

## PERSPECTIVE

# Sex, gender, sexual orientation, and more: Sexual diversity in Alzheimer's research needs a new lens to achieve inclusive research and generalizable results

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**Abstract**

Diversity, Equity, and Inclusion (DEI) efforts in Alzheimer's disease and related dementia (ADRD) research are guiding the adoption of two-step self-report questions that capture research participants' identity based on categories of sex, sexual orientation, and gender identity. The intent is to facilitate inclusion and representation of sexual and gender minoritized (SGM) communities in ADRD research. The data from using these questions are on a collision course with another National Institute of Aging initiative, which is aimed at understanding sex differences in ADRD mechanisms. Here, we critically analyze the goals and methods of the two initiatives. We propose that, in addition to being SGM focused, DEI efforts are needed to expand how scientists consider and measure sexual diversity itself.

**KEYWORDS**

Alzheimer's disease research, diversity equity inclusion, measurement, sex/gender

**Highlights**

- Sex, sexual orientation, and gender identity (SSOGI) will be asked in ADRD studies.
- SSOGI data will expand representation of research participant identities.
- SSOGI data are on a collision course with sex differences research.
- Both emphasize sexual diversity (SD) largely as SSOGI identity categories.
- Diversity, Equity, and Inclusion efforts must develop SD methods in ADRD research.

## 1 | INTRODUCTION

Diversity, equity, and inclusion (DEI) practices are the backbone of efforts to enroll under-represented populations in clinical research studies.<sup>1</sup> Sexual and gender minoritized (SGM) populations, also known as the LGBTQI+ (Lesbian, Gay, Bisexual, Transgender, Queer/Questioning, Intersex, plus) communities, are among these populations. DEI efforts focused on LGBTQI+ populations are essen-

tial for mitigating historic marginalization of these groups in research. Yet, in their current form, DEI efforts aimed at LGBTQI+ populations risk reinforcing the harmful assumptions and gaps in knowledge that they seek to ameliorate.

LGBTQI+ populations contain sexual diversity across groups defined by sex assigned at birth, sexual orientation, and gender identity (SSOGI). They are seen to do this mostly across groups defined by social identities, including how a person identifies in terms of sex,

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and gender identities and sexual orientation. We provide in this paper a reminder that SSOGI data capture only a few aspects of sexual diversity and recommend that “sexual diversity” also include variations in identities, behaviors, physical traits, and other characteristics that inform the definition.

In this article, we demonstrate how DEI efforts to recruit and include LGBTQI+ populations are on a collision course with efforts to understand the influences of sex and gender in Alzheimer’s disease and related dementias (ADRD) research.<sup>2,3</sup> We argue that efforts aimed at increased inclusion of transgender identities through a new set of SSOGI data ultimately oversimplify sex and gender, ignoring the relevance of sexual diversity to all study participants while unintentionally pigeonholing questions about sexual diversity in LGBTQI+ communities. We review extant ADRD literature to show how analyses of social factors beyond individual identity can more thoroughly capture how sexual diversity shapes social and structural determinants of health as ADRD outcomes. We propose that, in addition to being LGBTQI+ focused, DEI efforts that expand how scientists consider and measure sexual diversity itself need to be envisioned.

## 2 | DEI EFFORTS FOCUSED ON SEXUAL DIVERSITY ARE USEFUL

DEI efforts have been developed to focus on sexual diversity with the intent of addressing two related issues in biomedical research. First, the representation of social and biological diversity of research samples. Inclusion of LGBTQI+ populations in research samples helps to broaden the generalizability of the results generated from those samples and helps to generate knowledge about the social and structural pressures that can disproportionately affect these populations. Research findings can be informative to both taking steps to improve the generalizability of research results and understanding social and structural pressures that lead to health and healthcare disparities. Inclusion of LGBTQI+ populations also facilitates buy-in from these populations about the value and applicability of scientific discoveries, while taking seriously a key social and structural determinant of health in often underserved populations.<sup>4</sup>

Second, inclusion of sexual diversity, broadly, helps achieve the goals of biomedical research. While people share far fewer differences than they do commonalities, sexual diversity refers to a range of social and physiological factors that contribute to those differences. For example, social categories based on sexual diversity ground both historical and present-day social injustices affecting biomedical science. Women continue to be underrepresented,<sup>5,6</sup> under cited,<sup>7</sup> and less often promoted in many areas biomedical research,<sup>6,7</sup> and 90% of drugs approved by the United States Food and Drug Administration lack sufficient data to determine their safe use during pregnancy.<sup>8</sup> Inclusion of a wide variety of aspects of sexual diversity in biomedical research is essential for ensuring equitable availability of interventions and care. Moreover, detailed study of sexual diversity in mechanisms may aid discoveries about causal pathways.

## 3 | DEFINITIONS OF SEX AND GENDER

A foundational problem affecting research on the influences of sex and gender (which we henceforth refer to as “sex/gender” to reflect the inseparability of the two concepts; see Rubin<sup>9</sup> and Butler<sup>10</sup>) is ongoing disagreement about what these terms mean. Much has been written, including in the biomedical sciences, about the varied definitions that have been used to describe both terms. A full accounting of this rich body of work is beyond the scope of this article. What we present here is, however, based in the principles that this scholarship has developed: namely, that “sex” is a historically contingent designation of a constellation of traits and processes, and, like gender, is socially constructed.<sup>11–15</sup> In the context of biomedicine specifically, this means that we cannot assume that we are all talking about the same thing when we say “male” or “female,” or “woman” or “man,” because what sex is routinely differs from one study to another.

This multiplicity of definitions is further complicated by efforts to split gender from sex. A distinction intended to integrate social factors into biomedicine. In 2016 and again in 2021, the National Institutes of Health (NIH) clarified its definitions for sex and gender with the intention of supporting scientists with a shared set of distinct concepts to guide the research process. The NIH defines sex as a biological concept that consists of chromosomal measurement, sex organs, endogenous hormones, and other features encoded in DNA that typically characterize differences between men and women (note the many traits that all come under the heading of “sex”). In contrast, NIH defines gender as consisting of enacted roles and behaviors that occur in historical and cultural contexts.<sup>16</sup>

By framing gender as a distinct social contributor, the influences of social factors on biomedical outcomes can become more obtuse. For example, in bench science, gender is considered irrelevant. Indeed, by focusing DEI interventions related to sex/gender on questions of identity, researchers may miss the ways that social experiences of gender influence biological outcomes. Moreover, the social experiences of gender exert incredibly varied effects because gender is not experienced in the same way by all people in a given category.<sup>17</sup> In ADRD research, this problem has numerous downstream consequences that ultimately limit how inclusion of sexual diversity can contribute to scientific understanding. The rest of this paper provides examples of this problem in action and offers a vision of DEI efforts that could serve as alternative approaches.

## 4 | SSOGI QUESTIONS

One of the most pressing areas for DEI intervention on behalf of sexual diversity in ADRD research, and a place where these problems immediately manifest, is data collection. SSOGI questions will soon be added to the National Alzheimer’s Disease Coordinating Center’s (NACC) Uniform Data Set version 4 (UDS 4). SSOGI questions use a two-step model that asks a person to report their sex assigned at birth and their current gender identity.

**TABLE 1** Summary of sex and gender self-report questions in Alzheimer's disease research

Sex	Gender	Sexual orientation
Subjects sex: 1. Male 2. Female	Please select your gender identity: 1. Male 2. Female	What is your sexual orientation? <sup>a</sup> 1. Bisexual 2. Gay 3. Lesbian 4. Straight (heterosexual) 5. Questioning or unsure 6. Other 7. Prefer not to answer
What sex do you consider yourself? 1. Male 2. Female 3. Don't know 4. Refused	Please select your gender identity: 1. Male 2. Female 3. Nonbinary/genderfluid	
What was your sex at birth? <sup>a</sup> 1. Female 2. Male		

Note: Questions are listed by frequency of appearance from highest to lowest in longitudinal cohort studies of older adults that were or are currently funded by the National Institute on Aging. Data from two Alzheimer's Disease Research Centers (ADRCs) are missing. One ADRC had no written protocol for asking these questions, and one ADRC had documentation that did not permit inclusion in the table: "Coordinators obtain study consent and, if applicable, brain donation consent ... Participant demographics and family history are also tabulated."

<sup>a</sup>Obtained from an existing source such as medical record, insurance record, or other secondary record.

The question about sex assigned at birth is expected to improve upon the existing model. It will expand the number of response categories to include an option for intersex individuals who have that status documented on their original birth certificate, and is more specific than the common approach which has been administered with lack of attention to the question structure or administration protocol (Table 1).<sup>18,19</sup> In some cases, for example, responses to the existing single-question model are not actually self-reported but rather what research staff documents, based on their own interpretation of a particular participant's gender presentation.

Some scientists have argued that the SSOGI approach of asking about self-report sex as assigned at birth and current gender identity would help discern between the constructs of sex and gender.<sup>20</sup> Some transgender men, for example, could be identified by the incongruence between two questions that ask, "What sex were you assigned on your original birth certificate?" (in this case, "female") and "What is your current gender identity?" (in this case, "male"). Introduction of these types of two-step identity questions may help promote cultural inclusivity of some SGM populations and build ADRD science toward better inventories of social groups participating in research. Kronk et al<sup>21</sup> offers such an example.

However, while the two-step question method ostensibly seeks to allow for increased specificity of sex and gender identification and greater inclusion of transgender populations, the approach risks solidifying an overly simplistic conception of social "gender" and biological "sex." Both of these items, like the previous one-question method,<sup>18</sup> rest on social and psychological concepts of identity. Social identity refers to people's self-categorizations in relation to their group memberships, and personal identity refers to how we define ourselves and what differentiates us from others within a social identity group.<sup>22,23</sup>

Here, at the time of enrollment in ADRD science, these aspects of identity are being used for biomedical classification without acknowledgement that neither is purely biological, nor purely social. In other words, "sex" is just as much of an individual identity as "gender," since it still relies on a social process of self-definition and distinction, and the two cannot be fully parsed from each other. In fact, there is often significant overlap in how participants answer these questions.

## 5 | PROBLEMATIC CONSEQUENCES OF SSOGI ANALYSIS ACROSS CATEGORIES

The typical approach to studying sexual diversity in biomedical science is troubled. Sex/gender identity data are analyzed, simultaneously, as both biological proxies (indirect measures of other features) and demographic classifiers (attributes of social groups used to describe samples), such that identity stands in for social influences or direct measures.<sup>18,19</sup> Research based on these data primarily asks questions about differences related to identity categories, with the implication that membership in the category itself causes that difference.

This approach has been used a lot in ADRD research, and many ADRD studies demonstrate that a wide range of factors differ between self-reported men and women, including cognitive performance, rates of dementia diagnosis, rates of atrophy and disease progression, functional outcomes, caregiving, and participation in research among many others.<sup>24-27</sup> Yet, little is known about the mechanisms of the differences.<sup>28</sup> Research progress is stymied, conducting comparisons that reveal group differences, without advancing what is known about causal pathways. In an attempt to overcome this issue (and conform to NIH definitions), some studies designate sex/gender identity responses

**TABLE 2** Case examples<sup>a</sup> of ways exclusive reliance on sex/gender identity categories undermine goals of biomedical science

Case example	Empirical implication	Equity implication
Men are more variable on most measures of quantitative and visuospatial ability, which necessarily results in more males at both high- and low-ability extremes.	The reasons why males are often more variable remain unknown.	This observation supports judgments and sets expectations for males/men.
Women tend to excel in verbal abilities, which are skills supporting high-level achievement in science and math as the subjects require the ability to communicate effectively and comprehend abstract ideas.	Factors that support strong verbal abilities remain unknown.	Despite this female advantage, women in science are under-cited <sup>7</sup> , and professionally under-recognized <sup>5,6</sup> relative to male counterparts.
Sex differences in science and math achievement and ability are smaller in the mid-range of the abilities' distribution than they are for those with the highest levels of achievement and ability.	A focus on normative identity groups may lead to average group effects that obscure meaningful differences and insights.	This may produce an extractive focus on transgender identities as a non-normative source of sexual diversity and position these groups as outliers without questioning normative categories.
Sex, gender identity, and sexual orientation categories are not expected to be stable over time. Biological factors, societal trends, and individual psychology change over the life course.	The interpretation of the measure(s) may not be the same over time and place.	Science may become seen as increasingly out of step with LGBTQIA+ needs and lose participant trust.
Use of SSOGI expands opportunities for some additional, historically marginalized identities. Identification with these categories is expected to be low. Practically speaking, the minority will be too small for analysis and be excluded.	Cells with low frequencies are often dropped from analysis.	The overwhelming majority reinforces the overlap of the two types of categories, gender and sex, thereby reinforcing normative groupings.

Abbreviation: SSOGI, sex assigned at birth, sexual orientation, and gender identity.

<sup>a</sup>Case examples adapted from Halpern et al., 2007.<sup>29</sup>

as either predominantly biological or social, when in daily life one informs the other in indistinguishable ways.

To make this point more plain, we describe two well documented case examples of the sex/gender differences in science and math achievement and ability (Table 2). There has been speculation about the underlying reasons for the differences, with consensus among scientists being that the effects could be indirectly related to differences in interests and specific brain and cognitive systems. The analysis of sex/gender identity groups has yielded no data on the causal mechanisms, which is a fundamental goal of biomedical science. The approach has, however, contributed to problematic stereotype threat, which we discuss later, and has potentially obscured identifying root causes as these differences are nonlinear; sex differences in science and math achievement and ability are smaller for the mid-range of the abilities distribution than they are for those with the highest levels of achievement and ability.

These limitations in the general approach are unlikely to be addressed in the replacement of the single self-report sex/gender question, which has been asked in ADRD science over recent decades, with two-step SSOGI questions. The introduction of the SSOGI questions also poses two distinct challenges. First, as long as there is an interest in splitting biological from social factors by way of discerning sex from gender, transgender populations may be conceptually reduced to solely the sexual diversity their data offer while they continue to lack equitable access to quality, informed healthcare. As data are developed from SSOGI items, those data will likely also be analyzed using the approach of between-group comparison. Thus, SSOGI responses that appear incongruous between two-step identity questions—sex

assigned at birth and current gender identity—may become a much sought after source and focus of sexual diversity.

Variance located in transgender populations along with that from analyses between categories of self-report men/males and women/females may, erroneously, be considered the primary sources of sexual diversity in ADRD research. In a prior review of peer-reviewed biomedical literature,<sup>19</sup> we found a heavy reliance on data from self-report identity questions ( $n = 1233$ , 97%). Most studies in our review used responses from self-report questions to characterize and compare research participants' sex or gender identities ( $n = 1233$  of 1398, 88%). Only about one in five empirical studies ( $n = 237$ , 18.7%) used structured self-report measures other than single-item sex/gender identity question in data analysis.

This approach to studying sexual diversity has informed the bulk of what is currently understood about sex and gender in ADRD research; studies have relied almost exclusively on between-group comparisons of self-report sex/gender identity measures.<sup>30–34</sup> The combination of sex/gender as proxy for some unspecified variable(s) and research objective being a search for difference renders invisible what variable matters and what targets might benefit from interventions. This ultimately results in less useful research for all populations. In each case, sex/gender is uncritically imbued with a range of meanings for which no evidence or rationale for the measure is given. As a result, our existing knowledge is built upon assumptions and ambiguities.

These limitations in combination with the NIH's contemporaneous goal of understanding the influences of sex and gender in ADRD research may lead to problems and missed opportunities if ADRD scientists do not intentionally guide the efforts. Funding and other

resources are motivating researchers to collect SSOGI data and to conduct research on the effects of sex and gender on disease risk, progression, and clinical presentation of ADRD, but more nuanced approaches are needed to avoid the pitfalls outlined above.<sup>2,3</sup>

## 6 | A NEW LENS FOR SEX, GENDER, SEXUAL ORIENTATION, AND, BROADLY, SEXUAL DIVERSITY

Approaches that are expansive of sexual diversity are essential to achieve the NIH's goals of discovering mechanisms of influence related to sexual diversity. Scientists also have a responsibility to ensure nuanced consideration of identity categories in biomedical research, to be sure, as these categories can have serious social consequences. This cannot, however, be the endpoint. What qualifies as sexual diversity and what constitutes the effects of sexual diversity must expand beyond identity categories. DEI approaches, across the totality of research activities,<sup>35</sup> will be crucial to this expansion.

Simply adding more categories, however, is inadequate; while including more cisgender women, and now increasingly, more transgender and intersex people, in biomedical research is certainly better than assuming a universal male subject, an additive approach still does not unburden sex/gender identity from the meanings it is given in research, or critically examine the specific factors that may inform specific pathways. Elsewhere, we have summarized a review of the measures of sexual diversity that have been used and published in the peer reviewed biomedical science.<sup>19</sup> In the following sections, we offer discussion to broaden the lens through which researchers approach sexual diversity in scientific investigations, with a focus on facilitating science that promotes social equity, discovers causal associations, and produces widely generalizable outputs (Table 3).

In the following two sections, we offer explanations of how sex/gender identity can operate as a social and structural determinant of ADRD outcomes. These discussions may be most useful if taken as case examples for considering sex/gender identity data beyond between-group comparisons in ways that reflect efforts to expand conceptual frameworks, rather than defaulting to adding measures. We describe pathways through social policy and individuals' social and psychological experiences that may be shaped but not determined by sex/gender. These may reflect normative experiences for a given identity group rather than an inherent sex-based difference. By characterizing and studying these and other within-group factors, DEI efforts may be able to better characterize the sociocultural representation of research samples and guide analysis and interpretation of study findings.

## 7 | SEX/GENDER IDENTITY INFORMS SOCIAL POLICY AND HAS EFFECTS REINFORCED THROUGH SOCIAL POLICY

Sex/gender is a known social and structural determinant of health that is relevant to understanding ADRD outcomes.<sup>36,37</sup> Conceptual-

izing the influence of sex/gender through social systems offers ADRD researchers access to a tool for DEI science. The approach may help to more cogently situate individuals in systemic experiences; individuals can be linked to ADRD-relevant exposures driven by sex/gender identity. This permits consideration of (1) sex/gender representation in ADRD research samples to extend self-report identity to include social and psychological experiences that are informed by sex/gender, (2) systemic factors that may vary with time and place, and (3) more precise measures rather than using sex/gender as a proxy for unmeasured factors. Here, we explore the influences of sex/gender through systems of policy and psychology. We discuss applying this approach to characterizing and analyzing individuals in ADRD research.

Examining how social policy shapes and is shaped by sex/gender identity may help detect effects on ADRD outcomes related to sexual diversity. In turn, this may help identify specific features that can be measured to expand the variance captured by sex/gender identity questions alone. We discuss two ways sex/gender identity operates in social policy to determine ADRD outcomes: a modifier of risk and access to resources. Policies compound a society's architecture in two main ways, dictating a person's direct experiences and available resources. We offer examples of each.

Sex/gender specific policies determine individuals' experiences in ways that can alter dementia risk. One example of this is the Selective Training and Service Act of 1940, which made possible the Vietnam draft. Between 1964 and 1973, the US military drafted 2.2 million American men into military service. Another 1.4 million American men had already been inducted into the US military from 1954 to 1964, from the end of the Korean War until the escalation in Vietnam. These surviving individuals are now part of the current US aging population.

Participation in the military impacts ADRD risk by, among other factors, increasing exposure to environmental toxins and poor air quality, traumatic brain injuries, and cardiovascular damage related to alcohol, tobacco, and poor sleep. Military service also alters the course of survivorship, an issue researchers contend with frequently in ADRD research studies. The draft had many consequences to individuals that were, to be sure, the result of being men at a moment when membership in that category was linked to military participation. However, the increased risks, despite being sex/gender linked, were neither a result of personal identity nor an inherent biological state; they reflect consequences of the social construction of experience through policy.

Indeed, men had very different experiences based on how they chose to contend with the prescribed nature of military participation. In addition to the millions who were required to serve in the military, the draft also caused many young American men to volunteer for the armed forces. By volunteering—before potentially being drafted—they would have more of a choice of the military division in which they would serve. Presumably, those who volunteered would have chosen less hazardous posts than those who did not have a choice.

For young men who did not support the Vietnam war, the draft shaped their risk of ADRD through their efforts to avoid military participation. Some, for example, sought refuge in college as the Selective Service granted deferments of service to college students with an academic ranking in the top half of their class. This offers an instance of

**TABLE 3** Action steps to improve study of sexual diversity in Alzheimer's disease and related dementia research

Goal	Approach	Rationale
Health and social equity	Use gender informed theory.	Maximize beneficial interpretations and minimize potential harms by using theories that consider the specific needs and cultural biases of consequence to investigating and interpreting study effects.
	Conceptualize the influence of sex/gender through social systems as an investigative tool.	Identify pathways for structural influences on ADRD outcomes and opportunities to mitigate detrimental effects.
	Disconnect biological from social identity.	Avoid biological essentialism.
	Include sexual diversity experts and use the most appropriate measures. Interdisciplinary expertise on measurement, sociology, and/or physiology or other areas may also be appropriate given the range of effects that can be due to sexual diversity. In the absence of resources to appropriately undertake these tasks, do not take on issues of sexual diversity in the project.	It's essential to conduct sound quality research on sexual diversity. If not properly situated to conduct a study, invest in building toward it, rather than conduct an inferior version that risks perpetuating harms.
Generalizability	Assess research protocols and settings for sexism and gender bias, such as that introduced by stereotype threat.	Create a safe and welcoming space for colleagues and research participants and ensure quality in data collection.
	Categorize and characterize research participants according to multiple aspects of sexual diversity.	Evaluate the representation, or lack thereof, of social groups and transparently report the findings.
Identification of causal pathways	Conceptualize the influence of sex/gender through social systems as an investigative tool.	Evaluate the representation, or lack thereof, of social groups. For example, men may be proportionally represented in a sample but those who are veterans, which are a significant swath of the general population of certain ages, may be unrepresented.
	Categorize, or if appropriate ask participants to categorize themselves, into groups based on properties of sexual diversity that are relevant to question under study.	Improve methods to identify causal pathways.
	Select features of sexual diversity more theoretically relevant and proximal to the mechanism under study. This may include structural features, such as those created by social policy.	Improve research designs to identify causal pathways.

Abbreviation: ADRD, Alzheimer's disease and related dementia.

how a segment of a sex/gender identity group may have had exposure to a factor, namely higher education, that is known to mitigate ADRD risk. Categorization by sex/gender nor education would, on their own, provide this more nuanced information. Thus, underscoring the importance of studying intersectionality in sexual diversity.

There are substantive differences within sex/gender categories that may be the consequence of social policies. While there has been some investigation as to the effects of this on ADRD outcomes, much of the variance remains unexamined. Moreover, these effects are not commonly recognized or appreciated as aspects of sexual diversity in ADRD research. However, policy that influences—in some cases even dictates—individuals' lived experiences based on sex/gender also informs an individual's identity and behaviors, which in turn affect a person's health and wellbeing.

Another example of social policy's intersection with sex/gender is how it influences the populations in ADRD research. This occurs in several ways: access to care, prioritization of resources and support, and participation in research. In the American context, availability of

socioeconomic resources shapes access to ADRD diagnosis and care, and US policy generally is designed to support spousal relationships and some parent-child relationships.<sup>38</sup> Historically, and in many places globally, policy-based definitions of these relationships have focused on heterosexual spousal dyads and parent-child relationships; access to health insurance, inheritance, and various tax benefits, for example, are linked to marriage in the United States, which until very recently was limited to heterosexual couples and continues to be informed by structural sex/gender influences.<sup>39</sup> In ADRD research and care, spousal dyads are the most prominent relationship type between research participants and study partners and between patients and care partners.<sup>40</sup> This reflects the resource support from public policies related to finance, education, military, and occupation. In these dyads, men are often the primary beneficiaries of the financial and resource wealth while women access this wealth through their husbands.

The effects of these conditions on women are particularly stark. Women with ADRD are more likely than men to be institutionalized in a nursing home in the later stages of the disease course. Some

sources suggest that this sex/gender disparity is because men possess the financial resources—due to higher education, earning potential, career options—to pay for institutional care and lack the social skills to care for their spouses at home. It is also possible that, due to excess morbidity, potentially from exposure to war, manual labor jobs, and other social factors, men of some times and places may be generally less able to care for their spouses. Economists estimate that women bear six times the costs associated with ADRD as compared to men because of the informal care they deliver, thanks to expectations that women will serve as caregivers.<sup>41</sup> These are instances of potentially modifiable variables exerting significant effects on disease outcome, which would be rendered invisible if considered to be a product of sex/gender itself.

While it may seem daunting to consider the effects of broad social disparities arising from policies acting on sex/gender, DEI initiatives can build research processes that recognize these disparities. These processes can ensure that studies' recruitment and enrollment practices have mechanisms to offset these disparities. Changes that result from these efforts may aid in counteracting policies and systemic issues that have granted certain life chances to some and not others. Further advancing DEI efforts to generate a context-informed understanding of sex/gender may aid in addressing the representation of a fuller range of sexual diversity in research, and generating knowledge that can drive social policy.

## 8 | SEX/GENDER IDENTITY AFFECTS A PERSON'S SOCIAL AND PSYCHOLOGICAL EXPERIENCES

Understanding how an individual's sex/gender identity impacts daily life may help improve DEI strategies for recruitment, reduce bias between participating groups, and improve clinical research effectiveness by better explicating mechanisms, and informing development of individual-level interventions aimed at modifying ADRD outcomes. For example, relatively fewer men than women participate in ADRD research.<sup>42</sup> The men who do participate are also more likely to be married, and have children, than men with other sociocultural correlates.<sup>42</sup> Men, on average, also have a lower intention to join an ADRD research registry.<sup>43</sup> These findings raise questions about the sociocultural and psychological factors that may be supporting these outcomes.

Socially-created and reinforced gender patterns, such as those associated with an illness narrative, may affect ADRD research participation. A 2019 study conducted by Law that used gender-informed theory to understand participation of men in reproductive research concluded that men lacked a narrative that supported their participation, and therefore did not participate, leading to low representation of men in this research.<sup>44</sup> In other words, men tended not to perceive their participation as making a valuable contribution to the research. Given that AD disproportionately affects women, it seems plausible that men could experience a similar lack of relevance with respect to ADRD research.

Similar to how sex/gender identity may correlate with factors affecting participation in research, sex/gender identity may correspond to social and psychological experiences that can influence the research

experience. Because sex/gender identity shapes social experiences, it can exert differential effects in social situations, such as research settings. Some of these effects, such as stereotype threat, are evident in findings from psychological and social experiments.<sup>45</sup> Sex/gender identity can affect experiences of stereotype threat. Women experiencing stereotype threat can show substantially reduced short-term memory capacity relative to women in a low-stereotype threat condition and men.<sup>45</sup> The mechanism is thought to be that stereotype threat either increases or decreases situationally-specific anxiety.<sup>45</sup> Both memory effects and anxiety are key patient outcomes in ADRD.<sup>46</sup> Understanding these effects is crucial for ensuring the research environment does not differentially effect certain groups of participants.

In a well-known study by Spence, Steele, and Quinn, women performed substantially worse than equally qualified men on a test that was described as having gender differences in performance.<sup>47</sup> The difference in performance was eliminated when the stereotype threat was lowered by describing the test as not producing gender differences. The degree to which research settings and tasks might induce gender specific results warrants attention. DEI efforts that routinely examine gender effects may help ensure research practices are not introducing unintended effects through their choice of methods and protocols, and thus ensure more accurate research results.

## 9 | CONCLUSION: ACTION STEPS FOR A NOVEL APPROACH TO DEI INITIATIVES IN ADRD RESEARCH

In this paper, we have described how understandings of sexual diversity in ADRD have focused almost exclusively on identity. With the adoption of SSOGI items, the number of categories may increase. The continued focus on identity is likely to place the new data on a problematic trajectory with efforts to explicate influences of sex and gender on disease mechanisms. Thus, DEI efforts are needed across the continuum of research activities to broaden the focus on sexual diversity. To this end, we outlined examples that explore the influences of sex/gender identity through systems of policy and psychology.

The ADRD field has relied heavily on sex/gender identity with the goals of extrapolating social, psychological, and biological influences on ADRD mechanisms. The addition of SSOGI questions to the collection of standard demographic data in ADRD science raises concerns for how these data may be exploited as the major, if not only, source of sex/gender variance used by ADRD scientists. This presents a two-part problem for ADRD scientists as it may stymie the benefits that are anticipated from including SGM populations and burden individuals with unforeseen consequences of participation in research, while also hindering efforts to explicate the effects of sexual diversity on ADRD mechanisms.

Sexual diversity is vast, encompassing many qualities that include behaviors, life experiences, and genetics, among others. We propose that one avenue for expanding the aspects of sexual diversity that are considered in ADRD research is to capture those features that

have been the subject of social policy. In our examples, we identified veteran status and spousal relationship experiences as potential areas for further consideration. Understanding the effects of sex/gender identity via social policy may be useful for identifying experiences that are likely to affect large subpopulations and can be linked to specific time periods. These features add value for researchers, who study time dependent mechanisms (i.e., age) and aim to generate knowledge that is applicable to large populations. This approach of using policy analysis to identify features of the experience of sex/gender diversity also has other benefits. DEI efforts to enhance sociocultural representation rely on understanding what groups are missing from research samples and appreciating the value that would be added by their participation in the research process. By analyzing policy to identify relevant covariates, researchers may be able to (1) compare and contrast effects across geopolitical boundaries and time periods that do and do not have specific policies, and (2) anticipate the types of measures that might be needed as populations age that have experienced given policies.

This in turn avoids the use of sex/gender identity as an oversimplified biological proxy. Identity has historically served as a proxy for biological measures including chromosomes, gonads, hormones, genitals, metabolism, immune system, and stature, among others.<sup>48,49</sup> This has unnecessarily introduced vagueness into research and prevented more specific understandings of the physiological processes relevant beyond merely categorization as male/man or female/woman. Measures of biological variance, independent of identity category, are needed to characterize and assess biological diversity.

Over recent decades, for example, sex differences in careers in science and mathematics have become well-known and often discussed. Yet, little is known about what drives these differences. We suspect a significant reason for the stymied progress is the rigid and overdetermined categorization of sexual diversity. More specifically, while categorization of self-report identity is not itself a problem, the social consequences and downstream psychological pressures associated with the rigid and overdetermined meanings of the categories are problems. The scientific pursuit of understanding influences of sexual diversity and promoting social justice are better contributors to science than reification of social groupings.

DEI science is positioned to offer the field new tools to overcome these pitfalls with a new lens for sexual diversity in ADRD. To do so, DEI focused on sexual diversity are needed across the spectrum of research activities. Currently, data on sexual diversity have been almost exclusively obtained from self-report identity questions in ADRD research. Policy analyses and psychological models may be useful in expanding what is considered part of sexual diversity. This approach may aid in identifying additional features that, if routinely assessed, may offer details to more fully assess the representation of research samples. Sociological measures, including veteran status and schooling, may be useful for categorizing social impacts of sex/gender identity on individuals. Focusing on the social and psychological effects stemming from the social treatment of individuals on the basis of sex/gender identity—such as stereotype threat reactions—may offer novel and useful insights in clinical research.

## AUTHOR CONTRIBUTIONS

Shana D. Stites and Beans Velocci co-wrote the article. Shana D. Stites contributed the initial draft.

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## CONFLICT OF INTEREST STATEMENT

The authors have no conflicts to disclose. Author disclosures are available in the [supporting information](#).

## HUMAN PARTICIPANT PROTECTION

The Institutional Review Board of the University of Pennsylvania approved all procedures involving human subjects.

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