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Sexual and Gender Minority Health in Neurology: A Scoping Review

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Abstract

Importance: Little is known about the neurologic health needs of the sexual and gender minority (SGM) community.

Objective: The goal of this scoping review is to describe the current state of science in SGM health in neurology and highlight areas of knowledge and gaps to guide future research.

Evidence Review: The authors searched PubMed, Embase, Web of Science, PsycINFO, CINAHL, and Biosis Previews including all articles published before April 12,2020 using a search string encompassing SGM descriptors and neurologic disorders. A total of 8359 items were found and entered into EndNote, with 2921 duplicates removed. Blinded abstract review was performed by the authors in duplicate, with conflicts settled through consensus, followed by a duplicate full text review to identify the 348 articles eligible for data abstraction. Articles presenting primary data about an identified adult SGM population addressing a clinical neurology topic were included. Descriptive statistics were used for the abstracted variables.

Findings: Of the 348 articles, the largest proportion were published in the United States (50.3%) and were case reports/series (58.9%). Most (72.4%) included gay/bisexual cisgender men, and 247 studies (71.0%) assessed neurologic disorders in HIV+ individuals. Race/ethnicity was identified in 31.9% of studies. The most common subject themes were neuroinfectious disease (57.5%), cognitive neurology (17.2%), cerebrovascular disease (4.6%), and autism (4.6%).

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Conclusions: More rigorous research in a wider range of neurologic topics and inclusive of more sociodemographic diversity is gravely needed. Systematic collection of sexual orientation and gender identity in the electronic health record and in population health surveys would be an important step forward in neurologic health equity for the SGM community.

INTRODUCTION

Little is known about the neurologic health needs of sexual and gender minorities (SGMs; i.e. those in the lesbian, gay, bisexual, transgender, and queer [LGBTQ+] spectrum). Understanding an individual's identity is essential for patient-centered communication, which improves patient satisfaction and reduces health disparities. SGM identity directly impacts a variety of neurologic conditions, including epilepsy,[1] dementia,[2] and stroke.[3,4] Neurologists receive little to no dedicated SGM health training,[5] which may lead to conscious or unconscious behaviors that contribute to existing disparities.[6] A 2018 study of U.S. neurologists, for example, found a discrepancy between SGM-related medical knowledge and self-reported comfort in caring for SGMs.[3] Nearly half of respondents believed that sexual orientation and gender identity (SO/GI) had no bearing on the management of neurologic illness.[3] This scoping review describes the current state of science in SGM health in neurology, highlighting areas of knowledge and gaps to inform future research.

METHODS

Guided by an experienced medical librarian (EW), the authors developed, tested, and finalized a PubMed search utilizing MeSH and keywords with SGM descriptors[7] and neurologic disorders (Supplement 1). The disorders were compiled based on clinical expertise, the National Institute of Neurologic Disorders and Stroke website,[8] and prior research.[9] This search was modified for Embase, Web of Science, PsycINFO, CINAHL, and Biosis Previews.

The search encompassed studies published prior to April 12, 2020 and discovered 8359 items. All results were added to EndNote and duplicate items (n=2921) removed (Figure 1). The articles were uploaded to Rayyan[10] for title and abstract screening based on defined inclusion/exclusion criteria (Table 1). Two reviewers performed blinded screening, with conflicts resolved by discussion. A set of 534 articles was downloaded and added to Google Sheets. Two reviewers performed full-text screening, with conflicts resolved through consensus, resulting in 348 articles retained for analysis using a data abstraction form developed, piloted, and tested by the authors. Descriptive statistics were used to analyze the extracted variables.

RESULTS

Most of the articles were published in the U.S. (Table 2). Case reports/series accounted for 58.9% of the total. Most articles included gay/bisexual cisgender men. Race/ethnicity was identified in 31.9% of studies. Five studies (1.4%) focused on individuals over age 60. The

most common subjects were neuroinfectious disease (n=200, 57.5%), cognitive neurology (n=60, 17.2%), cerebrovascular disease (n=16, 4.6%), and autism (n=16, 4.6%) (Table 2).

HIV and Neurology

The predominant theme in SGM neurologic health literature was pathology associated with HIV. In nearly all these studies, SO was included solely as a risk factor for HIV. Two hundred-forty-seven studies discussed the neurologic health of HIV+ individuals, including 173 (86.5%) of the neuroinfectious disease studies and 54 (90%) of the cognition studies (for full references by topic, see Supplement 2). Of the HIV-related studies, 99 case studies/series, 5 cohort studies, 5 case-control, and 21 cross-sectional studies described opportunistic infections or risk factors for infections in HIV+ individuals. Fifteen case reports described neurologic symptoms of primary HIV infection. Fourteen case reports and one cross-sectional study described neurologic manifestations of chronic HIV.

Other neurologic pathologies studied in connection with HIV were central pontine myelinolysis, myelopathy, neuropsychiatric disorders, status epilepticus, peripheral neuropathy, myopathy, motor neuron disease, CNS tumors, and cerebrovascular disease. However, the focus of these studies was on HIV/AIDS, not explicitly SO/GI.

Neuroinfectious disease

Most studies describing neuroinfectious disease in the absence of HIV were case reports/series (25/27, 92.6%) among cisgender gay men (24/27, 88.9%). Most of these reports described syphilis (12/25, 48%). Four case reports/series from the 1980s described men with toxoplasmosis and progressive multifocal leukoencephalopathy (PML) without explicit discussion of HIV. Other case reports described gay men with adenovirus encephalitis, herpes encephalitis, cytomegalovirus encephalitis, shigellosis-associated encephalitis, gonococcal meningitis, and varicella zoster meningitis. Two studies assessed the epidemiology of and risk factors for an outbreak of invasive meningococcal disease in men who have sex with men (MSM) in New York City in 2012.[15,16]

Cognition

There were six studies that examined cognition in SGMs independent from HIV. Flatt et al. found that approximately 25% of 210 LGBT participants reported subjective cognitive decline (SCD). Those with depression, reporting functional impairment, and people of color were significantly more likely to experience SCD (odds ratio [OR]=2.9 [95% confidence interval [CI] 1.3–6.9], OR=2.6 [95% CI 1.1–6.5], and OR=2.5 [95% CI 1.1–7.8], respectively).[17] A study assessing SCD using 2016 Behavioral Risk Factor Surveillance System (BRFSS) data found no difference in SCD between SGM and non-SGM respondents after adjustment.[18] The only study to examine mild cognitive impairment (MCI) and dementia found no significant difference in the risk of MCI/dementia in same-sex couples compared with opposite-sex couples.[19]

The other three studies were qualitative: one was a case study describing an elderly person with dementia questioning their gender identity[20], and the other two were qualitative studies exploring the experiences of SGM individuals with dementia, their caregivers, and

providers.[21,22] These studies described similar themes: the impact of dementia on SO/GI (e.g. concealment versus disclosure, transitioning versus de-transitioning), conflict with family of origin, stigma around dementia and SGM identity, intimate relationships as safe spaces, and the vital need for inclusive healthcare services.[21,22]

Cerebrovascular disease (CVD)

Of the 12 CVD studies independent from HIV, eight (66.7%) were case reports/series. Most (8/12, 66.7%) included transwomen: four case reports of ischemic stroke in transwomen taking estrogen, one report of a transwomen with bilateral non-arteritic ischemic optic neuropathy, two reports of transgender women with cerebral venous sinus thrombosis, and one case series of stroke, transient ischemic attack and subarachnoid hemorrhage in eight transwomen.[23] This series found disproportionate rates of stimulant use, tobacco, hepatitis C, HIV and prior stroke in transwomen compared with the general population.[23]

Two large cross-sectional studies examined vascular disease in transgender individuals, with stroke included as an outcome.[24,25] One case-control study used an algorithm to identify transgender individuals in the Kaiser system.[24] In the transfeminine cohort (n=2842), risk of stroke was higher compared with ciswomen (adjusted hazard ratio [aHR] 1.9, 95% CI 1.3–2.6) but not cismen (aHR 1.2, 95% CI 0.9–1.7). In 853 transfeminine individuals who initiated gender affirming hormones after enrollment, risk of ischemic stroke was greater compared with ciswomen (aHR 2.9, 95% CI 1.5–5.5) and cismen (aHR 2.3, 95% CI 1.2–4.3). There was no difference in stroke risk in the transmasculine cohort (n=2118) compared with the cisgender cohort, with a small overall number of strokes (16).[24] Using 2014–2017 BRFSS data, another study found that transwomen were more likely to report ischemic stroke than ciswomen (aOR 1.88, 95% CI 1.16–3.03) but not cismen (aOR 1.62, 95% CI 0.99–2.63). Transmen and gender nonconforming individuals had no increased risk of stroke compared with cisgender people.[25]

The three cross-sectional analyses of CVD in SM individuals found conflicting results. A study of SM elders using National Health Interview Survey (NHIS) data found SM women were more likely to report stroke compared with heterosexual women (aOR 2.12, 95% CI 1.57–2.87), and lesbians were more likely than bisexual women to report stroke (aOR 2.79, $p<0.05$). There was a trend toward lower reported stroke in SM men compared with heterosexual men, however this was not statistically significant.[26] Another study found no difference in the odds of stroke between gay/lesbian and heterosexual respondents using 2014–2016 BRFSS data, but higher odds of stroke in bisexual women compared with heterosexual women (aOR 1.45, 95% CI 1.01–2.12).[27] A study using NHIS data found that white SM women were more likely to report stroke compared with white heterosexual women (prevalence ratio [PR] 1.91, 95% CI 1.16–3.15). Black SM women were more likely to report stroke compared with white heterosexual women (PR 4.51, 95% CI 2.16–9.39) and Black heterosexual women (PR 3.25, 95% CI 1.63–6.49). Latinx SM women had no difference in stroke compared to Latinx or white heterosexual women, nor were there differences in stroke for SM men compared with their heterosexual counterparts.[28]

Autism and Gender Identity

Of the 57 papers discussing transgender neurologic health, 16 (28.1%) investigated the potential association between gender dysphoria and autism spectrum disorder (ASD). Most (n=9, 56.3%) found a positive correlation. In one study, the prevalence of autistic traits consistent with ASD in 91 transpeople was 5.5% compared with 0.5–2% in the general population.[29] A study of individuals with ASD found rates of transgender identity 20–40 times higher than population estimates.[30] Another study, however, found similar rates of autistic traits between transgender and cisgender individuals.[31] They argued that higher Autism Spectrum Quotient scores may not indicate ASD "as the difference between groups…related to social behaviors" that "may be a reflection of transgender people's high social anxiety levels due to negative past experiences".[31] All the autism studies argued for increased awareness around this potential association and the importance of inclusive care for neurodiverse and gender diverse individuals. The three qualitative studies assessing experiences of transpeople with ASD identified themes of discrimination due to dual identities, lack of inclusive healthcare, and how these identities affect self-exploration and understanding of both GI and ASD.[32–34]

CNS tumors

HIV-associated malignancies (n=11), and meningiomas in transwomen (n=6) were two main themes in the SGM neurologic malignancy literature. Most were case reports/series (16/18, 88.9%). Six case reports explored the potential link between gender affirming hormone use and meningiomas in transwomen. The authors suggest a pathophysiologic mechanism between hormone-responsive meningiomas and feminizing hormones, including pathology showing progesterone and estrogen receptor positivity in 4/6 of the reports.[35–38] A retrospective case review of 3,928 transpeople echoed these findings.[39] This study compared the incidence of benign brain tumors in transpeople with those in the general Dutch and European populations. In transwomen, incidence of meningiomas and prolactinomas were higher than in ciswomen (standard incidence ratio [sIR] 4.1, 95% CI 1.9–7.7; sIR 4.3, 95% CI 2.1–7.9, respectively) and cismen (sIR 11.9, 95% CI 5.5–22.7; sIR 26.5, 95% CI 12.9–48.6, respectively). In transmen, incidence of somatotrophinomas was higher compared with cisgender people (sIR 22.2, 95% CI 3.7–73.4). The authors did not recommend routine screening, however, as the occurrence of these tumors was rare.[39]

Sleep

Nine studies examined sleep in SGM individuals with conflicting results. Each study defined short sleep duration differently (≤5 hours to ≤ 7 hours), and each relied on self-reported sleep duration/disturbances. One study found disparities in sleep duration and quality for SM people of color[40], while another did not.[41]

Dai and colleagues used 2014 BRFSS data to examine the association between sleep duration and health outcomes in SGM individuals. They found a higher prevalence of very short sleep duration (≤5 hours) in SGM respondents compared to non-SGM respondents (17.4% versus 12.2%, $p<0.0001$), most prevalent in gender nonconforming individuals (35.5%), lesbians (19.7%), and bisexual women (19.6%). They also found very short sleep

duration was associated with an increased odds of reporting stroke among SGM individuals (aOR 4.1, 95% CI 2.2–7.6).[42]

Three studies examined sleep in transgender individuals. One assessed the sleep electroencephalogram (EEG) of seven transwomen before and 3-months after initiation of hormones, finding an increase in stage 1 sleep and beta activity in non-rapid eye movement sleep after estrogen initiation.[43] One study used multicenter observational data of transgender individuals in Germany and found that sleep quality, measured by the Pittsburgh Sleep Quality Index (PSQI), was associated with quality of life in both transwomen and transmen ($r= -0.622$, $p<0.001$; $r= -0.530$, $p<0.001$, respectively). Rates of poor sleep (PSQI ≥ 5) were high for transwomen (79.2%) and transmen (81.2%).[44] The third study explored restless leg syndrome (RLS) in transgender individuals, finding a higher prevalence of RLS in those taking estrogen compared with testosterone (20% versus 9.3%), although not statistically significant and a small sample size (6 and 4, respectively).[45]

Headache

Headache literature in SGM individuals is sparse: four case reports and two cross-sectional studies. Three case reports described transpeople with idiopathic intracranial hypertension (IIH). The authors suggest a potential pathophysiologic link between gender affirming hormones and IIH. The fourth case, published in 1968, described migraine attributed to repression of sexual identity in a gay man through a psychoanalytic context.

Using data from a gender clinic in The Netherlands, one study found the prevalence of migraine in 50 transwomen was 26%, comparable to prevalence in ciswomen.[46] A study from Canada found that SM men had 50% greater odds of migraine compared with heterosexual men (OR 1.5, 95% CI 1.13–1.99), and found no difference between SM and heterosexual women.[47]

Multiple sclerosis

Three case reports and three cross-sectional studies included SGM individuals with multiple sclerosis (MS). Two case reports included SGM individuals, but discussed other concerns. The third described the progressive course of MS in a transman despite use of testosterone, suggesting a complex role of hormones in MS.[48]

Using linked English Hospital Episode Statistics and mortality data,[49] one study found an association between gender identity disorder diagnosis and MS in transwomen (adjusted risk ratio [aRR] 6.63, 95% CI 1.81–17.01, p=0.0002) but not transmen.[49] Two studies investigated experiences of SGM individuals with MS, finding no difference in healthcare utilization or disease modifying therapy use, but significant differences in continuity of care,[50] satisfaction with care,[50,51] and comfort in discussing sexual health with clinicians[51] compared with non-SGM peers.

Traumatic Injuries

Three traumatic brain injury (TBI) studies included transgender individuals. One case report described a transwoman's recovery from polytrauma, including one sentence about her

identity.[52] A qualitative study described experiences of violence for Toronto sex workers. Four of the 10 participants were transwomen. Nine participants had at least one prior TBI but the paper didn't explore transwomens' experiences compared with ciswomen.[53] The third study assessed concussion after bicycle accidents; three respondents identified as transgender, however the study didn't discuss GI.[54] The remaining study, a case report from 1988, described a spinal cord injury in a cisgender gay man with HIV.[55]

Movement disorders

The movement disorders literature in SGM individuals included five case reports/series, three of which described opportunistic infections in SM men with HIV.[56–58] Another case report described a gay man with HIV with acute extrapyramidal symptoms and Wernicke's pathology on autopsy.[59] The fifth case, published in 1960, discussed the psychiatric versus neurologic etiology of acquired spasmodic torticollis in a gay man.[60]

Neuromuscular disorders

Two case reports discussed neuromuscular disorders in HIV negative SGM individuals. One described a transman with hypokalemic thyrotoxic periodic paralysis exacerbated by testosterone. The authors mentioned that testosterone was stopped, however didn't discuss the consequences of this decision.[61] The other case described a transwoman with spinal bulbar muscular atrophy despite undetectable androgen levels. The authors postulated this was due to spironolactone's action as a selective androgen receptor modulator.[62]

Epilepsy

A single epilepsy study included gay men. This retrospective chart review assessed metabolic factors associated with status epilepticus in HIV+ individuals. Only 28/68 participants were gay, and there was no discussion of SO.[63]

Other neurologic topics

A cross-sectional study using the Centers for Medicare & Medicaid Services (CMS) Chronic Conditions Data Warehouse claim records compared chronic diseases in transgender Medicare beneficiaries with cisgender beneficiaries. They found that transgender individuals had higher prevalence of autism (3% versus 0.3%), epilepsy (10.5% versus 3.3%), fibromyalgia (37.2% versus 20.7%) and migraine (14.8% versus 4.4%) compared with cisgender peers, and lower prevalence of dementia (10.2% versus 11%) and stroke (9% versus 11.2%); however, there were differences by age of entitlement. They found that 71.4% of transgender individuals (versus 16.7% cisgender) were entitled to benefits due to disability rather than age.[64]

Another study used NHIS data to investigate SO and health outcomes. Lesbians had higher prevalence of stroke (PR 1.96, 95% CI 1.14–3.39) and functional limitation (PR 1.17, 95% CI 1.02–1.34) compared with heterosexual women. Bisexual women reported higher prevalence of functional limitations, but not stroke (PR 1.41, 95% CI 1.15–1.73). Bisexual men reported lower prevalence of stroke (PR 0.04, 95% CI 0.005–0.26), and all SM men reported higher prevalence of functional limitation, compared with heterosexual men.

This study found no significant difference in sleep duration between SM and heterosexual individuals.[65]

One study described the symptoms and natural history of PHACE syndrome in 18 individuals, one of whom was transgender, however did not distinguish the experience of the transgender participant.[66]

Neurologic health of intersex individuals

The sole study on neurologic health of intersex individuals was a case series of three individuals with differences in sex development due to a WT1 gene mutation who presented with hypomyelinating leukodystrophy, leading to a constellation of neurologic symptoms including gait instability, incontinence, weakness, and seizures.[67]

DISCUSSION

This scoping review highlights a number of deficiencies in the current science on SGM neurologic health. The literature is skewed towards HIV-related pathology, predominantly focused on young SM cisgender men, was comprised primarily of case reports/series, and largely omitted racial/ethnic considerations.

While the dedicated attention to HIV in SGM individuals was reasonable at the onset of the epidemic, the persistent connection between HIV and SGM health leaves many unexplored aspects of SGM health. Focusing on HIV in SGM individuals may lead to the incorrect conclusion that HIV is not a concern in other communities, and may reinforce the link between SGM identity and illness. Lastly, this focus may detract necessary attention and funding away from other health concerns in the SGM community, such as vascular disease and cancer.

The neurologic literature in SGM individuals also suffers from many limitations. Some studies examined sexual orientation (e.g. lesbian, gay) while other assessed behavior (e.g. MSM), limiting comparability across studies. The lack of analyses incorporating other sociodemographic factors that impacted health, such as race/ethnicity, socioeconomic status, and immigration/refugee status, limits the generalizability of this research to much of the SGM community. The few studies that examined neurologic health through an intersectional lens found greater disparities in SGM individuals of color, highlighting an important gap in our current understanding of SGM neurologic health. Research in SGM elders is similarly lacking, as is research in particular groups within the larger SGM umbrella, such as lesbians, gender non-binary or intersex individuals, or those who identify as queer, pansexual or asexual.

CONCLUSIONS

Systematic research on the neurologic health of SGM individuals is desperately needed. Large cohort studies with representation of diverse SGM individuals are essential. Collection of SO/GI in electronic health records, patient registries, and in all population health surveys is necessary to advance our neurologic care for this underserved community.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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KEY POINTS

Question:

What is the current state of science in sexual and gender minority (SGM) health in neurology?

Findings:

Most of the studies were case reports/series (n=205, 58.9%) and discussed the health of sexual minority cisgender men (n=252, 72.4%). The most common subjects were neuroinfectious disease (n=200, 57.5%), cognitive neurology (n=60, 17.2%), cerebrovascular disease (n=16, 4.6%), and autism (n=16, 4.6%). Two hundred and forty-seven studies (71.0%) discussed neurologic complications of HIV.

Meaning:

More rigorous research in a broader range of neurologic topics is needed to understand the current neurologic health needs of the SGM community.

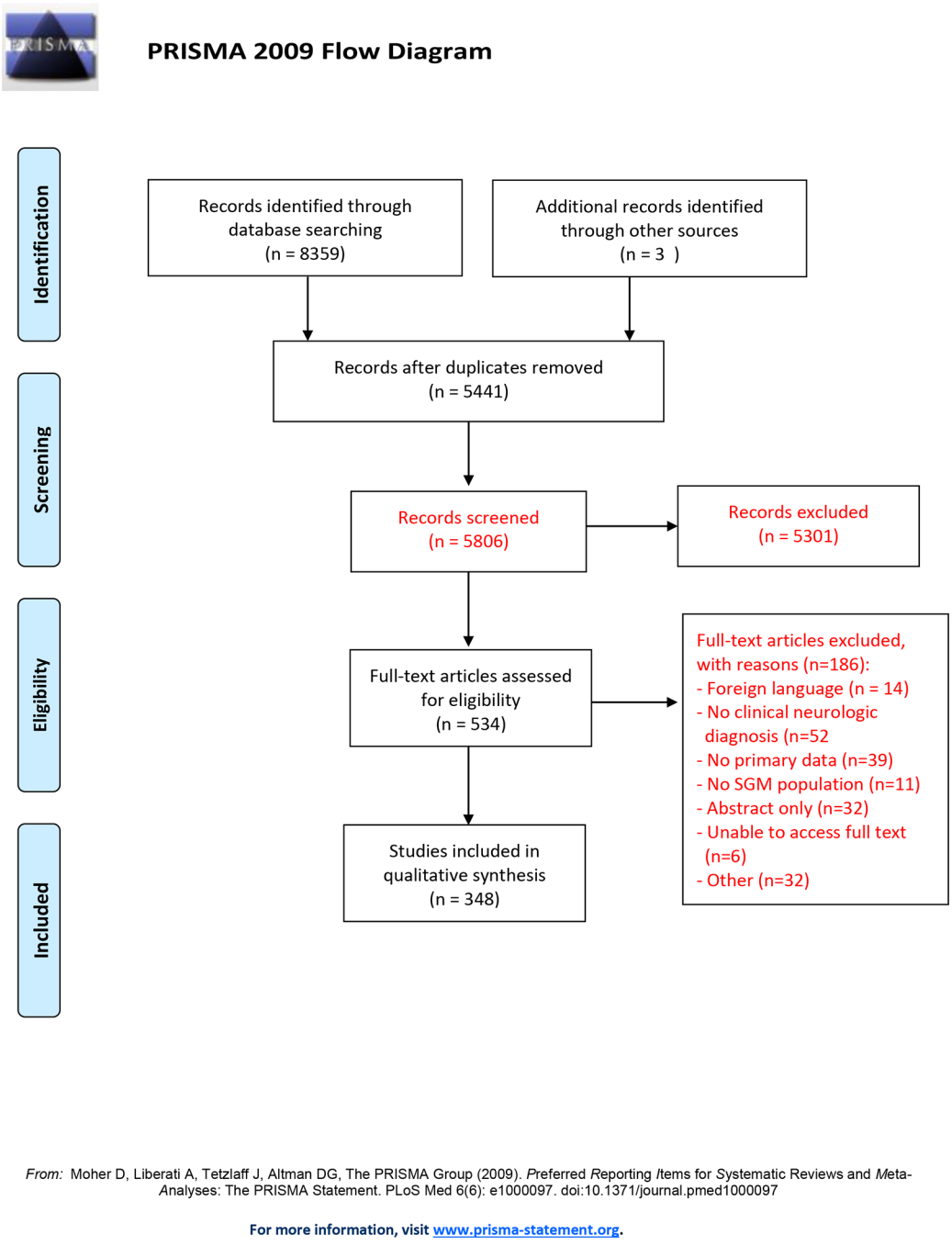

Figure 1.

PRISMA Flow Diagram: Scoping Review of Sexual and Gender Minority (SGM) Health in Neurology

Table 1:

Inclusion and exclusion criteria for article review

Inclusion criteria	Adult (age ≥ 18)
	Comprised of primary data
	Addresses clinical neurology
	Includes an identified LGBTQ+ population
	All years of publication included
	Case reports/series included
Exclusion criteria	Review articles, syntheses, books/book chapters, opinion pieces, sociological or theoretical articles, letters to the editor
	Autopsy studies, neurophysiology studies, or neuroanatomical studies without clinical information provided
	Addresses complications of HIV treatment or other treatments (chemotherapy, antibiotics, etc.)
	Foreign language
	Non-human research

Table 2:

Study characteristics of the articles eligible for full text review

	Number of studies (%) n=348
Country of origin	
Australia	12 (3.4)
Belgium	2 (0.6)
Brazil	7 (2.0)
Canada	10 (2.9)
China	1 (0.3)
Croatia	1 (0.3)
Czech Republic	1 (0.3)
Denmark	6 (1.7)
England	36 (10.3)
Finland	1 (0.3)
France	17 (4.9)
Germany	18 (5.2)
India	1 (0.3)
Ireland	2 (0.6)
Israel	1 (0.3)
Italy	16 (4.6)
Japan	7 (2.0)
Mexico	1 (0.3)
Netherlands	12 (3.4)
Russia	1 (0.3)
South Korea	3 (0.9)
Scotland	1 (0.3)
Spain	7 (2.0)
Sweden	1 (0.3)
Switzerland	3 (0.9)
Taiwan	1 (0.3)
Thailand	2 (0.6)
United States	175 (50.3)
Multiple (UK & Italy)	1 (0.3)
Year of publication	
<1979	3 (0.9)
1980–1989	87 (25.0)
1990–1999	102 (29.3)
2000–2009	52 (14.9)
2010–2019	93 (26.7)

	Number of studies (%) n=348
2020	11 (3.2)
Sexual orientation / behavior (n=297)	
Lesbian only	0 (0)
Gay only	193 (65.0)
Men who have sex with men	19 (6.4)
Bisexual only	15 (5.1)
Gay and bisexual men	44 (14.8)
Other or multiple sexual orientations[1]	26 (8.8)
Gender identity[2]	
Transgender women	24 (6.9)
Transgender men	6 (1.7)
Both transgender women and men	12 (3.4)
Cisgender only	289 (83.0)
Gender inclusive / multiple gender identities	15 (4.3)
Type of study	
Case report / series	205 (58.9)
Cohort study	35 (10.1)
Case-control study	7 (2.0)
Cross sectional study	95 (27.3)
Qualitative study	5 (1.4)
Mixed methods study	1 (0.3)
Race/ethnicity	
Exclusively white	18 (5.2)
Exclusively Black/African American	10 (2.9)
Majority white	51 (14.7)
Majority Black/African American	3 (0.9)
Country of origin provided	23 (6.6)
Race/ethnicity not specified	237 (68.1)
Neurologic topic	
Autism	16 (4.6)
Cognition	60 (17.2)
Epilepsy	1 (0.3)
Headache	6 (1.7)
CNS tumors	15 (4.3)
Movement disorders	2 (0.6)
Multiple sclerosis	6 (1.7)
Neuro-infectious disease	176 (50.6)
Neuro-ID and other topic (cognition, neuromuscular, movement disorders, multiple sclerosis, tumors, vascular)	24 (6.9)

	Number of studies (%) n=348
Neuromuscular	2 (0.6)
Sleep	9 (2.6)
Trauma	4 (1.1)
Cerebrovascular disease	16 (4.6)
Other neurologic topics	11 (3.2)
Studies about HIV	247 (71.0)

[1] Gay and lesbian (n=4); gay, bisexual and lesbian (n=14); men who have sex with men (MSM) and men who have sex with men and women (n=2); inclusive of all sexual orientations (n=6)

[2] Two studies missing because of unclear gender identity of the participants