Received: 9 May 2022 | Revised: 19 July 2022 | Accepted: 23 August 2022

DOI: 10.1002/dad2.12359

Alzheimer's & Dementia
Diagnosis, Assessment & Disease Monitoring

REVIEW ARTICLE

A systematic review of measures of gender and biological sex: Exploring candidates for Alzheimer's disease and related dementias (AD/ADRD) research

Shana D. Stites PsyDMSMA[1] | **Hannah Cao MSW**[2] | **Richard James MSLIS**[3] | **Kristin Harkins MPH**[4] | **Cameron Coykendall BA**[4] | **Jason D. Flatt PhDMPH**[5]

[1]Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA

[2]School of Social Policy and Practice, University of Pennsylvania, Philadelphia, Pennsylvania, USA

[3]University of Pennsylvania Libraries, Philadelphia, Pennsylvania, USA

[4]Division of Geriatric Medicine, Department of Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA

[5]Department of Social and Behavioral Health, School of Public Health, University of Nevada, Las Vegas, Nevada, USA

Correspondence
Shana Stites, University of Pennsylvania, 3615 Chestnut St. Philadelphia, PA 19104, USA.
Email: Stites@UPenn.edu

Funding information
National Institute on Aging, Grant/Award Numbers: U24AG058556, K23AG065442, K01AG056669, 3K23AG065442-03S1; the Alzheimer's Association, Grant/Award Number: AARF-17-528934

Abstract

Background: Gender and biological sex are social and structural determinants of health and umbrella concepts encompassing many distinct attributes. This systematic review summarizes measures of gender and biological sex published in the biomedical literature. The goal was to identify measures that may be useful to researchers studying Alzheimer's disease and Alzheimer's disease related dementias (AD/ADRD).

Methods: A search of PubMed, Embase, and PsycINFO (ProQuest platform) databases from 2000 to 2021 identified 1454 articles, which were then screened by five independent reviewers. Measures of gender and biological sex are summarized according to theoretical commitments and psychometric properties.

Results: Twenty-nine measures were identified that assessed gender-related constructs, and 4 were identified that assessed biological factors. Self-report instruments characterized aspects of gender, such as gender stereotypes, norms, and ideologies. One measure was developed with a focus on older adults (65+ years).

Discussion: We offer recommendations to guide measurement of gender in AD/ADRD research, including how the use of specific existing measures may help advance AD/ADRD research. The lack of gender measures for older adults limits AD/ADRD research. New measures may be needed to address lifespan and generational differences in gender factors.

Highlights

- A review of articles identifies 29 measures of gender in biomedical research.
- Gender is captured using multidimensional, self-reported concepts.
- One measure was developed with a focus on older adults (65+).

1 | INTRODUCTION

The United States (US) has set an ambitious national goal to understand the impact of sex and gender on the trajectories of brain aging and disease, phenotypes of dementia risk and responsiveness to treatment, and influences of gender on disease mechanisms.[1] The US government 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. The World Health Organization has a similar definition while also explicitly acknowledging the characteristics are not mutually exclusive, as there are individuals who possess both.[2] *Gender*, by contrast, is socially constructed and consists of enacted roles and behaviors that occur in historical and cultural contexts.[3] Achieving this national goal will require scrutinizing how sex and gender are understood and measured in Alzheimer's disease and Alzheimer's disease-related dementias (AD/ADRD) research.

Sex, also referred to as biological sex, and gender are well-known social and structural determinants of health (SSDoH). They shape environmental conditions where individuals are born, live, learn, work, and age. As a result, they can impact an individual's risk for AD/ADRD, ability to receive a diagnosis, and ability to optimize treatment and care.[4]

Studying sex and gender may help explain heterogeneity in cognitive, functional, biomarker, and interventional outcomes in AD/ADRD research and clinical care. Initiatives that bring a focus on sex and gender may also help improve inclusion and equity for sexual and gender minoritized (SGM) populations and reduce disparities in care for all patients. Advancing what is understood about how sex and gender impact experiences of AD/ADRD could lead to multiple opportunities to improve health outcomes and healthcare for individuals living with AD/ADRD and their families.

Measures are needed in order to access the benefits of studying sex and gender in AD/ADRD research. Sex and gender are broad concepts encompassing many distinct attributes.[1,3] The specific AD/ADRD outcomes they affect are highly varied.[5–7] Thus, their attributes influencing those outcomes are likely also varied. In other words, a gender measure intended to investigate its influences in caregiver decision-making will likely differ from one intended to investigate its influences on patient cognition. To discover specific influences of sex and gender in the AD/ADRD research, researchers need to develop standardized concepts and a repertoire of measures for characterizing sex and gender.

We conducted a review of the biomedical literature to summarize existing measures of sex and gender. The goal is to outline gaps and needs with respect to instrumentation for sex and gender in AD/ADRD research. Our findings may help researchers identify existing measures of sex and gender that would be relevant to their research programs and offer a guide for future research to advance study of sex and gender in AD/ADRD research.

1.1 | Basis of sex and gender informed studies in AD/ADRD research

The AD/ADRD outcomes that have been demonstrated to differ between men and women are far ranging, impacting many aspects of the disease experience from bench to bedside.[5–8] Pathological mechanisms have been shown to differ; women show greater severity in disease presentation, including greater hippocampal volume loss, memory decline, and functional impairment.[9–17] In addition, social policies and practices that affect a person's likelihood of seeking and receiving a diagnosis have differential effects on men and women. About two-thirds of persons diagnosed with Alzheimer's disease (AD) are women and 3 in 5 informal caregivers are women.[18] Moreover, studies have shown cognitive outcomes and risk factors for dementia are differentially impacted in SGM populations.[19–21]

How older adults protect their cognitive health, reduce their risk for cognitive decline, and manage cognitive changes can all also vary between men and women.[22] This may have important implications for the development, effectiveness, and translation of risk reduction programs and disease-modifying interventions. In addition, studies conducted over a century have shown gender affects older adults' cognitive outcomes.[23] This may impact baseline risk for dementia as well as methods for diagnosis and measurement.

Advancing what is understood of how sex and gender impact the experience of AD/ADRD could, in several ways, lead to opportunities to improve care for individuals living with AD/ADRD and their families. It could help explicate factors that modify risk, progression, diagnosis, and quality of life for persons directly affected by the disease and the persons who care for them.

RESEARCH IN CONTEXT

1. **Systematic review**: There have been public calls to advance study of sex and gender in AD/ADRD research. The authors reviewed literature using traditional (e.g., PubMed) sources to identify and summarize measures of sex and gender used in biomedical research.
2. **Interpretation**: Findings inform methods for measuring and investigating sex and gender effects in AD/ADRD research that builds upon existing biomedical science.
3. **Future directions**: The manuscript summarizes extant sex and gender measures, points to applications of sex and gender in AD/ADRD investigations, and summarizes the use of sex and gender measures in biomedical science. The manuscript accomplishes these goals with consideration of how the constructs of sex and gender can vary globally with cultural context.

2 | METHODS

2.1 | Data sources

We conducted a search in the PubMed, Embase, and APA PsycInfo (ProQuest platform) databases for citations matching text keywords related to sex and gender. The three databases offer comprehensive coverage of available sources sufficient to support this systematic review. The Cochrane Handbook recommends a minimum of three databases for systematic reviews. A 2017 review of systematic review

research that evaluated the precision in searching multiple databases found that a combination of Embase and Medline/PubMed recalled about 92% of citations that would be recalled by searching in all four of the databases used in their study (Medline, Embase, Web of Science, and Google Scholar).[24] In our study, we use Embase, Medline/PubMed, and PsycINFO as a third topically relevant database.

2.2 | Search period

Our search focused on articles published between January 2000 to December 2021. The original search covered 2000 to mid-2020. In 2022, we updated the search through the 2021 calendar year.

In selecting the year 2000 as the start year of our search period, we considered the state of the biomedical literature with respect to the concepts under study and key US governing bodies that would have influenced the definitions and study of these concepts. We estimated that by the year 2000, the concepts of sex and gender would have iteratively evolved in meaning and measurement in the biomedical literature as to lend to a meaningful review. The key term "gender identity", for example, was not detectable in the written corpus until the 1960s and then did not appear in any significant way until around 2000 (Appendix Figure 1).

2.3 | Derivation of text keywords used in article identification

We formulated search criteria to identify articles using key terms that were derived from social and scientific histories of the ideas of sex and gender and included search terms related to gender such as "measuring gender," "gender-measure," "sex/gender sensitivity," "gender-role," "sex roles," "gender-norm," "gender stereotypes," "masculine," "feminine," "male," "female," "masculinities," "femininities". We also included parameters to ensure our search located articles that involved a "measure," "inventory," "instrument," or "test". Primary search syntax is shown in the e-appendix A. Supplemental searches of indexed and non-indexed literature were also conducted.

To avoid limiting the articles recalled on sex and gender, we did not include terms for AD/ADRD in the search. We conducted an intentionally broad search of the literature studying sex and/or gender. Our goal is to identify and evaluate all measures of sex and gender being used in biomedical science for their potential relevance in AD/ADRD research.

2.4 | Abstract inclusion and exclusion criteria

To characterize the use of general categories of measures (structured self-report measures, biological measures, etc.), we retrieved all records, excluding only animal studies (n = 25) and non-article publication types (n = 31).

We use two sets of inclusion and exclusion criteria. To identify and characterize specific measures of sex and gender, we included articles that referenced a measure of sex and/or gender in the abstract. A priori exclusion criteria were: articles reporting on studies on non-human research samples, non-English articles, articles reporting on non-US residents, and if the publication types were book reviews and conference abstracts.

2.5 | Analysis of articles

After deduplication of results (n = 141 duplicates removed), 1454 citations were exported to the systematic review processing software platform Rayyan[25] for coding and analysis. A team of five reviewers independently screened each abstract recalled in the original search to determine inclusion and exclusion (n = 1419). Two reviewers independently screened each abstract in the updated search (n = 35). Screening decisions were blinded, according to evolving inclusion/exclusion criteria derived by group discussion. After individual screening was completed, results were unblinded and conflicts and concerns were resolved through group discussion.

From the pool of included abstracts, two researchers independently screened articles to identify those that reported at least one variable for sex and/or gender in human subjects. Screening flow is shown in Figure 1. For articles that referenced a measure of sex and/or gender in the abstract, we retrieved the measures and summarized them on the basis of their theoretical commitments and properties. We also examined the applicability of measures to AD/ADRD and aging research with special attention to considerations of older adult populations and global populations.

We report descriptive statistics (frequencies and percentages) for all retrieved records except for animal studies (n = 25) and non-article publication types (n = 31). The total number of records in this analysis was 1398. This approach to analysis allows us to summarize practices on the use and reporting of sex and gender measures independent of cultural setting.

3 | RESULTS

We identified 1398 articles that reported sex and/or gender data. We summarize the sex and gender measures used in US samples on the basis of their theoretical commitments and properties. We also discuss the applicability of the measures to AD/ADRD and aging research. Table 1 offers a list of key terms and their definitions to aid clarity in our reporting.

3.1 | Self-report measures of sex, gender, and sex/gender

Most studies in our review used responses from self-report questions to characterize research participants' sex or gender identity (n = 1233 of 1398, 88%). The term gender was used in the majority of studies (n = 671, 54.4%). We also found about one-third (n = 407) reported

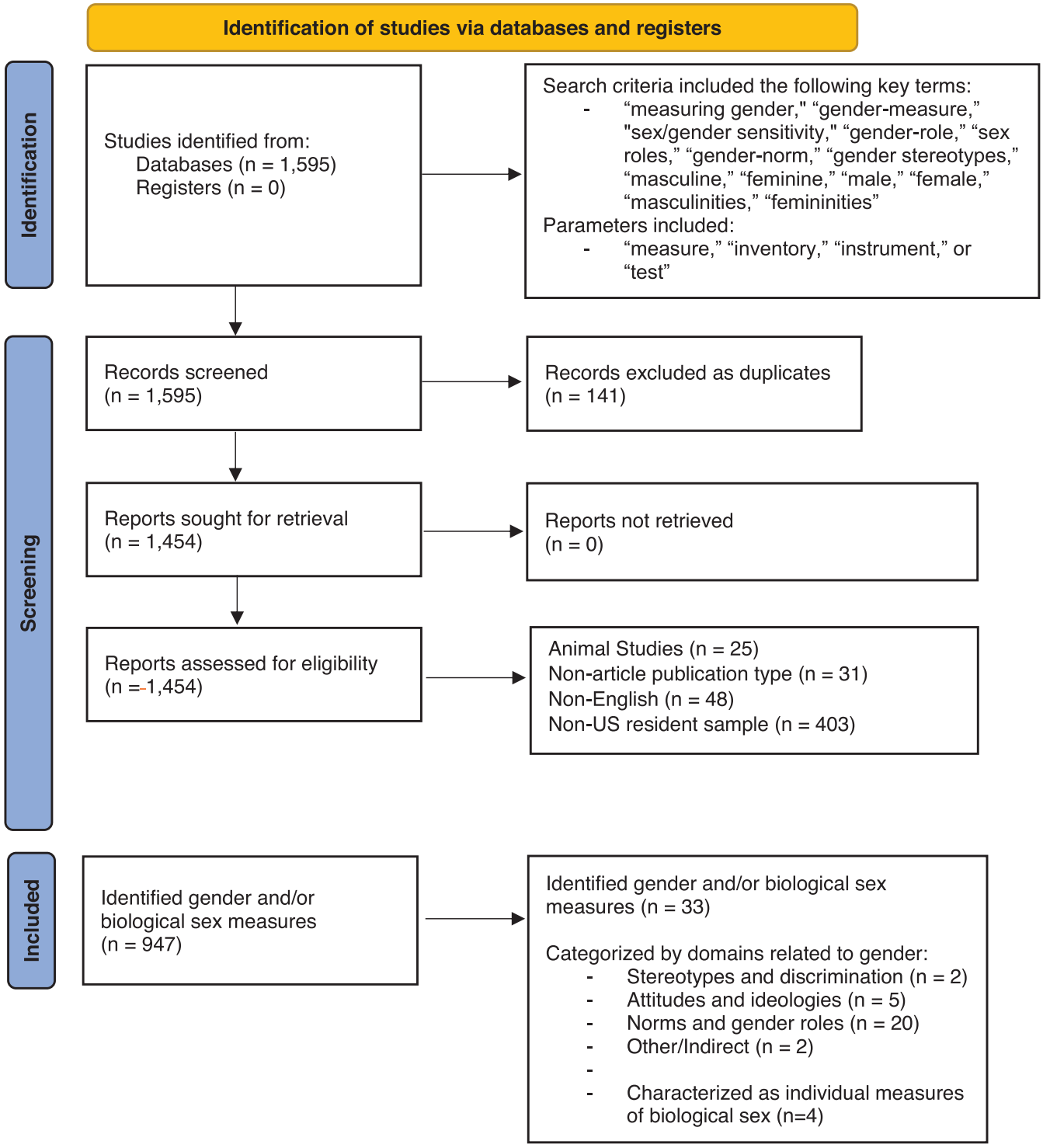


FIGURE 1 Screening flow of articles. *Note*: Excluded studies were: Animal studies = articles reporting on studies in non-human research samples. Non-english = articles published in languages other than English. Non-US resident samples = articles reporting on studies in research samples that do not include in United States residents. Excluded publication type = articles that reflect book reviews and conference abstracts.

responses to these identity questions using the term "sex". Some studies ($n = 155$), particularly those who included only men or only women, did not use either term.

In biomedical research, common practices for collecting sex/gender data ask research participants to self-identify or ask study staff members to make judgments as to which of these a priori categories best represent the participant.[26] Descriptions of the methods used to gather this information were not consistently reported.

We use the term "sex/gender" in reporting our findings when we could not discern that a concept pertained only to "sex" or "gender".

TABLE 1 Summary of sex and gender concepts reported in biomedical literature, 2000 to 2020

Concept	Definition
Gender norms	Gender norms define acceptable and appropriate actions for women and men in a given group or society. A common gender norm is that women and girls will and should do the majority of domestic work.
Person's sex as assigned at birth	An individual's assignment as male, female, or intersex based on observation of external genitalia at birth.
Biological sex	Sex is a biological concept that consists of chromosomal measurement, sex organs, endogenous hormones, and other features encoded in DNA that typically characterize differences across male, female, and intersex individuals.
Gender	Gender is socially constructed and consists of enacted roles and behaviors that occur in historical and cultural contexts.
Gender stereotypes	A gender stereotype is a generalized view or preconception about attributes, characteristics, or roles that are or ought to be possessed by, or performed by, women and men.
Gender ideology	Concerned with describing and explaining how views of men, women, and alternative gender categories differ across cultures.
Gender identity	An individual's internal sense of being a man, woman, or another identity.
Gender roles	Groups of attributes considered more appropriate for one sex or gender than another and have been shown to have both biological and social determinants.
Gender expression	Culturally ascribed ways that rights, responsibilities, and the identities of individuals are placed in relation to one another based on attributed gender categories.
Gender relations/relationships	Concept that captures culturally ascribed ways that rights, responsibilities, and the identities of individuals are placed in relation to one another based on attributed gender categories.
Gender role strain	Captures feelings of uncertainty that individuals may experience in doubting their abilities to fulfill culturally normative gender roles.

Single-item sex or gender identity questions, for example, are insufficient for distinguishing the social and biological concepts sex and gender. The items are typically used in biomedical science without definitions.[26] Thus, the reference being used by research participants when they are answering the questions is often unknown. Sophisticated versions of the questions may ask, for example, "what was your sex assigned at birth". This helps to narrow the definition, in this example, to genital sex. However, these types of questions are infrequently used ($n = 2$).

About a fifth of empirical studies ($n = 237$, 18.7) used structured self-report measures other than single-item sex/gender identity questions to gather data on gender. We identified 29 structured, multi-item measures of gender used in US-based samples (Table 2). Of the 29 gender measures we found, 27 were self-report tools. Respondents are asked to use Likert scales to rate how much they agree or affiliate with statements. Examples of statements are: (1) swearing/obscenity is unattractive in a woman, (2) men are expected to pay for all the expenses during a date, (3) it is the woman's responsibility to take care of the household, and (4) I feel bad about having multiple sexual partners.[32–34]

The 27 self-report measures assessed one or more of four domains related to gender: (1) stereotypes and discrimination, (2) attitudes and ideologies, (3) norms, and (4) gender/sex roles. We discuss the measures on each domain in order in this section. First, we identified two measures assessing stereotypes and discrimination. They aim to capture the intersectionality between race and culturally normative gender roles, and the effect on an individual's ability to behave according to those gender norms. Such measures of stereotypes and discrimination may be useful in studying effects of stigma and stereotyped threat in AD/ADRD patient and caregiver experiences. Stites et al.[27] offer discussion of the intersections between gender and AD stigma.

Second, we identified three instruments assessing attitudes. The instruments characterize respondents' reactions toward members of either their own or other genders. We also identified two measures that assessed gender ideologies, which are structural systems consisting of multiple attitudes, such as gender roles, norms, or behaviors.[28] Measures of attitudes and ideology may be useful in AD/ADRD studies of treatment experiences, research participation, and caregiver burden. Differences in gendered beliefs and attitudes, for example, may help explain disparities in anti-dementia medication use.[29]

Next, we identified three measures that assessed norms. Instruments measuring norms quantify respondents' affiliation with culturally determined gender roles. A closely related domain is sex roles, which are considered biologically determined such as breast feeding. Instruments in this category measure behavior characteristics in order to quantify how much respondents internalize or identify with the norms associated with a given role.

We found 19 measures of gender roles. The Bem Sex-Role Inventory (BSRI), for example, is a measure of masculinity and femininity. It includes a list of 60 personal qualities, such as ambitious, loyal, jealous; and asks respondents to rate themselves on a 7-point Likert scale.

Gender role measures may be useful for studying behaviors and activities that tend to be segregated between men and women. Social roles particularly relevant to AD/ADRD research include caregiving, housework, domestic financial responsibilities, and career choices.

TABLE 2 Summary of sex and gender measures reported in biomedical literature, 2000 to 2020

Domains	Instrument name	Year	Intended purpose of measure	# Items*	Reliability coefficient (alpha)	Used with older adults
Stereotypes and discrimination	African American Men's Gendered Racism Stress Inventory (AMGRaSI)[a]	2013	Gendered racism stress in African-American men w.r.t.: violence, absent fatherhood, athletic abilities	15	0.88	No
	Gendered Racial Microaggressions Scale (GRMS)[b]	2015	Gendered racial aggressions experienced by Black women	32	–	Yes (ages 19–68)
Attitudes and ideologies	Attitudes Towards Men Scale[c]	1983	Women's attitudes towards men	32	0.79	Yes (ages 18–63)
	Attitudes Towards Women Scale (AWS)[d]	1972	Attitudes and perceptions of the rights, roles, and privileges of women	55,25,15	–	–
	Attitudes Towards Women Scale for Adolescents (AWSA)[e]	1985	Adolescents' attitudes toward women	12	–	No
	Aging Men's Masculinity Ideologies Inventory (AMMII)[p]	2018	Masculinity ideologies w.r.t. aging men	15		Yes
Norms	Multicultural Masculinity Ideology Scale (MMIS)[q]	1998	Individual's adaptation and internalization of cultural norms w.r.t. how men behave	35	0.81–0.72	–
	Conformity to Masculine Norms Inventory (CMNI)[g,h]	2003	Men's conformity to US masculine norms	144	0.94	–
	Brannon Masculinity Scale (BMS)[i]	1984	Endorsement of masculine norms	110,58	-	-
	Male Role Norms Inventory (MRNI)[j,k,l]	1992	Traditional masculinity ideology	5,21,58	0.928	-
	Male Role Norms Scale (MRNS)[m]	1986	Men's endorsement of traditional male norms and attitudes towards appropriate role for women	57	-	No
	Measure of Men's Perceived Inexpressiveness Norms (M2PIN)[n]	2013	Men's perceptions of social norms regarding emotional inexpressiveness	10	0.89	Yes
	Peer Nomination Measure[o]	2002	Measure gender segregation and peer preferences	6	–	Yes
Gender/sex roles	Chinese Sex-Role Inventory (CSRI)[r]	1984	Self-identification with sex-role stereotypes in Hong Kong adolescents	51	–	No
	Bem Sex Role Inventory (BSRI)[s]	1974	Self-endorsement of feminine and masculine characteristics; androgyny	60	–	No
	Feminine Gender Role Stress Scale (FGRS)[t]	1992	Challenges to stereotypical feminine behaviors and coping skills	39	–	No
	Gender Role Beliefs Scale (GRBS)[u]	1996	Gender role ideology	20	0.89	No
	Gender Role Conflict Scale (GRCS)[v]	1986	Men's gender-role attitudes, behaviors, and conflicts (I) Men's situation-specific gender-role conflicts (II)	85,51, 37,16	0.75–0.85 (I) 0.51–0.76 (II)	No
	Gender Role Stereotypes Scale (GRSS)[w]	2012	Men and women's behaviors w.r.t. specific gender-role stereotypes and attitudes	8	0.75 (I) 0.78 (II)	Yes (ages 17–53)
	Sex-Role Egalitarianism Scale (SRES)[x]	1984	Measures the sex-role egalitarian features of an individual	95	0.81–0.97	–
	Labor Force Gender Index (LFGI)[y]	2016	Gender roles and institutionalized gender w.r.t. labor force	–	–	–
	Stereotypic Roles of Black Women Scale (SRBWS)[z]	2004	Perception and stereotypes of African American women	61, 34	–	Yes (ages 18–63)
	Role Conflict Questionnaire for Women (RCQW)[A]	1974	Potential gender-role conflicts that may affect women's self-image	252	–	–
	Masculine Gender Role Stress Scale (MGRS)[B]	1987	How men feel in situations that challenges their masculinity ("unmanly" or feminine behavior)	43	–	No
	The Macho Scale[C]	1977	Personality differences in sex-role stereotyping and sex discrimination	28	–	No
	Personal Attributes Questionnaire (PAQ)[D]	1978	Determine sex-typing of personality	24	0.67–0.78	–

(Continues)

TABLE 2 (Continued)

Domains	Instrument name	Year	Intended purpose of measure	# Items*	Reliability coefficient (alpha)	Used with older adults
Others	Self-Construal Scale[E]	1994	How people view themselves in relation to others	24	0.69–0.73	No
	Gender Implicit Association Test (GIAT)[F]	2000	Response latencies	–	–	No

Abbreviation: w.r.t., with respect to.

*Instruments with more than one number listed had multiple versions with varying numbers of items.

[a]Schwing AE. Development and validation of the African American Men's Gendered Racism Stress Inventory. Psychology of Men & Masculinity. 20120528;14(1):16. https://doi.org/10.1037/a0028272.

[b]Lewis JA, Neville HA. Construction and initial validation of the Gendered Racial Microaggressions Scale for Black women. https://doi.org/10.1037/cou0000062.

[c]Iazzo A. The Construction and Validation of Attitudes Toward Men Scale. The Psychological Record. 1983;33(3):371-378.

[d]Spence, Helmreich. Attitudes Towards Women Scale. Published online 1972.

[e]Galambos NL, Petersen AC, Richards M, Gitelson IB. The Attitudes Toward Women Scale for Adolescents (AWSA): A study of reliability and validity. *Sex Roles*. 1985;13(5-6):343-356. https://doi.org/10.1007/BF00288090.

[f]Mahalik JR, Morray EB, Coonerty-femiano A, Ludlow LH, Slattery SM, Smiler A. Development of the conformity to feminine norms inventory. *Sex Roles*. Published online 2005:417-435.

[g]Ludlow LH, Mahalik JR. Congruence between a theoretical continuum of masculinity and the Rasch Model: Examining the Conformity to Masculine Norms Inventory. *Journal of Applied Measurement*. 2001;2(3):205-226.

[h]Mahalik JR, Locke BD, Ludlow LH, et al. Development of the Conformity to Masculine Norms Inventory. *Psychology of Men & Masculinity*. 2003;4(1):3-25. https://doi.org/10.1037/1524-9220.4.1.3.

[i]Beere C. Brannon Masculinity Scale. In:; 1990. https://hdl.handle.net/2027/mdp.49015002877786.

[j]Levant RF, Richmond K. A review of research on masculinity ideologies using the Male Role Norms Inventory. *The Journal of Men's Studies*. 2007;15(2):130-146. https://doi.org/10.3149/jms.1502.130.

[k]Levant RF, Rankin TJ, Williams CM, Hasan NT, Smalley KB. Evaluation of the Factor Structure and Construct Validity of Scores on the Male Role Norms Inventory – Revised (MRNI–R). *Psychology of Men & Masculinity*. 2010;11(1):25-37. https://doi.org/10.1037/a0017637.

[l]Levant RF, Hall RJ, Weigold IK, McCurdy ER. Construct validity evidence for the Male Role Norms Inventory-Short Form: A structural equation modeling approach using the bifactor model. *Journal of Counseling Psychology*. 2016;63(5):534-542.

[m]Thompson EH, Pleck JH. The Structure of Male Role Norms. *American Behavioral Scientist*. 1986;29(5):531-543. https://doi.org/10.1177/000276486029005003.

[n]Wong YJ, Horn AJ, Gomory AMG, Ramos E. Measure of Men's Perceived Inexpressiveness Norms (M2PIN): Scale development and psychometric properties. *Psychology of Men & Masculinity*. 2013;14(3):288-299. https://doi.org/10.1037/a0029244.

[o]Strough, J, Covatto, A. (2002). Context and Age Differences in Same- and Other-gender Peer Preferences. Social Development. 11. 346 - 361https://doi.org/10.1111/1467-9507.00204.[p]Levant RF, Webster BA, Stanley JT, Thompson EH. The Aging Men's Masculinity Ideologies Inventory (AMMII): Dimensionality, variance composition, measurement invariance by gender, and validity. *Psychology of Men & Masculinities*. 20190307;21(1):46. https://doi.org/10.1037/men0000208.[q]Doss BD, Hopkins JR. The Multicultural Masculinity Ideology Scale: Validation from Three Cultural Perspectives. *Sex Roles*. 1998;38(9):719-741. https://doi.org/10.1023/A:1018816929544

[r]Keyes S. Measuring sex-role stereotypes: Attitudes among Hong Kong Chinese adolescents and the development of the Chinese sex-role inventory. *Sex Roles*. 1984;10(1):129-140. https://doi.org/10.1007/BF00287752.

[s]Bem SL. The measurement of psychological androgyny. *Journal of Consulting and Clinical Psychology*. 19740101;42(2):155. https://doi.org/10.1037/h0036215.[t]Gillespie BL, Eisler RM. Development of the feminine gender role stress scale. A cognitive-behavioral measure of stress, appraisal, and coping for women. *Behav Modif*. 1992;16(3):426-438. https://doi.org/10.1177/01454455920163008.[u]Kerr PS, Holden RR. Development of the Gender Role Beliefs Scale (GRBS). *Journal of Social Behavior & Personality*. 1996;11(5):3-16.

[v]O'Neil J, Helms B, Gable R, David L, Wrightsman L. Gender-role conflict scale: College men's fear of femininity. *Sex Roles*. 1986;14:335-350. https://doi.org/10.1007/BF00287583. [w]Mills MJ, Culbertson SS, Huffman AH, Connell AR. Assessing gender biases: Development and initial validation of the gender role stereotypes scale. *Gender in Management: An International Journal*. 2012;27(8):520-540. https://doi.org/10.1108/17542411211279715.

[x]Beere CA, King DW, Beere DB, King LA. The sex-role egalitarianism scale: A measure of attitudes toward equality between the sexes. *Sex Roles*. 1984;10(7):563-576. https://doi.org/10.1007/BF00287265, https://doi.org/10.1037/cou0000171. [y]Smith PM, Koehoorn M. Labor Force Gender Index. Published online 2016. [z]Thomas AJ, Witherspoon KM, Speight SL. Toward the Development of the Stereotypic Roles for Black Women Scale. *Journal of Black Psychology*. 2004;30(3):426-442. https://doi.org/10.1177/0095798404266061.

[A]Nevill D, Damico S. Development of a role conflict questionnaire for women: Some preliminary findings. *Journal of Consulting and Clinical Psychology*. 1974;42(5):743-743. https://doi.org/10.1037/h0037052.

[B]Baugher A.R., Gazmararian J.A. Masculine gender role stress and violence: A literature review and future directions. *Aggression Violent Behav*. 2015;24((Baugher A.R., yda1@cdc.gov; Gazmararian J.A.) Emory University Rollins School of Public Health, Department of Epidemiology, United States):107-112. https://doi.org/10.1016/j.avb.2015.04.002.

[C]Villemez WJ, Touhey JC. A Measure of Individual Differences in Sex Stereotyping and Sex Discrimination: The "Macho" Scale. *Psychol Rep*. 1977;41(2):411-415. https://doi.org/10.2466/pr0.1977.41.2.411.

[D]Spence JT, Helmreich RL. Masculinity and femininity: Their psychological dimensions, correlates, and antecedents. Published online 1978.

[E]Singelis TM. The Measurement of Independent and Interdependent Self-Construals. *Pers Soc Psychol Bull*. 1994;20(5):580-591. https://doi.org/10.1177/0146167294205014.

[F]Well S van, Kolk AM, Oei NYL. Direct and indirect assessment of gender role identification. *Sex Roles: A Journal of Research*. 2007;56(9-10):617-628. https://doi.org/10.1007/s11199-007-9203-7.

TABLE 3 Methods of assessing sex and gender concepts reported in biomedical literature, 2000 to 2020

Concept	Definition
Respondent rating scale	A set of closed-ended items used to characterize individual responses via levels of intensity related to particular beliefs, feelings, attitudes, or experiences. Total scores are mean of item ratings unless the count of attributes is most salient (i.e., number of symptoms versus mean agreement.).
Response latencies	Response latency is defined as the time in seconds that elapses between the delivery of the stimulus and the individual's response.
Social attributes indexes	A set of attributes used to characterize an individual with respect to a set of particular attributes.
Biological measures	Markers of processes or outcomes that are drawn from the body.

Using scales, such as those identified in this review, to characterize social roles, AD/ADRD researchers could garner more accurate insight into pathways that are driving AD/ADRD outcomes and, ultimately, inform interventions that can optimize patient and family outcomes.

One measure of gender segregation was identified, which estimated the mixture of a person's five friends and five colleagues who were men and women. Gender segregation is related to the concept of gender roles. Gender segregation, or sex segregation, is the physical, legal, or cultural separation of individuals based genital or reproductive sex. Gender segregation can be structurally imposed, for example, through social policies such as having unisex bathrooms and sports teams as well as in certain religious laws. It can also happen without structural antecedents given cultural histories and traditions. Gender segregation measures may be useful for studying relationship patterns and other social and structural factors that tend to be separate across genders.[30] AD/ADRD research may find gender segregation measures useful for understanding social isolation, loneliness, and social support, which can on their own be key AD/ADRD outcomes but are also recognized as important determinants of other AD/ADRD outcomes.

3.2 | Implicit association gender measures and multimetric composites

One tool we located that did not rely on a respondent's ratings was the Gender Implicit Association Test (GIAT).[35] The GIAT measures gender role identification through differences in an individual's response latencies when confronted with stereotypically congruent and incongruent pairings. Similarly, the Labor Force Gender Index (LFGI)[36] also does not rely on respondent ratings. The LFGI estimates a gender coefficient based on gender-biased social patterns, such as hours spent caring for children or working, level of education, and men-to-women ratio within the respondent's occupation. Methods of collecting sex and gender data are summarized in Table 3.

3.3 | Biological sex measures

In US-based samples, we found four studies reported collecting biological measures of sex (Table 4). Biological sex measures include markers collected from the body. Markers can be from chromosomes, gonads, hormones, genitals, and dimorphic characteristics.[37] Sexually dimorphic features vary and include metabolism, immune system, and stature.[38]

Three of the four measured endogenous hormones related to androgens levels ($n = 2$) and prenatal estrogen levels ($n = 1$). The fourth evaluated the sexually dimorphic quality of the ratio in the length between the index finger and ring finger on a hand ($n = 1$). Measures of biological sex may be useful in AD/ADRD research. They may help specify causal relationships. Estrogen levels, for example, may influence ventricular volume.[31] By measuring estrogen rather than relying on self-report sex as a proxy, researchers can more directly study the effects of biological sex on the brain.

3.4 | Considerations for aging and global populations

We discuss the applicability of extant sex and gender measures to aging and global populations. We focus on these two broad populations given their relevance to AD/ADRD research. We address available measures and considerations for gaps and goals.

3.4.1 | Older adults

Sex and gender measures have generally not been developed for older adults. Of the 29 tools identified in our review, only one, the *Aging Men's Masculinity Ideologies Inventory (AMMII)*,[39] was created to understand an aspect of gender as it operates in later life (≥65 years). The AMMII was developed in a sample of 601 (50.8%) cis-women, 577 (48.7%) cis-men, and less than 1% transgender and other, all between the ages of 31 and 95. The 15-item total score characterizes an individual's general later-life masculinity ideology.

AD/ADRD researchers may need to consider the validity and appropriateness of existing sex and gender measures when they consider using them. There are many differences known between older men and women.[40] Measures of gender and sex that are focused and specific may help discover what is causing those differences. In particular, biological sex measures, which can change developmental stage and environmental exposures, may help characterize sex effects on cognition over the life course.

TABLE 4 Summary of biologic sex measures reported in biomedical literature, 2000 to 2020

Authors	Title	Purpose	Year published	Journal	Biological trait being measured
Rammsayer, et al.	Sexual dimorphism in second-to-fourth digit ratio and its relation to gender-role orientation in males and females	Examine the association between 2D:4D ratio and gender-role orientation[a]	2007	Personality and Individual Differences	Androgens Prenatal estrogens Second to fourth digit (2D:4D) ratio
Troche, et al.	The relationship of digit ratio (2D:4D) and gender-role orientation in four national samples	Examine the influence of nationality on the relationship between 2D:4D ratio and gender-role orientation[a]	2007	Journal of Individual Differences	2D:4D ratio
Makrantonaki, et al.	Androgens and ageing of the skin	Review the role of androgens in the initiation of skin aging	2009	Current opinion in endocrinology, diabetes, and obesity	Androgens
Batista et al.	Psychosexual Aspects, Effects of Prenatal Androgen Exposure, and Gender Change in 46,XY Disorders of Sex Development	Examine the impact of prenatal sexual steroid exposure and external genital virilization on human psychosexual development	2019	The Journal of clinical endocrinology and metabolism	Prenatal sexual steroid exposure external genital virilization

[a]Role orientation as measured by the Bem Sex Role Inventory (BSRI).

3.4.2 | Time and place as considerations in gender measures

Because it is a culturally defined construct, gender can vary across societies and generations. No measures that we found addressed social and generational change directly in the design or development of the instruments. In other words, extant measures appear bound to the specific historical and cultural point when they were constructed. This may be a limiting factor to their use as they may lack cultural relevance and appropriateness. Researchers may need to consider these issues when considering using existing sex and gender measures.

As social events unfold, such as war, economic shifts, and medical advances (i.e., birth control, family planning, etc.), the effects of sex and gender on individuals can change. Individuals may be, for example, drafted into wartime conflicts that predispose them to cardiovascular risks of dementia from tobacco, head injury, or psychological risks of dementia due to depression, stress, or other factors. This means sex and gender effects can differ from one place to another and from one time to another. Sex/gender disparities are documented worldwide but their magnitude and character varies.[41]

Addressing time and place is essential for advancing measurement and study of sex and gender effects in AD/ADRD science. This is essential for being inclusive and responsive to cultural customs. Some cultures incorporate a variety of gender identities, such as Two-Spirit individuals of the Indigenous North American peoples,[42] Hijras of India,[43] and bissu of the Bugis in Indonesia.[44] In the US, for example, gender inequality changed notably from 1970 to 2018,[45] suggesting the gendered experiences of older Americans may differ by generation. Moreover, individuals' responses on gender measures are influenced by the terms and vocabulary, which can have or lose relevance based on time and place.

When conducting our analyses, we observed that many of the measures identified in the US sample were also being used in other nations. The Conformity to Masculine Norms Inventory, for example, appeared frequently in both groupings. We also noticed the countries represented in the data were heavily skewed toward the West; the bulk of studies were from the US ($n = 947$). Among others, there were 15 studies reporting on Japanese samples and 3 from Africa. Notably, similar measures, like the BEM Sex Role Inventory, a gender measure developed in the US in the 1970s,[60] were being used across these culturally heterogeneous settings.

4 | DISCUSSION

We conducted a review of 20 years of biomedical literature in order to inventory measures used to study the effects of sex and gender in medicine. We found most studies in our review used responses from self-report questions to characterize research samples based on the composition of men and women ($n = 1233$, 88%). About a fifth of empirical studies ($n = 237$, 18.5%) used structured measures other than single-item sex/gender identity questions to gather data on gender, and a few studies reported collecting biological sex measures ($n = 4$).

The goal of the current review was to identify whether there may be extant sex and gender measures that could be useful for advancing the study of sex and gender in AD/ADRD research. This contrasts with

prior studies that have focused on synthesizing results from studies of sex/gender differences in AD/ADRD outcomes.[5–7] Our study identified measures of sex and gender and raised the question: Are there existing measures capturing aspects of sex and gender that would be relevant to AD/ADRD research? Three elements seem relevant in evaluating the answer to this question: a measure's content, its suitability for older adults, and psychometric qualities. We discuss our findings with respect to each. We also discuss sex and gender constructs potentially relevant to AD/ADRD research for which there are currently no measures.

Our findings showed that existing measures of gender varied in focus, including gender stereotypes and discrimination, attitudes and ideologies, and social role responsibilities. Most of the instruments we found measured attitudes and ideologies. These measures may be useful in studying treatment seeking, research participation, and caregiver burden. They may help explicate ways that gendered attitudes and ideologies influence prejudicial beliefs about AD/ADRD,[46] which in turn can impact access to care, willingness to receive care, adherence to care recommendations, and willingness to participate in research.[47]

Another category of gender measures that we identified were those instruments that characterized social roles. In the US, gendered social roles include a range of activities that have historically been segregated between men and women such as childcare and caregiving, housework, domestic financial duties, and career pursuits (e.g., nurse, teacher vs. fire/police).[48] Many of these activities are relevant to AD/ADRD research and care. Moreover, science of what is understood about determinants of social role behaviors is an evolving area. Emerging data, for example, show social roles can have both biological and social determinants.[49] Social roles measures may be useful in AD/ADRD research for studying disparities in access to care, caregiving, and participation in research. They may also aid efforts to detect early cognitive declines that manifest in performance of household and financial responsibilities.

In AD/ADRD, gender roles can change as a consequence of dementia. Both members of a spousal dyad, for example, may experience this as one partner transitions to cognitive and functional decline and the other takes on caregiving responsibilities. The transitions can lead to gender role strain, which captures feelings of uncertainty that individuals may experience in doubting their abilities to fulfill culturally normative gender roles.[50]

We found multiple measures that capture gender role strain and stress. The Masculine Gender Role Stress scale lists situations (i.e., being perceived as gay, being less athletic, telling a spouse you love him/her) and asks respondents to rate how much each situation causes them stress.[51] Similarly, the Feminine Gender Role Stress Scale lists situations (i.e., Feeling pressured to engage in sexual activity, Having your car break down on the road, Trying to be a good parent *and* excel at work, Trying to get your spouse to take responsibility for child care) across five factors (i.e., Fear of unemotional relationships, Fear of physical unattractiveness, Fear of victimization, Fear of behavior assertively, and Fear of not being nurturant).[34]

While gender role strain may apply to any person, the construct was developed to capture role transition at the onset of disability – particularly roles connected to a person's expression of gender identity. The gender role strain paradigm may be useful for appreciating the demands of gender-specific roles on individuals and the congruence of those demands with the individual's public persona. This is a unique challenge in AD/ADRD as the lives of individuals with dementia are transformed by onset of cognitive and functional impairments. Moreover, the gender role strain paradigm may inform models of stress and resilience and explaining heterogeneity in patient and caregiver outcomes.

In examining the available measures of gender, only one was developed with older adults in mind. Research is needed to evaluate the relevance, performance, and sufficiency of gender measures in older adults. While sex and gender measures seem to be often assembled based on expert consensus,[52,53] empirical studies are needed to evaluate sex and gender measures in individuals for whom they are intended. Such studies would also allow for the evaluation of measures in older adults with varying sociocultural characteristics. This is important as aspects of sex and gender may vary across social and biological groups.

The psychometric qualities of the existing gender measures in the biomedical literature varied in suitability for AD/ADRD research as based on measures' length, temporal sensitivity, and method of administration. Structured instruments identified in our review ranged in length from 5 to 252 items. Instruments with items in the upper bounds of this range are infeasible in AD/ADRD research. Moreover, items on all 29 instruments reflected fixed notions of masculinity and femininity. That is, they are anchored to the generation and historical period in which they were developed. This may present a limitation of their use in AD/ADRD research and care given that older adults demonstrate generational differences in gender expression, ideologies, attitudes, and other areas.[54,55]

The method of administration was largely via self-report. All but 2 of the 29 identified gender measures, in addition to the self-report sex/gender identity items, were self-report tools that asked respondents to rate how much they agreed or identified with statements. This approach seems useful for capturing individuals' experiences, beliefs, attitudes, and identity. However, self-report data have limitations. They are unable to capture some elements of sex and gender that may be relevant to AD/ADRD research and care.

Self-report metrics tend to conflate sex and gender independent of the specific structure of a given item. That is, for most individuals, how they identify their sex is consistent with how they identify their gender. Other types of data collection – such as biological measures, like endogenous hormones, passive data collection, like smartwatches, and implicit metrics, like the GIAT,[35] and multimetric composites like the LFGI,[36] may enhance study of sex and gender effects. They may offer measurement approaches that are less influenced by social reporting bias, that capture more of the broad array of ways sex and gender can influence individuals, and that more directly assess biological variability in sex.

While there are some methods and measures available that may help characterize effects attributable to sex and gender, we found instead a heavy reliance on data from self-report identity questions (n = 1233, 97%). Only about 1 in 5 empirical studies (n = 237, 18.7%)

used structured self-report measures other than single-item sex or gender identity questions to gather data on gender. These findings are consistent with those from a recent review by Rechlin et al.[56] Moreover, our findings on the limited use of the sex and gender methods and measures by biomedical researchers offer a possible explanation for Rechlin and colleagues' conclusion that "progress to date has not been sufficient to address the importance of sex differences in research for discovery and therapeutic potential for neurological and psychiatric disease."

Lack of validated life course and population-specific measures (i.e., measures designed for older adults) may also explain the lack of progress on understanding sex and gender effects in biomedical research. There may be aspects of gender that are relevant to AD/ADRD research that do not yet have published measures. First, gender expression and its related trait constellations may be useful in elucidating components of sex and gender disparities in AD/ADRD risk[57] and aid efforts aimed at conceptualizing these disparities as correlates of AD/ADRD risk factors.[58] Gender expression captures how individuals perform their gender. In other words, gender-informed behaviors. Some scholars have referred to this as "doing femininities and masculinities,"[59] which refers relatively enduring personality traits that are often conceptualized along continuums representing masculinity, femininity, and androgyny.[60] Studies of gender expression may help discover whether there may be gendered behaviors that modify risk of AD/ADRD.

The concept of gender relations (e.g., social support) may also be relevant in AD/ADRD research and care. Gender relations capture culturally ascribed ways that rights, responsibilities, and identities of individuals are placed in relation to one another based on attributed gender categories.[61] Unequal gender relations among men, women, and alternative gender categories matter in AD/ADRD. The disparities impact caregiving, care arrangements, participation in research, and risk of clinical symptoms, whereby women are known to disproportionately incur these burdens.[62–64] Little is known about marginalized groups. Influences of disparities in gender relations may also spill over to impact dynamics within gender categories. Some of the ways this occurs may be relevant to AD/ADRD research and care. For example, women may offer support to other women in order to facilitate overcoming barriers to participating in AD/ADRD research.[65]

We found no measures that characterized both sex (biological) and gender (sociological). Measures we found offered ways to characterize social and institutional factors of gender but did not incorporate any appraisals of biological factors. The inverse is true for the four biological measures of sex that we found, including endogenous hormones ($n = 3$) and sexually dimorphic quality of digit ratio ($n = 1$). The measures of biological sex that we found may be useful in AD/ADRD research as they may capture variance that is otherwise lost or missed in self-report measures and thereby help explicate how sex influences disease mechanisms.[5,6,62] Moreover, sex and gender are dynamic systems that can and do influence each other. Well-specified measures that independently capture both sex and gender may help foreground a more complete context for scientific investigations and aid in advancing knowledge of reciprocities between sex and gender as well as disentangling their individual roles. This, in turn, would be useful in understanding their effects over the life course and influences on disease mechanisms. In addition, an approach that offers a more complete context for investigations would also recognize that science is situated in historical and cultural contexts that influence understanding of sex and gender, particularly in ways that limit or misconstrue what is known about women.[66] This also includes SGM populations.

Clinical interviews to collect data on sex and gender life course experiences may also aid AD/ADRD science, in addition to psychosocial coefficients and biological metrics. Structured clinical interview data could aid in capturing development histories and life span experiences that could garner information relevant to understanding AD/ADRD risk. For example, transition from perimenopause to postmenopause, as well as changes in sexual function can all be indicators of endogenous hormone states that can impact cognitive function and neural anatomy.[67–69]

5 | LIMITATIONS

Because gender is a major focus of this study and gender is a social construct that can vary across cultures, we only included articles with US-based research samples in the analysis of specific measures. However, when possible, we summarize the general types of measures in human subjects' studies, independent of the cultural or national origin of study samples. We found the undertaking informative for understanding the state of the science on sex and gender measures from a global perspective. When conducting our analyses, we observed that many of the measures identified in the US sample were also being used in other nations. There is a need for future research to understand the context dependency of sex and gender measurement. Currently, some studies may be conflating gender effects with acculturation effects. Moreover, there were no studies from many countries, some notably in which sex and gender may have the most oppressive effects. There is a need to expand study of sex and gender measurement to increasingly heterogeneous and culturally divergent populations.

Because we could not identify, analyze, and contextual measures by culture group or nationality, the applicability of our findings to countries outside the US is limited. Specific recommendations may not be applicable. Moreover, there may be versions of some measures that are relevant to countries outside the US that are not listed in our results. Our approach and conclusions regarding the further study of sex and gender in AD/ADRD research may be useful for advancing this line of research in the US and elsewhere. In addition, our search did not include all possible data sources or years. It is possible that we may have inadvertently missed relevant scholarship even though we likely identified the bulk of this information.

6 | CONCLUSION

Existing sex and gender measures may add value to AD/ADRD studies, particularly those related to understanding social and psychological

aspects of patient and caregiver experiences and those that aid in characterizing biological diversity. Further study is needed to validate existing measures in older adult samples and new instruments may also be needed to address temporal aspects of gender that change across generations. Advancement in measurement of sex and gender in AD/ADRD research may aid improvements downstream in patient care.

ACKNOWLEDGMENTS

The authors wish to thank Andrew Peterson, PhD, Emily Largent, PhD, Jason Karlawish, MD, Justin Clapp, PhD, and all the members of the Penn Program on Precision Medicine for the Brain (P3MB). This research was supported by the Research Centers Collaborative Network (RCCN) of the National Institute on Aging (NIA) (U24AG058556). Dr. Stites is supported by the Alzheimer's Association (AARF-17-528934) and the National Institute on Aging (K23AG065442). Dr. Flatt is supported by the National Institute on Aging (K01AG056669). The funders had no role in the design and conduct of the study; collection, management, analysis, or interpretation of the data; preparation or approval of the manuscript; and decision to submit the manuscript for publication.

CONFLICT OF INTEREST

The authors report no conflicts of interest. Author disclosures are available in the supporting information.

ORCID

Shana D. Stites PsyDMSMA https://orcid.org/0000-0003-3994-4343
Richard James MSLIS https://orcid.org/0000-0003-1672-0259
Kristin Harkins MPH https://orcid.org/0000-0001-5360-1043
Cameron Coykendall BA https://orcid.org/0000-0002-4983-401X
Jason D. Flatt PhDMPH https://orcid.org/0000-0003-1244-738X

REFERENCES

1. Milestone 2D National Institute on Aging. Accessed February 28, 2021. http://www.nia.nih.gov/researcSh/milestones/disease-mechanisms/milestone-2-d
2. Defining sexual health. Accessed July 10, 2022. https://www.who.int/teams/sexual-and-reproductive-health-and-research/key-areas-of-work/sexual-health/defining-sexual-health
3. Including Women and Minorities in Clinical Research Office of Research on Women's Health. Accessed February 22, 2019. https://orwh.od.nih.gov/research/clinical-research-trials/nih-inclusion-policy/including-women-and-minorities-clinical
4. Hill CV, Perez-Stable EJ, Anderson NA, et al. The national institute on aging health disparities research framework. *Ethn Dis*. 25(3):245-254. doi:10.18865/ed.25.3.245
5. Snyder HM, Asthana S, Bain L, et al. Sex biology contributions to vulnerability to Alzheimer's disease: a think tank convened by the Women's Alzheimer's Research Initiative. *Alzheimers Dement*. 2016;12(11):1186-1196. https://doi.org/10.1016/j.jalz.2016.08.004
6. Nebel RA, Aggarwal NT, Barnes LL, et al. Understanding the impact of sex and gender in Alzheimer's disease: a call to action. *Alzheimers Dement*. 2018;14(9):1171-1183. https://doi.org/10.1016/j.jalz.2018.04.008
7. Ferretti MT, Martinkova J, Biskup E, et al. Sex and gender differences in Alzheimer's disease: current challenges and implications for clinical practice: position paper of the Dementia and Cognitive Disorders Panel of the European Academy of Neurology. *Eur J Neurol*. 2020;27(6):928-943. https://doi.org/10.1111/ene.14174
8. Mielke MM, Aggarwal NT, Vila-Castelar C, et al. Consideration of sex and gender in Alzheimer's disease and related disorders from a global perspective. Alzheimers Dement. Published online April 8, 2022. https://doi.org/10.1002/alz.12662
9. Sundermann EE, Biegon A, Rubin LH, et al. Does the female advantage in verbal memory contribute to underestimating Alzheimer's disease pathology in women versus men? *J Alzheimers Dis*. 2017;56(3):947-957. https://doi.org/10.3233/JAD-160716
10. Hua X, Hibar DP, Lee S, et al. Sex and age differences in atrophic rates: an ADNI study with n = 1368 MRI scans. *Neurobiol Aging*. 2010;31(8):1463-1480. https://doi.org/10.1016/j.neurobiolaging.2010.04.033
11. Holland D, Desikan RS, Dale AM, et al. Alzheimer's Disease Neuroimaging Initiative. Higher rates of decline for women and apolipoprotein E epsilon4 carriers. *AJNR Am J Neuroradiol*. 2013;34(12):2287-2293. https://doi.org/10.3174/ajnr.A3601
12. Lin KA, Choudhury KR, Rathakrishnan BG, et al. Marked gender differences in progression of mild cognitive impairment over 8 years. *Alzheimers Dement (N Y)*. 2015;1(2):103-110. https://doi.org/10.1016/j.trci.2015.07.001
13. Sundermann EE, Biegon A, Rubin LH, et al. Better verbal memory in women than men in MCI despite similar levels of hippocampal atrophy. *Neurology*. 2016;86(15):1368-1376. https://doi.org/10.1212/WNL.0000000000002570
14. Sundermann EE, Maki PM, Rubin LH, et al. Female advantage in verbal memory: evidence of sex-specific cognitive reserve. *Neurology*. 2016;87(18):1916-1924. https://doi.org/10.1212/WNL.0000000000003288
15. Skup M, Zhu H, Wang Y, et al. Sex differences in grey matter atrophy patterns among AD and aMCI patients: results from ADNI. *Neuroimage*. 2011;56(3):890-906. https://doi.org/10.1016/j.neuroimage.2011.02.060
16. Barnes LL, Wilson RS, Bienias JL, et al. Sex differences in the clinical manifestations of Alzheimer disease pathology. *Arch Gen Psychiatry*. 2005;62(6):685-691. https://doi.org/10.1001/archpsyc.62.6.685
17. Filon JR, Intorcia AJ, Sue LI, et al. Gender differences in Alzheimer disease: brain atrophy, histopathology burden, and cognition. *J Neuropathol Exp Neurol*. 2016;75(8):748-754. https://doi.org/10.1093/jnen/nlw047
18. Women and Alzheimer's. Alzheimer's Disease and Dementia. Accessed July 11, 2022. https://alz.org/alzheimers-dementia/what-is-alzheimers/women-and-alzheimer-s
19. Flatt JD, Cicero EC, Lambrou NH, et al. Subjective cognitive decline higher among sexual and gender minorities in the United States, 2015-2018. *Alzheimers Dement (N Y)*. 2021;7(1):e12197. https://doi.org/10.1002/trc2.12197
20. Perales-Puchalt J, Gauthreaux K, Flatt J, et al. Risk of dementia and mild cognitive impairment among older adults in same-sex relationships. *Int J Geriatr Psychiatry*. 2019;34(6):828-835. https://doi.org/10.1002/gps.5092
21. Flatt JD, Johnson JK, Karpiak SE, et al. Correlates of subjective cognitive decline in lesbian, gay, bisexual, and transgender older adults. *J Alzheimers Dis*. 2018;64(1):91-102. https://doi.org/10.3233/JAD-171061
22. Jancke L. Sex/gender differences in cognition, neurophysiology, and neuroanatomy. *F1000Res*. 2018;7:F1000. 10.12688/f1000research.13917.1
23. Mielke M, Vemuri P, Rocca W. Clinical epidemiology of Alzheimer's disease: assessing sex and gender differences. *Clin Epidemiol*. 2014;6:37-48. https://doi.org/10.2147/CLEP.S37929

24. Bramer WM, Rethlefsen ML, Kleijnen J, et al. Optimal database combinations for literature searches in systematic reviews: a prospective exploratory study. *Syst Rev*. 2017;6(1):245. https://doi.org/10.1186/s13643-017-0644-y
25. Ouzzani M, Hammady H, Fedorowicz Z, et al. Rayyan – a web and mobile app for systematic reviews. *Syst Rev*. 2016;5(1):210. https://doi.org/10.1186/s13643-016-0384-4
26. Stites SD, Cao H, Harkins K, et al. Measuring sex and gender in aging and Alzheimer's research: results of a national survey. *J Gerontol Ser B*. 2022;77(6):1005-1016. https://doi.org/10.1093/geronb/gbab226
27. Stites SD, Milne R, Karlawish J. Advances in Alzheimer's imaging are changing the experience of Alzheimer's disease. *Alzheimers Dement (Amst)*. 2018;10(1):285-300. https://doi.org/10.1016/j.dadm.2018.02.006
28. Pelletier R, Khan NA, Cox J, et al. Sex versus gender-related characteristics: which predicts outcome after acute coronary syndrome in the young? *J Am Coll Cardiol*. 2016;67(2):127-135. https://doi.org/10.1016/j.jacc.2015.10.067
29. Frontiers | Gender Disparities in Anti-dementia Medication Use among Older Adults: Health Equity Considerations and Management of Alzheimer's Disease and Related Dementias | Pharmacology. Accessed April 23, 2022. https://www.frontiersin.org/articles/10.3389/fphar.2021.706762/full
30. Mehta C, Wilson J, Smirles KES. Gender segregation and its correlates at midlife and beyond. *Int J Aging Hum Dev*. 2021;93(2):675-699. https://doi.org/10.1177/0091415020974624
31. Kantarci K, Tosakulwong N, Lesnick TG, et al. Effects of hormone therapy on brain structure. *Neurology*. 2016;87(9):887-896. https://doi.org/10.1212/WNL.0000000000002970
32. Galambos NL, Petersen AC, Richards M, et al. The Attitudes Toward Women Scale for Adolescents (AWSA): a study of reliability and validity. *Sex Roles*. 1985;13(5-6):343-356. https://doi.org/10.1007/BF00288090
33. Spence JT, Helmreich R. The attitudes toward women scale: an objective instrument to measure attitudes toward the rights and roles of women in contemporary society. *Catalog Sel Doc Psychol*. 1972;2(66).
34. Gillespie BL, Eisler RM. Development of the feminine gender role stress scale. A cognitive-behavioral measure of stress, appraisal, and coping for women. *Behav Modif*. 1992;16(3):426-438. https://doi.org/10.1177/01454455920163008
35. van Well S, Kolk AM, Klugkist IG. Effects of sex, gender role identification, and gender relevance of two types of stressors on cardiovascular and subjective responses: sex and gender match and mismatch effects. *Behav Modif*. 2008;32(4):427-449. https://doi.org/10.1177/0145445507309030
36. Smith PM, Koehoorn M. Labor force gender index. Published online 2016.
37. Karkazis K. The misuses of "biological sex". *Lancet North Am Ed*. 2019;394(10212):1898-1899. https://doi.org/10.1016/S0140-6736(19)32764-3
38. Clayton JA. Applying the new SABV (sex as a biological variable) policy to research and clinical care. *Physiol Behav*. 2018;187:2-5. https://doi.org/10.1016/j.physbeh.2017.08.012
39. Levant RF, Webster BA, Stanley JT, et al. The Aging Men's Masculinity Ideologies Inventory (AMMII): dimensionality, variance composition, measurement invariance by gender, and validity. *PMM*. 21(1):46. https://doi.org/10.1037/men0000208
40. Smith J, Baltes MM. The role of gender in very old age: profiles of functioning and everyday life patterns. *Psychol Aging*. 1998;13(4):676-695. https://doi.org/10.1037//0882-7974.13.4.676
41. Carmel S. Health and well-being in late life: gender differences worldwide. *Front Med*. 2019;6:218. Accessed April 24, 2022. https://www.frontiersin.org/article/10.3389/fmed.2019.00218
42. Wilson A. How we find ourselves: identity development and two spirit people. *Harvard Educ Rev*. 2010;66(2):303-318. doi:10.17763/haer.66.2.n551658577h927h4
43. Nanda S. Hijras. In: *The International Encyclopedia of Human Sexuality*. American Cancer Society; 2015:501-581. https://doi.org/10.1002/9781118896877.wbiehs207
44. Graham S. It's like one of those puzzles: conceptualising gender among bugis. *J Gend Stud*. 2004;13(2):107-116. https://doi.org/10.1080/0958923042000217800
45. England P, Levine A, Mishel E. Progress toward gender equality in the United States has slowed or stalled. *Proc Natl Acad Sci*. 2020;117(13):6990-6997. https://doi.org/10.1073/pnas.1918891117
46. Sandberg LJ. Dementia and the gender trouble? Theorising dementia, gendered subjectivity and embodiment. *J Aging Stud*. 2018;45:25-31. https://doi.org/10.1016/j.jaging.2018.01.004
47. Mena E, Bolte G, Study Group ADVANCEGENDER. Intersectionality-based quantitative health research and sex/gender sensitivity: a scoping review. *Int J Equity Health*. 2019;18(1):199. https://doi.org/10.1186/s12939-019-1098-8
48. Roos P, Stevens L. Integrating occupations: changing occupational sex segregation in the U.S. from 2000 to 2014. *Demogr Res*. 2018;38(5):127-154. https://doi.org/10.4054/DemRes.2018.38.5
49. Adelson SL. Development of AACAP practice parameters for gender nonconformity and gender discordance in children and adolescents. *Child Adolesc Psychiatr Clin N Am*. 2011;20(4):651-663. https://doi.org/10.1016/j.chc.2011.07.001
50. Luyt R. Beyond traditional understanding of gender measurement: the gender (re)presentation approach. *J Gend Stud*. 2015;24(2):207-226. https://doi.org/10.1080/09589236.2013.824378
51. Eisler RM, Skidmore JR. Masculine gender role stress: scale development and component factors in the appraisal of stressful situations. *Behav Modif*. 1987;11(2):123-136. https://doi.org/10.1177/01454455870112001
52. PhenX Toolkit: Protocols. Accessed May 8, 2021. https://www.phenxtoolkit.org/protocols/view/11801
53. PhenX Toolkit: Protocols - Gender Identity. Published June 2019. Accessed May 18, 2021. https://www.phenxtoolkit.org/protocols/view/11801
54. Cichy KE, Lefkowitz ES, Fingerman KL. Generational differences in gender attitudes between parents and grown offspring. *Sex Roles*. 2007;57(11):825-836. https://doi.org/10.1007/s11199-007-9314-1
55. Scott J, Alwin DF, Braun M. Generational changes in gender-role attitudes: britain in a cross-national perspective. *Sociology*. 1996;30(3):471-492. https://doi.org/10.1177/0038038596030003004
56. Rechlin RK, Splinter TFL, Hodges TE, Galea LAM. An analysis of neuroscience and psychiatry papers published from 2009 and 2019 outlines opportunities for increasing discovery of sex differences. *Nat Commun*. 2022;13(1):2137. https://doi.org/10.1038/s41467-022-29903-3
57. Ferretti MT, Martinkova J, Biskup E, et al. Sex and gender differences in Alzheimer's disease: current challenges and implications for clinical practice. *Eur J Neurol*. 2020;13:928-943. https://doi.org/10.1111/ene.14174
58. Krieger N. Genders, sexes, and health: what are the connections – and why does it matter? *Int J Epidemiol*. 2003;32(4):652-657. https://doi.org/10.1093/ije/dyg156
59. Alex L, Fjellman Wiklund A, Lundman B, Christianson M, Hammarström A. Beyond a dichotomous view of the concepts of 'sex' and 'gender' focus group discussions among gender researchers at a medical faculty. *PLoS One*. 2012;7(11):e50275. https://doi.org/10.1371/journal.pone.0050275
60. Bem SL. The measurement of psychological androgyny. *J Consult Clin Psychol*. 42(2):155. https://doi.org/10.1037/h0036215

61. Ron P. Offspring caring for their elderly parents: the effect of social support and gender-role orientation on these caregivers' well-being. *Illn Crisis Loss*. 2008;16(3):183-201. https://doi.org/10.2190/IL.16.3.a
62. Mielke M, Vemuri P, Rocca W. Clinical epidemiology of Alzheimer& disease: assessing sex and gender differences. *CLEP*. 2014;6:37-48. https://doi.org/10.2147/CLEP.S37929
63. Chappell NL, Dujela C, Smith A. Caregiver well-being: intersections of relationship and gender. *Res Aging*. 2015;37(6):623-645. https://doi.org/10.1177/0164027514549258
64. Gibbons C, Creese J, Tran M, et al. The psychological and health consequences of caring for a spouse with dementia: a critical comparison of husbands and wives. *J Women Aging*. 2014;26(1):3-21. https://doi.org/10.1080/08952841.2014.854571
65. Stites SD, Largent EA, Gill J, Harkins K, Karlawish J, What predicts who becomes a study partner in an AD cohort study? *Alzheimers Dement*. 2020;16(S7):e043404. https://doi.org/10.1002/alz.043404
66. Einstein G. Situated neuroscience: exploring biologies of diversity. In: Bluhm R, Jacobson AJ, Maibom HL, eds. *Neurofeminism: Issues at the Intersection of Feminist Theory and Cognitive Science. New Directions in Philosophy and Cognitive Science*. Palgrave Macmillan UK; 2012:145-174. https://doi.org/10.1057/9780230368385_8
67. Conde DM, Verdade RC, Valadares ALR, Mella LFB, Pedro AO, Costa-Paiva L. Menopause and cognitive impairment: a narrative review of current knowledge. *World J Psychiatry*. 2021;11(8):412-428. https://doi.org/10.5498/wjp.v11.i8.412
68. He L, Guo W, Qiu J, et al. Altered spontaneous brain activity in women during menopause transition and its association with cognitive function and serum estradiol level. *Front Endocrinol (Lausanne)*. 2021;12:652512. https://doi.org/10.3389/fendo.2021.652512
69. Kaur M, Kaur M. Is cognitive performance of women sensitive to the severity of menopausal symptoms? *Menopause*. 2022;29(2):170-177. https://doi.org/10.1097/GME.0000000000001910

How to cite this article: Stites SD, Cao H, James R, Harkins K, Coykendall C, Flatt JD. A systematic review of measures of gender and biological sex: Exploring candidates for Alzheimer's disease and related dementias (AD/ADRD) research. *Alzheimer's Dement*. 2022;15:e12359. https://doi.org/10.1002/dad2.12359

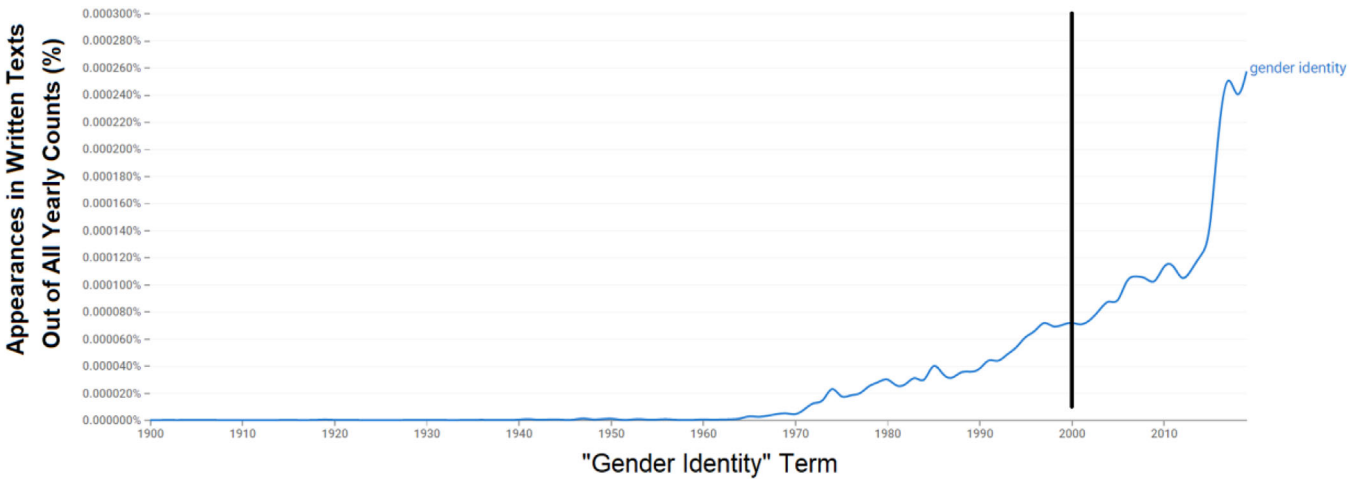
APPENDIX A

Sample Search (PubMed): ("measuring gender"[tiab] OR gender-measure*[tiab] OR "sex/gender sensitivity"[All Fields] OR "Gender role attitudes" OR ((gender-role*[All fields] OR "sex roles"[tiab] OR gender-norm*[tiab] OR "gender stereotypes" OR "gender stereotyping" OR "stereotypical" OR social-construct*[tiab] OR socially-constructed [tiab]) AND (masculine* OR feminin* OR male[tiab] OR female[tiab])) OR "masculinities" OR "femininities" OR "gender practice" OR "hegemonic masculinity" OR "conformity to masculine norms" OR "conformity to feminine norms") AND (Measurement[tiab] OR Measuring OR measure* OR "personality inventory" OR "inventory"[tiab] OR instrument* OR "Current Procedural Terminology"[Mesh] OR "Terminology as Topic"[Mesh] OR "psychological tests"[All Fields] OR "psychological testing" OR "Standardized Nursing Terminology"[Mesh] OR "Systematized Nomenclature of Medicine"[Mesh] OR "Unified Medical Language System"[Mesh]) AND ("2000/01/01"[PDAT] : "3000/12/31"[PDAT]) AND English[lang].

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

APPENDIX B



Appendix B Figure 1. Line Graph of the Google Books corpus for the term "gender identity". *Note*: A line graph produced by Google Books Ngram Viewer, which is an online search engine that charts the frequencies of appearance of a set of strings using a yearly count of n-grams found in printed sources published between 1900 and 2019 in Google's text corpora in English.