



Cognitive Impairment in Sexual and Gender Minority Groups: A Scoping Review of the Literature

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Abstract

Purpose: The purpose of this review was to synthesize evidence on differences in cognitive impairment by sexual orientation/gender identity (SOGI) status.

Methods: A scoping review of the literature was conducted. Five databases (PubMed/Medline, Cumulated Index to Nursing and Allied Health Literature, Web of Science, PsycInfo, and Embase) were searched for primary articles comparing incidence or prevalence of cognitive impairment among sexual and gender minority (SGM) groups versus non-SGM groups. Two reviewers independently screened articles and conducted risk-of-bias assessment on eligible articles.

Results: Fifteen primary studies were eligible. Most studies ($n = 13$) were cross-sectional, with moderate to critical risk of bias. Among eight studies examining self-reported cognitive impairment, seven reported a higher prevalence among some SGM groups versus non-SGM groups. Among seven studies using objective measures of cognitive impairment, three examined prevalence of clinician-documented diagnosis of dementia, of which two reported a higher prevalence specifically among transgender versus cisgender individuals. Among the other four studies examining objective measures, two reported poorer cognitive performance or memory, one reported better performance, and another reported no difference. Comparisons across studies were challenging due to inconsistencies in how SOGI and cognitive impairment were operationalized, and the factors used for statistical adjustment; some studies adjusted for putative intermediary factors that potentially explain differences in cognitive impairment.

Conclusions: Whereas most published studies identified a positive relationship between SOGI status and self-reported cognitive impairment, evidence is mixed with regard to objective cognitive performance. Well-designed longitudinal, observational studies are needed, using objective measures of cognitive function, with careful consideration of confounding versus intermediary risk factors.

Keywords: aging, gender identity, health disparities, mental health, sexual orientation

Introduction

COGNITIVE IMPAIRMENT—FROM mild cognitive impairment (MCI) to dementia—is a major public health concern, given the rise in life expectancy and the consequent growth in populations of older adults across the world.¹ Approx-

imately 12%–18% of adults aged 60 and older have MCI, defined as a slight but measurable decline in cognitive abilities including memory and thinking skills.² Annually, about 10%–15% of individuals with MCI progress to dementia, characterized by physical changes in the brain and a decline in cognitive abilities severe enough to interfere with daily life.^{2,3}

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According to the World Health Organization more than 55 million people, globally, live with dementia, and this number is expected to reach 78 million by 2030 and 139 million by 2050.⁴ In 2019, the total societal cost of dementia was estimated at \$1.3 trillion (US Dollars).⁴ The most common cause of dementia is Alzheimer's disease (AD),² which is the seventh leading cause of death worldwide and is a major cause of disability and dependency among older adults.⁵

Understanding populations at high risk for cognitive impairment and associated modifiable risk factors is important for promoting awareness among health care professionals and the public, encouraging early screening and diagnosis, and implementing behavioral or social-support interventions. The 2020 report of the *Lancet* Commission on "Dementia Prevention, Intervention, and Care" estimated that modifying specific risk factors could prevent or delay up to 40% of AD-related dementia, globally.⁶

Numerous studies have found that sexual minority groups (i.e., lesbian, gay, bisexual, queer people, and those who do not identify as heterosexual) and gender minority groups (i.e., transgender, nonbinary, gender-diverse people and those with a gender identity that differs from sex assigned at birth) are more likely to have modifiable risk factors for cognitive impairment compared with their cisgender heterosexual counterparts. These factors include smoking, excessive alcohol consumption, depression, obesity, high blood pressure, cardiovascular disease (CVD), and diabetes.^{7–18}

Moreover, individuals belonging to sexual and gender minority (SGM) groups are less likely to be partnered, married, and have children than their non-SGM (i.e., cisgender, heterosexual) peers and, thus, may be more likely to experience social isolation with age, which could hasten cognitive decline. Minority stress, due to anticipated or experienced homophobia, biphobia, or transphobia, is also a potential contributing factor to, and cause of other risk factors for, cognitive impairment in SGM groups.^{14,19}

Evidence, however, is mixed on whether SGM groups are more likely to have cognitive impairment compared with non-SGM groups. Studies have found a higher prevalence of subjective cognitive decline (SCD) (i.e., self-reported experiences of declining memory or worsening confusion) in SGM versus non-SGM adults and a higher prevalence of diagnosed dementia in transgender versus cisgender Medicare beneficiaries.^{18,20,21} Yet, another study found no difference in the onset of MCI among older adults in same-sex partnerships (SSPs) versus opposite-sex partnerships (OSPs), which the authors used as a proxy for sexual orientation.²²

These studies differed in terms of SGM groups examined, populations from which samples were drawn, how cognitive impairment and SGM groups were operationalized, and whether statistical adjustment was performed for confounding factors. To our knowledge, a comprehensive synthesis and appraisal of this growing literature has not been conducted. We performed this scoping review to examine the current state of evidence on differences in cognitive impairment by sexual orientation/gender identity (SOGI) status.

Methods

Search strategy

We conducted a scoping review of the published literature to identify articles describing cognitive impairment among SGM

groups, with findings reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses Guidelines.²³ Search terminology was developed in collaboration with a medical librarian. The search string included a variety of key terms describing SGM groups and cognitive impairment (Appendix 1).²⁴ PubMed/Medline, Cumulated Index to Nursing and Allied Health Literature, Web of Science, PsycInfo, and Embase were searched on February 5, 2022 for articles published since database inception through the search date. This study did not involve human subjects and therefore, Institutional Review Board approval was not required.

Citation screening

Identified citations were imported into an Excel spreadsheet for screening. Two independent reviewers (R.J.R. and A.S.R.) examined titles and abstracts for eligibility criteria. Specifically, citations were included if they described primary studies examining the incidence or prevalence of cognitive impairment by SOGI and excluded if they described reviews or commentaries; however, we scanned the reference lists of relevant secondary articles for primary studies that were not captured in our systematic search. Citations were also excluded that described studies of HIV/AIDS-related dementia, conference abstracts, and those not published in English.

Selected citations were compared between the two reviewers, and disagreement was resolved by consensus with co-authors (J.D.F. and Z.A.M.). Citations were advanced to the full-text review stage if the abstract was not available.

Among potentially eligible citations, two reviewers (R.J.R. and A.S.R.) examined the full text of articles to confirm they met eligibility criteria. Disagreement between reviewers was resolved by consensus with co-authors. Citations that passed both title/abstract screening and full-text article evaluation were included in the scoping review (Fig. 1).

Data extraction, management, and quality assessment

One reviewer extracted relevant study information into a standardized data extraction template and the second reviewer checked the accuracy of the extraction. Outcomes included percentages or point estimates (e.g., odds ratios [ORs] or hazard ratios) with measures of precision (e.g., confidence intervals [CIs]). When proportions were reported instead of ORs or when standard errors were reported instead of 95% CI, we calculated ORs and 95% CI for comparative purposes, applying methods described elsewhere.^{25,26}

Study quality was assessed using tools provided by Cochrane.²⁷ In brief, the study design, handling of confounding, and exposure/outcome measurement were rated as having low, moderate, serious, or critical risk of bias. An overall bias score was also qualitatively assigned; however, issues of confounding contributed more heavily to the overall score.

Based on our understanding of the extant literature, we categorized variables used in studies as potential confounders (i.e., associated with SOGI status and risk factors for cognitive impairment) or intermediary factors (i.e., potentially on the causal pathway between SOGI status and cognitive impairment), so that studies could be assessed on whether authors appropriately handled confounding and/or whether they "over adjusted" for factors that explain relationships.

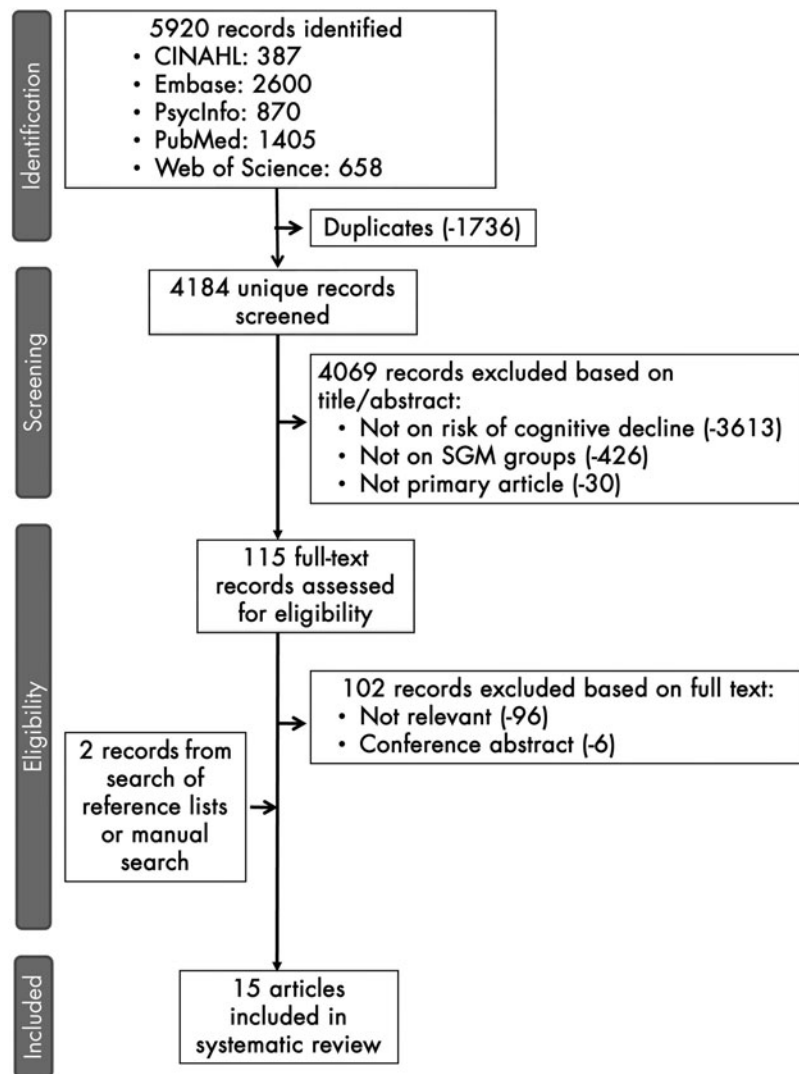


FIG. 1. Study eligibility flow diagram.

We further categorized studies based on whether cognitive impairment was measured subjectively (i.e., self-report) or objectively (i.e., cognitive performance tasks or documented clinical diagnosis). We use the term “subjective cognitive impairment” (SCI) to generically refer to self-reported problems with memory and related cognitive symptoms, whereas we use the term “SCD” to indicate self-reported worsening of these symptoms.

The following *sociodemographic variables* were categorized as confounders: age, sex, race/ethnicity, education, employment status, income, and health insurance status. The following variables were categorized as intermediary factors: *health behaviors* (smoking status, alcohol use, physical activity), *mental health* (depression, anxiety, social connections, stress), *physical conditions* (CVD, diabetes, body mass index [BMI], sleep problems), and *household characteristics* (marital status, household size).

Our working assumption was that there is no direct causal relationship between SOGI status and cognitive impairment. Rather, the relationship is completely mediated by indirect associations between risk factors (i.e., intermediary factors listed previously) that are attributable to SOGI status and lead to cognitive impairment.

Results

Article identification

A total of 4184 citations were identified, of which 115 (2.7%) were selected for full-text review based on initial eligibility screening of titles/abstracts. Upon full-text evaluation, 13 studies from the database searches were considered eligible; one additional study was identified from the reference lists of eligible articles and another study was identified that was recently published after the database search was conducted. In total, 15 studies were included in this scoping review.^{18,20,22,28–39} Total agreement between reviewers on citation selection was 98%, with a kappa statistic of 0.666, corresponding to substantial agreement.⁴⁰

Study characteristics

The 15 studies were published between 2017 and 2022, with data collected between 2005 and 2020. Ten of 15 studies included middle-aged to older adults (≥ 45 years),^{20,22,28,30,33–36,38,39} and the other 5 studies included younger people (≥ 16 or 18 years).^{18,29,31,32,37} Twelve studies were conducted on samples from the United

States,^{18,20,22,28,30,31,33–35,37–39} two were conducted on samples from the United Kingdom,^{29,32} and one was conducted on a sample from Canada.³⁶

Eight studies examined cognitive impairment based on subjective measures in SGM groups versus non-SGM groups (Table 1)^{20,28–34}; five were rated as having moderate risk of bias,^{28,29,32–34} two were rated as having serious risk of bias,^{20,30} and one was rated as having critical risk of bias.³¹

Seven studies examined cognitive impairment based on objective measures among SGM groups versus non-SGM group or by SSP versus OSP status (Table 2)^{18,22,35–39}; three studies were rated as having moderate risk of bias,^{22,35,37} three were rated as having serious risk of bias,^{36,38,39} and one was rated as having critical risk of bias.¹⁸

Across the 15 studies, major sources of bias included study design (i.e., most studies were cross-sectional), limited statistical adjustment for confounding variables or inappropriate statistical adjustment for potential mediating variables and, in the case of subjective outcomes, the use of self-report to measure cognitive impairment.

Findings from the 15 studies are described hereunder. Evidence for subjective and objective measures of cognitive impairment is summarized separately. Also evidence is summarized separately for SGM versus non-SGM groups and SSP versus OSP groups, as the interpretation and implications of findings are different.

Subjective measures of cognitive impairment among SGM versus non-SGM groups

Among eight cross-sectional studies, seven reported statistically significant associations between SOGI status and SCI; however, these relationships differed by groups or subgroups evaluated, whether statistical adjustment was performed, and the factors included for statistical adjustment. Study details are given in Table 1 and described hereunder.

In a study among US adults ≥ 45 years of age using 2013–2018 data from the National Health Interview Survey, Fredriksen-Goldsen et al. found that sexual minority versus heterosexual individuals had higher odds of SCI after adjusting for sociodemographic factors.²⁸ In this study, sexual minority versus heterosexual individuals also had higher odds of more severe and frequent SCI, as well as the extent of and limitations due to SCI. Stratified by gender, the authors found similar results for sexual minority men and women on prevalence of SCI and limitations due to SCI versus their heterosexual peers; however, sexual minority women, but not men, had an increased odds of severity, frequency, and extent of SCI.

In another study of US adults ≥ 45 years of age using 2015–2018 data from the Behavioral Risk Factor Surveillance System (BRFSS), Flatt et al. found that SGM groups had increased odds of SCD versus non-SGM groups, after adjusting for sociodemographic and household factors, as well as health status, but the relationship was attenuated with further statistical adjustment for depressive disorder.²⁰

Likewise, in a cross-sectional study of 2007 Adult Psychiatric Morbidity Survey data from England conducted by Jacob et al., among a sample of people ≥ 16 years of age, after adjusting for sociodemographic and household factors, sexual minority versus heterosexual individuals had higher odds of self-reported concentration complaints²⁹; yet, this ef-

fect was nullified when further adjusting simultaneously for smoking status, alcohol dependency, stress, depression, anxiety, sleep problems, and obesity.

In this study, mediation analysis revealed that smoking status, alcohol dependency, depression, and perceived stress each attenuated this relationship by 0.9%, 5.0%, 4.6%, and 7.0%, respectively, although not completely.²⁹ However, any anxiety, sleep problems, and the number of stressful life events nullified the relationship between self-reported concentration complaints and sexual orientation, each reducing effect sizes by 10.9%, 11.0%, and 13.4%, respectively. No relationship was found between self-reported memory complaints and sexual orientation.

By contrast, a study of women ≥ 65 years of age from the 2015 BRFSS, by Seelman, reported increased odds of SCI, as measured by self-reported serious difficulty concentrating, remembering, or making decisions, among bisexual women compared with heterosexual women but not lesbian or gay women, after adjusting for sociodemographic and household factors.³⁰ Stratified by age, sexual minority women (gay/lesbian/bisexual) combined showed increased odds for SCI among those 70–79 years, but not those aged 65–69 or 80+ years.

Whereas Flatt et al.²⁰ and Jacob et al.²⁹ showed that the relationship between SOGI status and subjective measures of cognitive impairment was mitigated by risk factors, namely depression and anxiety/stress, respectively, another study using BRFSS data (2014–2015) of adults ≥ 18 years of age, conducted by Streed Jr et al., reported increased odds of SCI among gender minority versus cisgender individuals, even after adjusting for depression and various other risk factors including alcohol consumption, smoking, and BMI.³¹

In a study from the United Kingdom, using 2015–2017 cross-sectional data from the National Health Service England, General Practice patient survey, among >1.3 million adults ≥ 18 years of age, Saunders et al. reported increased odds of self-reported dementia diagnosis among sexual minority versus heterosexual individuals, after adjusting for sociodemographic factors. Stratified by age, sexual minority men and women tended to have increased odds of self-reported dementia diagnosis in younger (<55 years) but not older (≥ 55 years) groups.³²

In another study of adults ≥ 45 years of age from the BRFSS from 2016, Brown and Patterson showed no difference in odds of SCD among SGM groups compared with non-SGM groups before statistical adjustment or after adjustment for sociodemographic and household factors, depression, and diabetes³³; however, subgroup analysis showed that gender minority individuals had increased odds of SCD compared with cisgender individuals on crude analysis, but not after statistical adjustment for demographic and health factors.

Nelson and Anzel, using 2016 Health and Retirement Study data among adults ≥ 50 years of age, showed that sexual minority versus heterosexual individuals had no statistically significant differences in SCI, after adjusting for sociodemographic and health factors.³⁴

Objective measures of cognitive impairment among SGM versus non-SGM groups

Four cross-sectional studies examined objective cognitive impairment by SOGI status, of which two measured cognitive

TABLE 1. CHARACTERISTICS OF COMPARATIVE STUDIES EXAMINING SUBJECTIVE MEASURES OF COGNITIVE IMPAIRMENT

<i>Author, publication Year</i>	<i>Data source, country, study year(s)</i>	<i>Study design sample (n)</i>	<i>Measure of cognitive impairment</i>	<i>Odds ratios (95% CI)</i>	<i>Statistical adjustment</i>	<i>Risk of bias</i>
Flatt et al. (2021) ²⁰	Behavioral Risk Factor Surveillance System, United States, 2015– 2018	Cross-sectional Adults 45+ years SGM (<i>n</i> = 3520) Non-SGM (<i>n</i> = 115,608)	Confusion or memory loss that is happening more often or is getting worse	1.26 (1.05–1.51)* 1.23 (1.03–1.47)* 1.15 (0.97–1.37)	Age, race/ethnicity, education, income, health insurance status, marital status + Health status + Depressive disorder Missing confounder(s): sex	Study design: moderate Confounding: serious Measurement: moderate Overall: serious
Fredriksen- Goldsen et al. (2022) ²⁸	National Health Interview Survey, United States, 2013–2018	Cross-sectional Adults 45+ years Sexual minority (<i>n</i> = 2421) Heterosexual (<i>n</i> = 105,731)	Difficulty remembering or concentrating <i>Severity of difficulty</i> remembering or concentrating <i>Frequency of difficulty</i> remembering or concentrating <i>Extent of difficulty</i> remembering or concentrating <i>Limitations due to</i> difficulty remembering or concentrating	1.5 (1.3–1.8)* 2.0 (1.3–3.1)* 1.6 (1.1–2.2)* 1.8 (1.2–2.6)* 1.7 (1.4–2.1)*	Age, race/ethnicity, income, education, survey year Age, race/ethnicity, income, education, survey year Age, race/ethnicity, income, education, survey year Age, race/ethnicity, income, education, survey year Missing confounder(s): sex	Study design: moderate Confounding: moderate Measurement: moderate Overall: moderate

(continued)

TABLE 1. (CONTINUED)

<i>Author, publication Year</i>	<i>Data source, country, study year(s)</i>	<i>Study design sample (n)</i>	<i>Measure of cognitive impairment</i>	<i>Odds ratios (95% CI)</i>	<i>Statistical adjustment</i>	<i>Risk of bias</i>
Jacob et al. (2021) ²⁹	Adult Psychiatric Morbidity Survey, United Kingdom, 2007	Cross-sectional Persons 16+ years Sexual minority (n = 501) Heterosexual (n = 6809)	Concentration complaints Memory complaints	1.40 (1.12–1.76)* 0.99 (0.75–1.3) 1.19 (0.96–1.47)	Age, sex, race/ethnicity, education, employment status, income, marital status +smoking status, alcohol dependency, stress, depression, anxiety, sleep problems, obesity Age, sex, race/ethnicity, education, employment status, income, marital status +smoking status, alcohol dependency, stress, depression, anxiety, sleep problems, obesity	Study design: moderate Confounding: moderate Measurement: moderate Overall: moderate
Seelman, ³⁰ (2019)	Behavioral Risk Factor Surveillance System, United States, 2015	Cross-sectional Women 65+ years Lesbian/gay (n = 158) Bisexual (n = 188) Heterosexual (n = 34,361)	Serious difficulty concentrating, remembering or making decisions	Lesbian/gay: 1.11 (0.49–2.53) Bisexual: 2.41 (1.10–5.76)* Lesbian/gay/bi 65–69 years 1.14 (0.46, 2.80) 70–79 years 3.78 (1.50–9.54)* 80± years 0.96 (0.30–3.02)	Age, race/ethnicity, education, income, home ownership status, household size Age, race/ethnicity, education, income, home ownership status, household size Age, race/ethnicity, education, income, home ownership status, household size Age, race/ethnicity, education, income, home ownership status, household size Missing confounder(s): sex	Study design: moderate Confounding: serious Measurement: moderate Overall: serious

(continued)

TABLE 1. (CONTINUED)

<i>Author, publication Year</i>	<i>Data source, country, study year(s)</i>	<i>Study design sample (n)</i>	<i>Measure of cognitive impairment</i>	<i>Odds ratios (95% CI)</i>	<i>Statistical adjustment</i>	<i>Risk of bias</i>
Streed Jr et al. (2017) ³¹	Behavioral Risk Factor Surveillance System, United States, 2014–2015	Cross-sectional Adults 18+ years Gender minority (<i>n</i> = 1443) Cisgender (<i>n</i> = 314,550)	Serious difficulty concentrating, or remembering, or making decisions	1.56 (1.27–1.93)*	Age, race/ethnicity, education, employment status, alcohol consumption, smoking, BMI, relationship status, children in household, depression Missing confounder(s): sex	Study design: moderate Confounding: critical Measurement: moderate Overall: critical
Saunders et al. (2021) ³²	NHS England GP Patient Survey, United Kingdom, 2015–2017	Cross-sectional Adults 18+ years Sexual minority women (<i>n</i> = 15,597) Sexual minority men (<i>n</i> = 18,557) Heterosexual women (<i>n</i> = 731,164) Heterosexual men (<i>n</i> = 585,208)	Self-reported dementia	Sexual minority women 1.6 (1.3–1.9)* Sexual minority men 1.3 (1.1–1.6)*	Age, ethnicity, deprivation, region Age, ethnicity, deprivation, region	Study design: moderate Confounding: low Measurement: moderate Overall: moderate
Brown and Patterson, (2020) ³³	Behavioral Risk Factor Surveillance System, United States, 2016	Cross-sectional Adults 45+ years SGM (<i>n</i> = 1094) Non-SGM (<i>n</i> = 35,640)	Confusion or memory loss that is happening more often or is getting worse	All SGM groups 1.24 (0.94–1.63) 1.23 (0.93–1.64) 0.88 (0.63–1.24) Gender minority 2.18 (1.01–4.70)* 2.21 (0.99–4.88) 1.59 (0.69–3.71)	Crude Age, gender, race/ethnicity + education, income, employment, marital status, depression, diabetes Crude Age, gender, race/ethnicity + education, income, employment, marital status, depression, diabetes	Study design: moderate Confounding: moderate Measurement: moderate Overall: moderate
Nelson and Andel, (2020) ³⁴	Health and Retirement Study, United States, 2016	Cross-sectional Adults 50+ years Sexual minority (<i>n</i> = 140) Heterosexual (<i>n</i> = 3574)	Self-rated memory	1.25 (0.93–1.71) 1.35 (0.98–1.96)	Age, sex, education + health status, depression, ever smoking, drinking behavior, physical activity, obesity Missing confounder(s): race/ethnicity	Study design: moderate Confounding: moderate Measurement: moderate Overall: moderate

Bold text under the Statistical Adjustment column indicates the adjustment of potential intermediary factors.

*Statistically significant at $p < 0.05$.

BMI, body mass index; CI, confidence intervals; GP, general practitioner; NHS, National Health Service; SGM, sexual and gender minority.

TABLE 2. CHARACTERISTICS OF COMPARATIVE STUDIES EXAMINING OBJECTIVE MEASURES OF COGNITIVE IMPAIRMENT

Author, publication year	Data source, country, data year(s)	Study sample	Measure of cognitive impairment	Outcomes (95% CI)	Statistical adjustment/matching	Risk of bias
Dragon et al. (2017) ¹⁸	Medicare Claims, United States, 2015	Cross-sectional Adults 18+ years Transgender (n = 7454) Cisgender (n = 39,136,229)	Diagnosis of dementia	≤65 years Transgender: 6.9% Cisgender: 4.8% [[OR = 1.47 (1.32–1.63)]]* ≥65 years Transgender: 18.2% Cisgender: 12.2% [[OR = 1.60 (1.43–1.79)]]*	Crude	Study design: moderate Confounding: critical Measurement: low Overall: critical
Perales-Puchalt et al. (2019) ²²	National Alzheimer's Coordinating Center's Uniform Dataset, United States, 2005–2017	Longitudinal Adults 55+ years SSP (n = 307) OSP (n = 4750)	MCI or dementia based on DSM criteria on clinical assessment	MCI HR = 0.92 (95% CI = 0.72–1.18) 1.05 (0.83–1.32) Dementia 1.14 (0.76–1.71) 1.21 (0.73–2.00)	Crude Age, sex, center, education, APOE-e4 allele, living alone Crude Age, sex, center, education, APOE-e4 allele, living alone Missing confounder(s): race/ethnicity	Study design: low Confounding: moderate Measurement: low Overall: moderate
Hsieh et al. (2021) ³⁵	National Social Life, Health, and Aging Project, United States, 2015–2016	Cross-sectional Adults 50+ years Sexual minority (n = 81) Heterosexual (n = 3486)	Poor cognitive performance (18-item MGA)	OR = 2.07 [[(95% CI = 1.77–2.37)]] * 1.91 [[(1.63–2.19)]]* 2.07 [[(1.76–2.38)]]* 2.00 [[(1.69–2.31)]]* 1.95 [[(1.66–2.24)]]* 1.83 [[(1.58–2.08)]]*	Age, gender, race/ethnicity, education Age, gender, race/ethnicity, education + depression and anxiety Age, gender, race/ethnicity, education + physical comorbidity Age, gender, race/ethnicity, education + smoking, drinking, exercise Age, gender, race/ethnicity, education + marital status + close family + living with others + community participation Fully adjusted	Study design: moderate Confounding: low Measurement: low Overall: moderate

(continued)

TABLE 2. (CONTINUED)

Author, publication year	Data source, country, data year(s)	Study sample	Measure of cognitive impairment	Outcomes (95% CI)	Statistical adjustment/matching	Risk of bias
Stinchcombe and Hammond, (2022) ³⁶	Canadian Longitudinal Study on Aging, Canada, 2010–2015	Cross-sectional Adults 45–85 years Homosexual (<i>n</i> = 619) Bisexual (<i>n</i> = 173) Heterosexual (<i>n</i> = 36,057)	Memory (The Rey Auditory Verbal Learning Test: immediate and 5-minute delay recall) Executive function (Mental Alteration Test and Animal Naming Fluency)	Memory Lesbian/Gay 0.22 <i>[[</i> (95% CI = 0.08–0.35) <i>]]</i> * Bisexual 0.26 <i>[[</i> (0.00–0.50) <i>]]</i> * Executive Function Lesbian/Gay 0.02 <i>[[</i> (–0.10 to 0.14) <i>]]</i> Bisexual 0.13 <i>[[</i> (–0.10 to 0.34) <i>]]</i>	Age, sex, race/ethnicity, education, income, employment status, health conditions, health behaviors, marital status, social standing Age, sex, race/ethnicity, education, income, employment status, health conditions, health behaviors, marital status, social standing	Study design: moderate Confounding: critical Measurement: low Overall: serious
Guo et al., (2022) ³⁷	OneFlorida EHR, United States, 2012–2020	Cross-sectional Adults 18+ years Transgender (<i>n</i> = 1784) Cisgender (<i>n</i> = 35,285)	Diagnosis of ADRD	All ages Transgender: 1.7% Cisgender: 0.8% <i>OR</i> = 2.14 <i>[[</i> (1.47–3.13) <i>]]</i> * 18–49 years Transgender: 1.1% Cisgender: 0.3% <i>OR</i> = 3.70 <i>[[</i> (2.11–6.47) <i>]]</i> * 50± years Transgender: 3.5% Cisgender: 2.2% <i>OR</i> = 1.61 <i>[[</i> (0.96–2.71) <i>]]</i>	Matched on age, race/ethnicity Matched on age, race/ethnicity Matched on age, race/ethnicity Missing confounder(s): sex	Study design: moderate Confounding: moderate Measurement: moderate Overall: moderate

(continued)

TABLE 2. (CONTINUED)

<i>Author, publication year</i>	<i>Data source, country, data year(s)</i>	<i>Study sample</i>	<i>Measure of cognitive impairment</i>	<i>Outcomes (95% CI)</i>	<i>Statistical adjustment/matching</i>	<i>Risk of bias</i>
Liu et al., (2021) ³⁸	Health and Retirement Study, United States, 2000–2016	Cross-sectional Adults 50+ years living with a partner SSP (<i>n</i> = 196) OSP (<i>n</i> = 23,473)	Cognitive impairment (composite score)	OR = 1.78 <i>[[</i> (95% CI = 1.65–1.91) <i>]]</i> * 1.33 <i>[[</i> (1.25–1.41) <i>]]</i> * 1.78 <i>[[</i> (1.65–1.91) <i>]]</i> * 1.69 <i>[[</i> (1.58–1.80) <i>]]</i> * 1.73 <i>[[</i> (1.61–1.84) <i>]]</i> * 1.32 <i>[[</i> (1.25–1.39) <i>]]</i> * 1.26 <i>[[</i> (1.15–1.37) <i>]]</i> *	Age, sex, race/ethnicity, education, total household income Age, sex, race/ethnicity, education, total household income + marital status Age, sex, race/ethnicity, education, total household income + smoking and drinking behavior Age, sex, race/ethnicity, education, total household income + depression Age, sex, race/ethnicity, education, total household income + self-rated health Fully adjusted Fully adjusted + same sex*female interaction	Study design: moderate Confounding: low Measurement: low Overall: serious
Manca and Venneri, (2020) ³⁹	National Alzheimer's Coordinating Center's Uniform Dataset, United States, 2005– 2019	Case-control Adults 55+ years MCI/AD (<i>n</i> = 40; 20 SSP, 20 OSP) Controls (<i>n</i> = 40; 20 SSP, 20 OSP)	Cognitive performance (MMSE, Semantic Fluency Test, Trail Making Test, Logical Memory Test (immediate and delayed recall) Digit Span test (forward and backward recall)	See publication for data	Matched on sex, age, years of education, global cognitive functioning status, diagnosis, and APOE status Missing confounder(s): race/ethnicity	Study design: critical Confounding: moderate Measurement: low Overall: serious

*Statistical significance at $p < 0.05$.

Italicized text denotes point estimates calculated from proportions or CIs calculated from standard errors. Bold text under the Statistical Adjustment column indicates the adjustment of potential intermediary factors. Italicized, bracketed text under the Outcomes column indicates that ORs and or 95% CI were calculated.

AD, Alzheimer's Disease; ADRD, Alzheimer's disease and related dementias; APOE, apolipoprotein E; DSM, Diagnostic and Statistical Manual of Mental Disorders; EHR, electronic health records; HR, hazard ratio; MCI, mild cognitive impairment; MGA, Montreal Cognitive Assessment; MMSE, mini-mental state examination; OR, odds ratio; OSP, opposite-sex partnership; SSP, same-sex partnership.

function and two utilized clinical diagnoses of dementia. Study details are given in Table 2 and briefly described hereunder.

One analysis of adults ≥ 50 years of age from the 2015–2016 US National Social Life, Health, and Aging Project, reported that sexual minority individuals had higher odds of cognitive impairment compared with heterosexual individuals based on performances on the 18-item survey-adapted Montreal Cognitive Assessment after adjusting for sociodemographic and health factors, health behaviors, and social connections.³⁵ In stepwise models, many of these factors only slightly impacted the magnitude of the effect size. However, only mental health conditions were found to be statistically significant mediators.

In contrast, using data from 2010 to 2015 in the Canadian Longitudinal Study on Aging among adults aged 45–85 years, Stinchcombe and Hammond found that homosexual and bisexual participants had better performance on memory tests than heterosexual participants, but not on executive function tests, after adjusting for sociodemographic, household, and physical and mental health factors, as well as health behaviors.³⁶

Among two studies that examined diagnoses of dementia, both found a higher prevalence among transgender versus cisgender individuals. In a study by Dragon et al, using 2015 Medicare claims data, the authors showed that transgender beneficiaries were more likely to have a documented diagnosis of dementia among those < 65 years of age (6.9% transgender vs. 4.8% cisgender adults) and those 65 years of age and older (18.2% transgender vs. 12.2% cisgender adults)¹⁸; however, the study authors did not adjust for potential confounders.

In the second study, Guo et al. found that transgender individuals from an electronic health records-based cohort, OneFlorida, from 2012 to 2020 had a higher prevalence of a documented dementia diagnosis than cisgender individuals matched on age and race/ethnicity.³⁷ When stratified by age, the authors found that younger transgender individuals (18–49 years) had a higher prevalence of dementia than age and race/ethnicity-matched cisgender individuals; however, this relationship was not statistically significant among older transgender individuals (≥ 50 years) compared with their cisgender counterparts.

Although the authors did not explore mediators of this relationship, they reported that transgender individuals were more likely to have established risk factors for dementia than their cisgender counterparts, including ever smoking, alcohol use disorder, depression, diabetes, and obesity, among other factors.

Objective measures of cognitive impairment by partnership type

Three studies examined cognitive impairment based on objective measures by partnership type, as a proxy for sexual orientation. Study details are given in Table 2 and briefly described hereunder. One study reported poorer cognitive performance among people in SSPs. Liu et al. explored cross-sectional data from the US Health and Retirement Study from 2000 to 2016 among adults ≥ 50 years of age in cohabitation within another person.³⁸ People in SSPs compared with OSPs had higher odds of cognitive impairment,

as measured by a composite score for immediate and delayed word recall, serial subtraction, and backward counting, after adjusting for sociodemographic factors. This relationship was partially mitigated when adjusting for self-rated health status or depression and was most pronouncedly mitigated when adjusting for marital status.

In this study, mediation analysis showed that marital status explained $\sim 52\%$ of the effects of partnership type on cognitive impairment, whereas health behaviors had no effect, and depression and physical health status each had small effects.³⁸ An interaction between partnership type and gender was not statistically significant, indicating that the composition of the partnership (i.e., male-female, male-male, or female-female) did not influence observed relationships.

The other two studies reported mixed findings for the association between cognitive performance and partnership type. One study was a case-control study using 2005–2019 data from the National Alzheimer's Coordinating Center's Uniform Dataset, which included 80 participants (40 with MCI/AD and 40 controls), with those in SSPs matched to those in OSPs on sex, age, years of education, global cognition functioning status diagnosis, and apolipoprotein E (APOE) allele status (a genetic risk factor for AD).³⁹

In this study, Manca and Venneri reported no differences by partnership type in clinical dementia rating or cognitive performance, except for performance on an auditory working memory task (Digit Span Backward), on which participants in SSPs performed worse than those in OSPs, including when restricting analyses to participants with known positive APOE status.³⁹

Among a subset of study participants with brain magnetic resonance imaging, the authors reported no significant partnership type-by-diagnosis interaction on regional gray matter volumes (GMV), and no main effect of partnership type on GMV. However, the pattern of cerebral atrophy differed by partnership type, where cerebral atrophy among those in OSPs was generally greater in medial temporal lobe regions, and atrophy among those in SSPs was more focused in fronto-limbic regions. The authors noted that this pattern of atrophy may be attributable to the higher rates of neuropsychiatric symptoms present in people in SSPs due to a predisposition for neuropsychiatric symptoms from chronic minority stress.

In a longitudinal study of 2005–2017 data from the National Alzheimer's Coordinating Center's Uniform Dataset, among participants at least 55 years of age, Perales-Puchalt et al. found no difference in the risk of MCI or dementia, as measured by clinical assessment using Diagnostic and Statistical Manual of Mental Disorders criteria, among those in SSPs versus OSPs, on crude analysis or after adjusting for sociodemographic and household factors, and presence of the APOE allele.²² Similar null findings were observed when analyses were stratified by gender.

Discussion

This scoping review identified 15 primary, comparative studies examining cognitive impairment by SOGI status. Included studies had moderate to critical risk of biases, due to their cross-sectional study designs, use of subjective measures of cognitive impairment, and/or how potential confounding was handled. Overall, although most studies showed an increased prevalence of SCI or SCD in SGM groups, the evidence for objective measures of cognitive impairment was

mixed; however, direct comparisons across studies are challenging because authors applied distinct eligibility criteria and measured exposures and outcomes differently.

As mentioned earlier, our working assumption is that the relationship between SOGI status and cognitive impairment is indirect and completely mediated by risk factors that are often more prevalent in SGM groups, such as mental health conditions (e.g., depression, anxiety, and stress) and health behaviors (e.g., smoking, excessive alcohol consumption), which are on the causal pathway to cognitive impairment. Accordingly, demonstration of a relationship between SOGI status and cognitive impairment may be dependent upon the conceptual model used and approach to statistical adjustment in analyses. Despite these issues, there are also concerns regarding the manner in which cognitive impairment and SOGI status are operationalized. We discuss these concerns hereunder.

We identified eight studies that examined cognitive impairment using subjective measures; for example, study participants were asked to report whether they had issues with concentration or memory. Measures of SCI or SCD are not validated diagnostic instruments and may be unreliable in classifying objective cognitive impairment, especially among those with increased psychological stress or cognitive dysfunction.⁴¹

Seven studies from our review used objective measures of cognitive impairment, of which three evaluated cognitive impairment via documented diagnosis in claims data or by clinical assessment and four directly evaluated cognitive performance. Using EHR data has the potential for introducing biases. First, and in general, SGM groups are less likely to interact with the health care system than non-SGM groups, which may lead to underdiagnosis of some conditions in the former.⁴² Second, and specific to studies from this scoping review, transgender individuals may be more likely to be under psychiatric care as part of their gender-affirming treatment than cisgender individuals and, thus, may also be more likely to undergo cognitive assessment, leading to a diagnosis of dementia.^{18,37}

Among the four studies that directly measured performance on cognitive tasks, two studies used partnership type as a proxy for sexual orientation, which is also a concern.^{38,39} For example, by definition sexual minority individuals who are not in a partnership (i.e., single, widowed, or divorced) are excluded. Indeed, older SGM adults are twice as likely to be single and live alone compared with older non-SGM adults.⁴³

Furthermore, this definition also excludes SGM individuals who are in a partnership but do not categorize it in binary or heteronormative terms. Evidence suggests that individuals, regardless of SOGI status, who are not partnered or married are at greater risk for social isolation and loneliness, potentially hastening cognitive decline with age.^{44,45} Thus, partnership type as a proxy for sexual orientation excludes people who are potentially at higher risk for cognitive impairment.

Relatedly, one study required married or partnered individuals to be cohabitating, which excluded people living apart from their partner or spouse.³⁸ The authors adjusted for whether the cohabiting partners were married or not and found that this explained >50% of the association between partnership type and cognitive performance.

They attributed this observation to individuals in SSPs being unmarried because they experience discrimination, which in turn increased their minority stress and, consequently, their risk of cognitive impairment; however, there may be many reasons why people in SSPs are not married, including

personal choice or historical and current sociopolitical factors. Further research is needed to disentangle the relationships between marital status, SOGI status, and cognitive impairment.

Several studies from this scoping review examined the relationship between SOGI status and cognitive impairment before and after adjusting for other variables, alone or in combination, revealing potential mediating factors. Flatt et al. reported that the increased prevalence of SCD among SGM groups was nullified when adjusting for depressive disorder.²⁰ However, symptoms of SCD (or SCI) may actually be a manifestation of depression, rather than neuropathologically related cognitive changes. Jacob et al. reported that the increased prevalence of SCI among sexual minority individuals was partially mitigated by adjusting for smoking status, alcohol dependency, depression, and perceived stress, and completely mitigated when adjusting for the number of stressful life events, any anxiety, and sleep problems.²⁹

Liu et al., however, found that the higher prevalence of objective cognitive impairment among participants in SSPs versus OSPs was mitigated primarily by adjusting for whether the couple was married or not (but this may just be a proxy of sexual orientation), whereas depression and self-reported health had much smaller impacts.³⁸ Similarly, Hsieh et al. found that having mental health conditions partially mediated the association between SOGI status and cognitive impairment.³⁵ These findings are consistent with a body of literature indicating that mental health conditions, like depression and high-risk lifestyle behaviors are more prevalent in SGM groups and are established risk factors for cognitive impairment.^{10–14,46}

Nevertheless, a study by Streed Jr et al. reported an increased risk of SCI among gender minority individuals, despite statistical adjustment for several putative risk factors, including depression, alcohol consumption, and smoking³¹; however, because stepwise analyses were not reported, we cannot know if and to what extent these factors impacted the relationship between gender identity and SCI.

Overall, the published literature currently suffers from several risks of biases, which stem from their designs (i.e., most studies are cross-sectional), limited statistical adjustment for confounding variables or inappropriate statistical adjustment for potential mediating variables and, in the case of subjective outcomes, the use of invalidated measures of cognitive impairment. On this basis, future well-designed longitudinal, observational studies are needed to elucidate the risk of cognitive impairment among SGM groups compared with non-SGM groups, using objective and clinically validated measures.

Furthermore, such studies ought to distinguish between confounding and mediating variables and appropriately incorporate these into analyses, so that factors along the causal pathway are accounted for in a manner that acknowledges their impact on observed relationships. In this scoping review, we have proposed that several sociodemographic factors are classified as confounders (e.g., age, sex/gender, race/ethnicity, education, employment status, income, and health insurance status), whereas the following variables are classified as putative intermediary factors: health behaviors (smoking status, alcohol use, physical activity), mental health (depression, anxiety, social connections, stress), physical conditions (CVD, diabetes, BMI, sleep problems), and household characteristics (marital status, household size).

Future studies are needed to assess these distinctions to work toward a validated conceptual model. Identification

of modifiable risk factors is particularly relevant to alleviate the global burden of cognitive impairment. Although effective treatments for cognitive impairment and dementia are lacking, more high-quality data on risk factors can assist clinicians in counseling patients about their risk and how to modify that risk with tools that are currently available.

In general, more cohort studies are also needed that collect SOGI data so that these groups are better represented in research. Studies identified in this review had very small samples of SGM groups likely because of nascent efforts to collect information on SOGI status.

Limitations

This scoping review has several limitations. First, it was restricted to databases of published research and did not include gray literature; thus, findings are potentially subject to publication bias. Second, the review was also restricted to articles in English; although, non-English citations were not identified in our search. Lastly, due to wide heterogeneity in terms of study designs, pooling of estimates across studies was not feasible.

Strengths

Despite these limitations, this study has important strengths. Our review builds upon a scoping review published in 2021, which evaluated neurological conditions in SGM groups.²⁴ Because the previous scoping review did not focus on comparative studies, our review provides, to the best of our knowledge, the first synthesis and appraisal of the literature on studies comparing risk of cognitive impairment by SOGI status and has identified key areas where future research is needed.

Conclusions

Studies have found higher prevalence of SCI or SCD among some SGM groups versus non-SGM groups and a higher prevalence of dementia diagnoses, specifically, among transgender versus cisgender individuals; yet findings are mixed regarding differences in cognitive performance. Well-designed longitudinal, observational studies using objective measures of cognitive function are needed, with careful consideration of confounding versus intermediary risk factors.

Authors' Contributions

R.J.R.: conceptualization, formal analysis, and writing (original draft); A.S.R.: conceptualization, validation, and writing (review and editing); Z.A.M.: conceptualization, validation, and writing (review and editing); J.D.F.: conceptualization, validation, and writing (review and editing).

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(Appendix follows →)

Appendix 1.

Search terms:

Terms are divided into three categories. The search should capture: (1 AND (2 OR 3)).

1. Variations on terms for LGBTQ+ groups

(bicurious[tiab] OR bisexual[tiab] OR bisexuality[MeSH Terms] OR bisexuality[tiab] OR bisexuals[tiab] OR “cross sex”[tiab] OR crossgender[tiab] OR F2M[tiab] OR (“female-to-male”[tiab] AND gender) OR gay[tiab] OR gays[tiab] OR “gender change”[tiab] OR “gender dysphoria”[tiab] OR “gender identity”[tiab] OR “gender minority”[tiab] OR “gender minorities”[tiab] OR “gender queer”[tiab] OR “gender transition”[tiab] OR genderqueer[tiab] OR GLB[tiab] OR GLBQ[tiab] OR GLBs[tiab] OR GLBT[tiab] OR GLBTQ[tiab] OR heteroflexible[tiab] OR homosexual[tiab] OR homosexuals[tiab] OR intersex[tiab] OR lesbian[tiab] OR lesbianism[tiab] OR lesbians[tiab] OR lesbigay[tiab] OR LGB[tiab] OR LGBQ[tiab] OR LGBS[tiab] OR LGBT[tiab] OR M2F[tiab] OR (“male-to-female”[tiab] AND gender) OR “men who have sex with men”[tiab] OR msm[tiab] OR ((nonbinary[tiab] OR “non-binary”[tiab]) AND gender) OR queer[tiab] OR “same gender loving”[tiab] OR “same sex attracted”[tiab] OR “same sex couple”[tiab] OR “same sex couples”[tiab] OR “same sex relations”[tiab] OR “sex change”[tiab] OR “sex reversal”[tiab] OR “sex transition”[tiab] OR “sexual and gender minorities”[tiab] OR “sexual and gender minority”[tiab] OR “sexual identity”[tiab] OR “sexual minorities”[tiab] OR “sexual minority”[tiab] OR “sexual orientation”[tiab] OR “sexual preference”[tiab] OR “trans female”[tiab] OR “trans male”[tiab] OR “trans man”[tiab] OR “trans men”[tiab] OR “trans people”[tiab] OR “trans woman”[tiab] OR “trans women”[tiab] OR “trans-sexuality”[tiab] OR transexual[tiab] OR transgender [tiab] OR “Transgender Persons”[Mesh] OR transgendered[tiab] OR transgenders[tiab] OR transsexual[tiab] OR transsexualism[MeSH] OR transsexualism[tiab] OR transsexuality[tiab] OR transsexuals[tiab] OR transvestite[tiab] OR “women loving women”[tiab] OR “women who have sex with women”[tiab] OR WSW[tiab] NOT (“laparoscopic gastric bypass”[tiab] OR “markov state model” OR “multiple source method”[tiab])) AND

(

2. Variation on terms for cognition/memory in combination with impairment/disorder

((cognition[tiab] OR cognitive[tiab] OR memory[tiab] OR neuropsych*[tiab] OR neurocog*[tiab] OR attention[tiab] OR “executive function”[tiab] OR language[tiab]) AND (impaired[tiab] OR impairment*[tiab] OR decline*[tiab] OR loss*[tiab] OR lost[tiab] OR deficienc*[tiab] OR deficient[tiab] OR deficit*[tiab] OR dysfunction*[tiab] OR disorder*[tiab])) OR

3. Variation on terms specific to impaired cognition or dementia

(Dementia[MeSH] OR Frontotemporal Dementia[MeSH] OR Alzheimer Disease[MeSH] OR Lewy Body Disease[MeSH] OR Cognition[MeSH:noexp] OR “Cognitive Reserve”[Mesh] OR Cognition Disorders[MeSH] OR Cognitive Dysfunction[MeSH] OR Memory Disorders[MeSH] OR Neurocognitive Disorders[MeSH] OR Mental Fatigue[MeSH] OR Functional Status[MeSH] OR Cognitive Aging[MeSH] OR Dementia, Vascular[MeSH] OR Memory Disorders[MeSH] OR Neurocognitive Disorders[MeSH] OR Attention[MeSH] OR Executive Function[MeSH] OR Language Disorders[MeSH] OR dementia[tiab] OR Alzheimer*[tiab])