau181 between Black and White research participants [39]. The study centered on 65 African Americans, of whom a mere 29 were *APOE ε4* carriers, which was the relevant gene. The researchers found lower levels of two key biomarkers, CSF t-tau and p-$tau_{181}$, in the African American participants compared to 504 White Americans. The lower levels of biomarker in African American individuals in the study were not statistically explained by the measure of comorbid cerebrovascular disease the researchers assessed. The researchers concluded that the lower levels of these biomarkers in African Americans were largely a function of *APOE ε4* carrier

status. The researchers suggest that if their findings can be confirmed with analyses in larger cohorts than there may be a need to adjust for differences in the performance of these biomarker measures across race groups.

Race adjustment, also known as race-correction, is the calculating of a result to account for differences in measurement or interpretation across race groups. It is commonly and controversially used in medical algorithms in several specialties, including cardiology, nephrology, urology, and obstetrics [40]. Many race-adjusted algorithms guide clinical decisions in ways that may direct more resources to White patients than to members of racial and ethnic minoritized populations [40, 41].

The researchers are appropriately cautious in discussing the potentiality of future use of race correction. They suggest further study is needed to confirm (or refute) their findings. They explain the study findings need to be replicated in larger cohorts and mention the need to examine factors—"influences of socioeconomic status, comorbid diseases, and other factors that may contribute to racial differences"—that may be confounding the results. Their study, like many others in AD/ADRD that examine racial differences in AD biomarkers, relies on a relatively small sample as only small racially diverse cohorts are currently available for study. This issue is in part the impetus for NIA's plan for increasing racial diversity in research samples.

Race correction, particularly when mentioned in the literature so early in the research process, warrants discussion in the broader AD/ADRD community. The idea will be repeated in the scientific narrative as scientists use this foundational study to develop plans for the next studies. Its suggestion as a future possibility raises the question: is race correction of a biomarker result an appropriate scientific goal?

We understand the authors to be suggesting that caution is needed until further work is conducted that confirms (or refutes) the finding. If confirmed, race correction could be a reasonable solution. However, we propose, first, that this focus—confirming or refuting use of race correction—is not an appropriate conceptual positioning given small sample sizes, uncertainty in how to interpret findings, recent development of biomarkers, and the wider goals of the field. Second, the proposition of race correction as a solution for race-based differences in biomarker results warrants scrutiny by the field because the reasoning that supports it is flawed and the practice risks harmful downstream effects on patient care.

While race-based adjustment may seem a readily available option, given its wide-spread and continued use in medicine, the practice has been shown to be problematic. The field of nephrology offers a recent example that has garnered national attention [42]. Black adults have higher rates of end-stage kidney disease and death due to kidney failure than the overall population. Race-based correction of glomerular filtration rate, or eGFR, was used to adjust for differences in kidney function in Black adults. This adjustment delayed referral to a specialist, reduced access to transplantation, or both [42]. The adjustment also reflects a flawed biological attribution of race [40, 43].

## THE SLIPPERY SLOPE: IGNORING RACISM'S ROLES IN AD/ADRD RESEARCH

### Are the racial differences in AD/ADRD biomarkers truly a function of race, or are they a function of racism?

A fundamental question underlying race-adjustment is whether the validity of AD/ADRD biomarkers differs by race. As most AD/ADRD samples privilege a specific population subgroup [44], the field currently does not yet have data to adequately address this question and is working to address this limitation.

In the absence of evidence that a biomarker test differs in its ability to detect disease across race groups, the question of race-adjustment is, rather, a proposition to address the consequences of structural and social inequalities. A race-based adjustment to a biomarker test result attributes the underlying causes of the difference to "race". This is, at best, uninformative and, at worst, leads to a misguided conclusion that race has direct biologic effects (that require correction).

Foremost, if the same level of biomarker has differential effects across races, science needs to understand what would be moderating the effect. Could it be a lifestyle factor? Environment reason? Moderator analyses may help explicate the conditions, "when" or "for whom", a race may be more strongly associated with an outcome [45]. In addition, mediator analyses that help establish "how" or "why" a factor causes an outcome may also be useful [45]. Studies in AD/ADRD, such as those conducted by Schindler et al and others [46–49], are suggesting that levels of an AD biomarker do not consistently correspond to a disease endotype because either the biomarker or endotype is being influenced by another variable (like *APOE* genotype or cardiovascular disease).

Stopping at "race" is insufficient. Scientists need to understand the disease mechanisms and, potentially, develop biomarkers that more closely link AD endotypes. Invariance of AD biomarker test results across racial groups raises a question for AD/ADRD scientists as to whether, rather than adjusting its interpretation, such a test should be translated from research into clinical care.

Adjusting biomarker benchmarks by race could make it more difficult for Black Americans with AD/ADRD and their families to be diagnosed and to receive treatments. This in effect could undermine distributive justice in emerging treatments. Moreover, further investigation could not only prevent harm but it could also have benefits, such as those that aid in identifying disease-modifying interventions.

It is troubling that biomarker technologies could be used in ways that facilitate structural and social inequities. It is also disconcerting to consider that the potential of biomarkers as a mechanism to help mitigate inequalities could go unrealized. Biomarker technology holds promise for allowing clinicians to identify the presence, type, and staging of pathologies that cause dementia. In this way, they potentially offer a more precise and culturally agnostic way to diagnose AD/ADRD [9]. Traditionally, clinical interviews and neuropsychological

assessments have been used to identify problems in a person's cognition and function. The problems, however, could be attributable to a number of pathologies and experiences.

In considering how to address gene and biomarkers that differ across race groups, a key step is conducting the studies that are needed to understand what might be causing the differences. There could be any combination of correlates that could potentially explain race-based differences in gene and biomarkers [29]. Another step may be to debate how such a difference would be translated from research to clinical care. Developing robust clinical interviews, for example, may be more instructive to medical care than systemic adjustment of a result to nullify the difference. Clinical interviews could help explicate relevant factors from a patient's history and guide their discussion in the context of risk appraisal, treatment decisions, and care planning.

There is a need for ongoing dialog among stakeholders—patients and family members, researchers, clinicians, and funding agencies—about how to address race and related constructs in AD/ADRD science. Polygenic risk scores (PRS), for example, have gained a lot of attention recently for their potential to serve as predictive and prognostic biomarkers; individuals with higher PRS may be at higher risk to develop AD symptoms, experience earlier onset, faster decline or more severe impairments [50, 51]. PRS, which are typically defined by genome-wide association studies (GWAS), need to account for ancestry and adjust for race [52]. Decisions and rationales that underlie methods warrant exposition in the field.

## HOW CAN AD/ADRD RESEARCHERS AVOID BAKING BIAS INTO NEW DISCOVERIES?

Conducting science that leads to equitable access and care for all patients and their families demands researchers counter structural bias, which is the tendency of systems to support certain outcomes. Practices are problematically biased when they confer advantage to some and disadvantage to others based on identity [53, 54]. There are ways scientists can help address structural bias (Table 1). While some strategies may have unavoidable costs associated with them (i.e., consulting fees, time), most do not require investments of time and effort above what would be expected in the routine conduct of rigorous science.

## STUDY DESIGN

### Follow the most current evidence

Currently, science broadly recognizes race as being socially constructed [13]. While race can have biologic correlates, it is not biologically verifiable or biologically defined. Considering race in AD/ADRD science is particularly helpful for understanding effects of cultural beliefs and attitudes, group behaviors, and socioeconomic policies. Ross and colleagues offer further discussion of the topic [55].

### Include race in a study's conceptual model if race will be examined in analyses

A researcher that collects data on participant "race" does so for a reason. Most often in the United States (US) this is done to satisfy funder reporting requirements of participant characteristics. Thus, given the purpose, race is typically measured as a self-report question with response categories defined by the federal government. Because the data are then available, researchers might examine them in analytic models without a priori planning. But appropriate consideration of a construct warrants use of a conceptual model, which demands *a priori* deliberation.

A conceptual framework illustrates what researchers expect to find by conducting a study. When race, ancestry, or another concept is included in a study, the conceptual framework maps out how the concept relates to the mechanisms being studied. From this conceptual framework emerges the rationales for measures and analyses. In GWAS, for example, both ancestry and self-report data are used. The conceptual framework could describe how ancestry informative markers (AIM) are used to define genetically homogenous populations by excluding extreme outliers while self-report race would be a subgroup characteristic used to covary social and structural influences of population architecture. In considering how race may operate in a study's conceptual model, Hill and colleagues [30], Stites and colleagues [29], and others offer discussions of how social and structural factors may correlate with health disparities and explain variance in AD/ADRD outcomes.

### Structure the study and its processes to disrupt structural bias

Scientists can set in place practices that make it more likely that divergent perspectives will be included and less likely that biased conventions may be carried forward as defaults. These practices include collaborating with research participants to co-create questions and projected outcomes [56], encouraging member-checking [57], collaborating on interpretation of results [58], and acknowledging the collective positionality of the research team [59].

## ANALYSIS

### Scrutinize metrics

A difference in a measure across race groups may be due to a number of factors that should be considered before concluding that a difference is attributable to race. Common factors to consider might characteristics of a measure and correlates of group membership.

Schindler and colleagues [48], for example, analyzed the accuracy of a set of biomarker tests in 76 pairs of Black and non-Hispanic white participants. The pairs were matched on age, gender, cognitive status, and *APOE* status. They found p-tau plasma tests (p-tau$_{181}$, p-tau$_{231}$) and neurofilament light (NfL) protein performed inconsistently as a measure of brain amyloidosis across African Americans and non-Hispanic White Americans in their sample. As they appropriately investigate and conclude, the error in the tests was likely due to differences in medical comorbidities between the study groups, not race.

Inspect the metrics being used in a study. Race, for example, may be measured as self-report racial identity, defined in a conceptual model as a "personal characteristic," and entered into

analysis as “a correlate of disease severity”. However, the metric and its conceptualization warrant inspection. They are expected to be synergistic. Self-report race reflects affiliation with a social group. In the case of Black race, it is a social group that is minoritized.

Race-based differences in disease severity may be better attributed to systemic racism, i.e., inadequate access to appropriate healthcare or poor environmental conditions, than personal health choices. In contrast to ancestry, race is a social construct and cannot cause a disease. As a modifier of social conditions, it can impact availability of treatment, access to care, and other factors. As a modifier of environmental factors, it can affect exposure to certain causal agents and confluences of risk factors, and susceptibilities that can impact on disease.

Moreover, some metrics, such as many PRS, have been developed in cohorts with European ancestry. As a consequence, they may lack validity in a sample based on a mismatch between the development samples and study populations. AD biomarkers also demonstrate variability in the degree to which they do or do not detect differences across racial groups. Garrett and colleagues (2019) that suggest biomarkers such as $A\beta_{42}$ and p-tau may differ less across races.

The need to scrutinize metrics is underscored by the data sharing efforts that have made it possible for researchers to use metrics they did not personally develop. PRS, for example, have wide availability in public use datasets, such as the Health and Retirement Study. Scientists may easily make an error in using a metric or interpreting a result due to not knowing underlying problems or limitations of a measure.

It is an important scientific goal to identify factors that contribute to differences in AD/ADRD outcomes across race groups.

## RESEARCH RESULT INTERPRETATION

### Avoid biologic essentialism

Research shows individuals who subscribe to biologic essentialism, or the belief that some social groups have an underlying biological *essence*, tend to endorse biased beliefs about individuals in those groups [61]. While there may be biologic correlates to groupings, race, and other demographic group characteristics, such as ethnicity, sexual orientation, sex/gender identity, ability, religion/spirituality, nationality, and socioeconomic status are predominantly sociocultural identities.

The differences in biomarker performance across racial groups suggests scientists need to be attentive to a broad array of possible consequences when the metrics are used. Deters and colleagues (2021), for example, showed how differences in amyloid results across racial groups lead to differential qualification for an AD prevention trial [49].

When a difference is observed across race groups, steps are needed to identify factors that might explain the difference and, potentially, to mitigate the effects of the difference. In the case that the difference is leading to exclusion and/or attrition in a clinical trial, a prudent approach may be initiating a substudy to investigate those effects. In addition, given that emerging evidence suggests some biomarkers may vary by ancestry, it may be

prudent for research studies to collect these data rather than relying on race as a proxy for this information. Dieters and colleagues (2021) study, for example, suggests collecting Ancestry data may be valuable as their results showed higher levels of African ancestry were associated with reduced amyloid levels [49].

As AD biomarkers are translated from research to routine clinical care, it will be essential to have professional groups like the *Advisory Group on Risk Evidence Education for Dementia (AGREED)* to offer information to guide clinicians on their interpretations, especially in the context of variable quality and strength in supporting evidence [37]. AGREED and other similar groups also provide a pathway to obtain direct input from patients, research participants, and other key stakeholders.

### Appreciate sociocultural diversity

The history of science has focused on the discovery of knowledge and its systemization. The topics and methods are largely the products of a Eurocentric worldview [62]. Critically examining assumptions and traditions in scientific practices is core to addressing biased artifacts of this history. An awareness of the narrowness of this history may aid scientists' ability to appreciate the many sociocultural groups who are unrepresented or subjugated in this history. As done by many researchers in the AD/ADRD field, articulating gaps in knowledge about sociocultural groups and listing limits of generalizability and representativeness are essential in reporting research results. Scientists show fidelity to research participants by being transparent about how data might be evaluated and how an individual might be categorized.

The history of race, particularly in the US, is grounded in the subjugation of people. Slavery and institutionalized bias have systematically limited access to social resources for BIPOC communities. While it is good social practice to avoid making poor judgments of an individual's character, such as attributing one's social position to a moral deficit or disease, the history of disenfranchisement underscores the need to elevate social groups based on positive contributions, or at minimum retain neutrality. Favor for biologic family structures, white collar professions, and university education are often grounded in this biased history and warrant careful interrogation.

In addition to structural bias, researchers often routinely address a range of biases to help the assure quality and integrity of studies [63]. This includes being aware of biases, e.g., selection bias, recall bias, and citation bias, and doing the work to mitigate them. There are specific steps a researcher can take to address each type of bias. To minimize selection bias, for example, participants should be recruited from the general population using rigorous criteria and they should be recruited into well designed, prospective studies. To help avoid citation bias, researchers can check registries for similar unpublished or in-progress trials prior to publication.

## CONCLUSION

Scientists are making discoveries that hold promise for revolutionizing AD/ADRD diagnosis and treatment. These advances could aid in undoing the racial and social biases that have

haunted the history of AD/ADRD research. But, if cultural bias spills over to affect how methods of AD/ADRD diagnosis are designed by scientists and used by clinicians, it may perpetuate sociocultural inequities in AD/ADRD, perhaps, even intensifying them [6, 64, 65]. We have seen first-hand in kidney disease how the failure to address social equity in research has translated to race-based injustices in clinical care [42].

Researchers and clinicians must practice in ways that are historically and scientifically informed. Methods that attempt to confirm aspects of race with biologic data reify historical injustices. They promulgate false ideas that may compromise the relationships between AD/ADRD scientists, participants, and broader public communities as individuals may feel their trust is compromised. Alternatively, using methods that promote social justice and equity begins with a question: How do my research methods align with social justice values?

Methods that adjust for race indiscriminately risk undermining two of the most promising parts of current advances in AD/ADRD science. They undermine the power of these advances for being able to identity potentially modifiable disease targets for intervention. Additionally, they pose a risk to the distributive justice of AD/ADRD treatments that are reliant on them.

In sum, to bring to bear advances in diagnosis and treatment, racial underrepresentation, and disparities must be addressed in AD/ADRD research. The NIA has laid out a strategic plan and increased funding to improve the racial representativeness in research samples [1]. Research is responding to these incentives, but scientists also need to improve their methods and approaches to ensure forward movement in scientific discovery. What scientific inquiries are prioritized, how methods are used, and how results are interpreted within a study and to the broader community, also need to improve to assure structural racism is not built into new discoveries. If proposed solutions are not grounded in pursuit of equity, inclusion, and justice, biases they introduce into the conduct of AD/ADRD science could perpetuate, or even worsen, disparities in AD/ADRD research and care.

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**Table 1**

Candidate Approaches to Promoting Equitable Scientific Practices by addressing Structural Bias

| Research Phase[a] | Step | Explanation |
|---|---|---|
| Study Design | Build a study using the most current evidence | Seek out the most current scholarship on the topic. This includes literature searches of PubMed and other repositories of scholarship. |
| | Include race in a study's conceptual model if race will be examined in analyses. | When race is included as a study variable, include it in the conceptual framework and map out how the construct relates to the mechanisms under study and other variables. |
| | Structure the study and its processes to disrupt systemic bias. | Collaborate with research participants to co-create questions and outcomes [56], encourage member-checking [57], collaborate on interpretation of results [58], and acknowledge the collective positionality of the research team [59]. |
| Analysis | Scrutinize metrics | A difference in a measure across race groups may be due to a number of factors that should be considered before concluding that difference is attributable to race. These factors can include characteristics of measure and biologic, social, and/or behavioral correlates of group membership. |
| | | Know the specifics of metrics – their strengths and limitations – that are being used in a study. This is a prime example of a situation in which a content expert may be particularly valuable. |
| Interpretation | Generate alternative explanations | Generate many factors that might explain observed differences and their alternatives. A sound alternative explanation is a credible one, supported by evidence and uninfluenced by bias. |
| | Avoid biologic essentialism | Biologic essentialism refers to beliefs that some social groups have an underlying biological *essence*. Individuals who subscribe to biologic essentialism tend to endorse biased beliefs about individuals in those groups [66]. While there may be biologic correlates to social groupings, race and other characteristics are predominantly sociocultural identities. |
| All phases | Appreciate sociocultural diversity | Maintain awareness of the history of science being largely grounded in a Eurocentric worldview. Examine critically assumptions and traditions to identify and address biased artifacts of this history. Strive for transparency in communication. |
| | Consult with content experts | Seek consultation, at any phase of the research process, when uncertain about the application of concepts. Sociologists, anthropologists, racial justice advocates, community partners are all potential sources of expertise. |

[a]Categorization is based on when the step may be most germane to the research process however the steps ought to be practiced throughout all phases of the scientific process.