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Sex Differences in Neurology: A scoping review protocol

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Sex Differences in Neurology: A scoping review protocol

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Abstract

Introduction: Sex and gender are independently important in health and disease but have been incompletely explored in neurology. This is in part contributed to by the pre-existing male bias in scientific literature that results in fewer females being included in clinical research and the often interchangeable use of sex and gender in the literature.

This scoping review intends to identify the advances as well as under-explored aspects of this field to provide a road map for future research. This paper outlines the methods for a scoping review of published, peer-reviewed literature on sex and gender differences in four subspecialty areas of neurology: demyelination, stroke, epilepsy, and headache.

Methods and Analysis: A detailed search strategy will be used to search 5 databases. Specific inclusion and exclusion criteria will be applied to capture relevant literature published from 2014-2020. Data will be collected and synthesized to provide an overview of information retrieved, a narrative synthesis of each subspecialty area, and map of results.

Ethics and Dissemination: Research ethics board approval was not required for this study. This study will aid in mapping recent trends in sex differences in four major neurological conditions and will help identify areas for further research. A manuscript will be compiled for publication and presentations of findings.

Registration Details: The final protocol is registered with the Open Science Framework (<https://osf.io/n937x/>).

Keywords: Sex, Gender, Neurology, Women's Issues, Scoping Review

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This will be one of the most comprehensive studies to date to summarize the available literature on sex and gender differences in four of the largest neurology subspecialties across diverse periods of hormonal changes
- Both quantitative and qualitative studies will be assessed.
- The review will cover five databases (Ovid MEDLINE, PsychINFO, Embase, Central Registry of Controlled Trials, Ovid Emcare).
- Grey literature, commentaries, cases, and pilot studies will not be included in the literature search.
- Due to the vast literature and broad topic, only studies published within the past 5 years will be included.

INTRODUCTION

Medicine has moved away from a ‘one size fits all’ model of care in favor of a targeted, precision-based medicine approach that recognizes the importance of population variables in health and disease. Of particular note are sex and gender, which have historically been used interchangeably or omitted as a variable in research design.[1] With the National Institute of Health’s (NIH) policy change requiring sex to be defined as a biological variable, research is moving towards an increasing understanding of how sex influences neurological illness and treatment.

The interchangeable use of sex and gender in medical literature disregards distinctions between biological factors and sociocultural norms. Sex refers to biological differences between male and females (e.g., hormonal and genetic differences).[2] Sex differences play an important role in disease prevalence, presentation and outcomes, as well as in treatment efficacy and tolerability.[3,4] Gender refers to socially constructed roles, behaviours, expressions, and identities of individuals (e.g., risk-taking behaviour, treatment by others).[2] Gender differences have been implicated in health behaviours and disease outcomes.[3] Both sex and gender are independently important in health and disease, interacting through an individual’s life course and resulting in different health and disease outcomes.

The extent of sex and gender differences in neurology is incompletely explored. There has historically been a male bias in scientific literature, particularly in neuroscience, with females excluded from clinical trials or fewer females than males recruited to clinical trials.[1] Although this discrepancy has been reduced in recent years, gaps in studies examining sex and gender differences remain in the literature. Despite recent research indicating that 85.5% of human neuroscience studies include both male and female participants, 73.5% of these studies did not analyze data by sex.[1] As well, males are exclusively studied 4 times as often as females.[1] To optimize care for patients with neurological conditions, it is important to understand how sex and gender each impact health and disease outcomes.

Therefore, this protocol is appropriately set for a scoping review of sex and gender differences across 4 neurology subspecialties: demyelination, stroke, headache, and epilepsy. These four subspecialty areas were chosen as they are among the largest

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2
3 subspecialties in neurology. Furthermore, these conditions commonly affect younger
4 adults, allowing for further evaluation of sex differences during periods of hormonal
5 changes (i.e., menstruation, pregnancy, menopause). The aims of the scoping are: a) to
6 systematically map the research conducted in these areas, and b) to identify any existing
7 gaps in knowledge. These findings may inform future research and ultimately enable
8 implementation of sex- and gender-specific strategies in clinical practice.
9

10 11 **METHODS**

12 **Scoping Review Aim**

13 The aim is to conduct a scoping review of sex differences in neurologic conditions, using
14 the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols
15 (PRISMA-P) guidelines.[5] The final protocol is registered with the Open Science
16 Framework (<https://osf.io/n937x/>).
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18

19 **Research Objectives**

20 This scoping review will explore how sex differences affect different aspects of patient
21 experiences in four subspecialty areas in neurology: demyelination, stroke, headache, and
22 epilepsy. The findings will be used to summarize research conducted in these areas and
23 identify any existing gaps of knowledge.
24
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26 The broad research question for this review is: How does sex impact the epidemiology,
27 pathophysiology, clinical presentation, response to intervention, and disease outcomes in
28 neurologic conditions?
29
30

31 **Identifying Relevant Studies**

32 **Participants**

33 Studies of participants with primary neurologic conditions in one of the four neurology
34 subspecialties (i.e., demyelination, stroke, headache, epilepsy) will be included. Primary
35 demyelination conditions will be considered as multiple sclerosis, neuromyelitis optica
36 spectrum disorders, and acute disseminated encephalomyelitis. Primary stroke conditions
37 will be considered as ischemic strokes, hemorrhagic strokes, and cerebral venous sinus
38 thrombosis (CVST). Primary headache conditions will be considered as migraines,
39 tension-type headaches, cluster headaches, paroxysmal hemicrania, hemicrania continua,
40 or short-lasting unilateral neuralgiform (SUNCT) headaches/short-lasting unilateral
41 neuralgiform headaches with autonomic symptoms (SUNA). Primary epilepsy conditions
42 will be considered as any epileptic seizures (i.e., non-epileptic events will not be
43 included). Studies of participants with primary diagnoses of neuromuscular conditions,
44 movement disorders, sleep disorders, neuro-infectious diseases, neuro-ophthalmology, or
45 neuro-oncologic conditions will not be included.
46
47
48

49 **Interventions**

50 Studies that explore sex or gender differences in neurology will be included in initial
51 review due to their often-interchangeable use in research. Ultimately, only studies
52 exploring true sex differences will be included. Sex will be defined as the biological
53 differences between males and females (e.g., hormonal, genetic). Gender will be defined
54 as social norms for men and women, including social constructs and attitudes.
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Inclusion and Exclusion Criteria

The scoping review will include (must meet all of the following):

1. Reviews, primary research (i.e., qualitative, quantitative, mixed methods)
2. Human adults ≥ 18 years
3. Sex- or gender-specific data as a primary objective of the study
4. At least one of the four neurologic subspecialties of interest (i.e., demyelination, stroke, headache, epilepsy)
5. Published in English language

The scoping review will exclude (must meet 1 of the following):

1. Abstracts, commentaries, editorials, letters to the editor, case reports, case series, animal studies, phase 1 and 2 studies, pilot studies
2. Duplicate studies, irrelevant studies, those with a wrong aim, availability in abstract form only, and multiple articles from the same study
3. Humans < 18 years
4. Primary objective is not sex-specific endpoint
5. Condition is not in one of the four neurologic subspecialties of interest (i.e., demyelination, stroke, headache, epilepsy)
6. Not published in English language

Search Strategy

The search strategy will be designed and conducted by an information specialist using terms for each of the main concepts found within the review's research questions. The search strategy will include broad terms related to each neurologic condition, their synonyms, sex or gender. The search strategy will first be validated in MEDLINE (Ovid) and subsequently translated in Cochrane Central Registry of Controlled Trials (Ovid), EMBASE (Ovid), Emcare (Ovid), and PsychINFO (Ovid). See supplementary file 1 for the search strategy syntax that will be used in MEDLINE (Ovid).

Free text terms will be run to identify additional relevant studies that were not identified with the controlled classifying terminology. Reference lists of relevant systematic reviews and all included articles will be reviewed to identify additional studies of relevance. Lastly, articles from authors of included studies will be sought for inclusion. Grey literature will not be searched. Given the rapidly evolving field and recent advances in sex and gender differences in person-centered medicine, studies will be limited to those published between 2014-2020.

Data Collection and Study Selection

Searches will be exported into EndNote software, with duplicates identified and removed. Study selection will involve a two-stage process:

1. Title and abstract review
2. Full-text review

For the first stage, two reviewers with the aid of Covidence software will screen the titles and abstracts of articles identified in the search and additional sources described. The

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3 inclusion/exclusion criteria will be tested on sample abstraction prior to beginning full
4 abstract review. At the second stage, full-text articles will be obtained and assessed again
5 by two reviewers to determine if they meet inclusion and exclusion criteria. Reasons for
6 exclusion will be documented for all articles at both stages. In the case of disagreement
7 not resolved by discussion, a third reviewer will be consulted. A complete PRISMA flow
8 chart and table of all included studies will be prepared for the final review.[5]
9
10

11 **Data Charting Process**

12 Reviewers will independently extract data using a standardized data collection form
13 designed for this study. Prior to implementation, the research team will review this form
14 to ensure all relevant information is accurately captured. Data charted will include, but
15 not be limited to: study citation, study methods (e.g., aim, design, population), key
16 findings, patient characteristics (e.g., pregnancy, menopause), neurologic condition, and
17 sex- and gender-specific information relevant to the patient experience (e.g.,
18 epidemiology, pathophysiology, risk factors, clinical features, diagnostics, medical and
19 surgical treatments, disease outcomes, psychosocial outcomes, and comorbidities). All
20 study outcomes will be reviewed, including both qualitative and quantitative results. Data
21 abstraction will occur concurrently by two independent reviewers. To ensure accuracy,
22 extracted information by each reviewer will be compared and discrepancies will be
23 discussed to ensure consistency between reviewers. Authors of eligible studies will be
24 contacted, if necessary, to obtain further information. The data will be compiled into a
25 single Microsoft Excel spreadsheet.
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30 The methodological quality of studies included for in-depth review will be examined, as
31 applicable, using a modified version of the Critical Appraisal Skills Program (CASP)
32 quality assessment tool for qualitative studies.[6] The Confidence in the Evidence from
33 Reviews of Qualitative research (CERQual) approach will be used to determine how
34 much certainty should be placed on findings from the review's synthesis.[7]
35
36

37 **Results Synthesis**

38 The neurology subspecialty areas previously identified will be used as a foundation to
39 organize results as an overview of all of the information retrieved and to establish the
40 extent and nature of the literature. The following presentation strategies will be used for
41 each subspecialty area:
42

- 43 1. Basic overview of amount, type, and distribution of included studies
- 44 2. Narrative synthesis and mapping of results
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48 A meta-analysis of quantitative results will not be performed as that is not part of scoping
49 review methodology.
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52 **Patient and Public Involvement**

53 No patient involvement.
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ETHICS AND DISSEMINATION

No ethical approval was required for this study as it is literature-based.

Given that sex and gender differences are not studied with consistent methods, the overview presented by this scoping review may provide clarity regarding what is currently known about sex and gender differences in neurology. This scoping review will map the recent trends observed in sex and gender difference research in neurology and identify subspecialty areas in need of further research. An understanding of sex and gender differences in neurology is necessary for implementation of sex- and gender-specific strategies to optimize patient care.

Knowledge translation will occur through presentation of results at relevant national and international conferences, and publication in a peer-reviewed journal. The study team will use their individual networks to encourage broad dissemination of results.

CONTRIBUTORSHIP STATEMENT

AP, EB, and GM initiated the project. AP and EB advised on study methods and revised the draft paper. EW and GM wrote the first drafts of the paper. All authors approved the final version of the paper.

FUNDING

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COMPETING INTERESTS

No authors have any competing interests to declare.

REFERENCES

- 1 Mamlouk GM, Dorris DM, Barrett LR, *et al.* Sex bias and omission in neuroscience research is influenced by research model and journal, but not reported NIH funding. *Front Neuroendocrinol* 2020;**57**. doi:10.1016/j.yfrne.2020.100835
- 2 What is gender? What is sex? Can. Institutes Heal. Res. 2020.https://cihr-irsc.gc.ca/e/48642.html (accessed 3 May 2021).
- 3 Connelly PJ, Azizi Z, Alipour P, *et al.* The Importance of Gender to Understand Sex Differences in Cardiovascular Disease. *Can J Cardiol* 2021;**37**:699–710. doi:10.1016/j.cjca.2021.02.005
- 4 Zucker I, Prendergast BJ. Sex differences in pharmacokinetics predict adverse drug reactions in women. *Biol Sex Differ* 2020;**11**:32. doi:10.1186/s13293-020-00308-5
- 5 Tricco AC, Lillie E, Zarin W, *et al.* PRISMA extension for scoping reviews (PRISMA-ScR): Checklist and explanation. *Ann. Intern. Med.* 2018;**169**:467–73. doi:10.7326/M18-0850
- 6 Critical Appraisal Skills Programme. CASP Qualitative Checklist. *CASP Online* 2018.
- 7 Lewin S, Glenton C, Munthe-Kaas H, *et al.* Using Qualitative Evidence in Decision Making for Health and Social Interventions: An Approach to Assess Confidence in Findings from Qualitative Evidence Syntheses (GRADE-CERQual). *PLoS Med* 2015;**12**. doi:10.1371/journal.pmed.1001895

August 18, 2020 Searches

Databases:

- Ovid Medline ALL
- Ovid Embase

August 19, 2020 Searches

Databases:

- Ovid Cochrane Central Register of Controlled Trials
- Ovid Emcare
- Ovid PsycINFO

August 18, 2020

Database(s): **Ovid MEDLINE(R) ALL** 1946 to August 17, 2020

Search Strategy:

#	Searches	Results
1	*sex factors/	5525
2	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 differenc*).ti,kf,hw.	33981
3	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 factor*).ti,kf,hw.	271950
4	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 compar*).ti,kf,hw.	5519
5	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 impact*).ti,kf,hw.	2812
6	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 influen*).ti,kf,hw.	6758
7	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 confound*).ti,kf,hw.	43
8	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 associat*).ti,kf,hw.	7924
9	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 link????).ti,kf,hw.	2182
10	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 contribut*).ti,kf,hw.	892
11	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 specific*).ti,kf,hw.	9851
12	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 distribut*).ti,kf,hw.	56980
13	or/1-12	365404
14	exp Epilepsy/	111569

15	epilep*.mp.	163872
16	seizur*.mp.	142544
17	seizing.mp.	554
18	aura?.mp.	11568
19	myoclonus/ [1966-1976]	5154
20	(dravet adj4 syndrom*).mp.	1003
21	myoclon*.mp.	17146
22	(atroph* adj4 dentatorubral-pallidoluysian).mp.	400
23	atypical inclusion body disease*.mp.	0
24	(biotin adj4 encephalopath*).mp.	8
25	naito-oyanagi.mp.	3
26	(haw river adj4 syndrome*).mp.	5
27	(may white adj4 syndrome*).mp.	2
28	lafora.mp.	644
29	merrf.mp.	642
30	fukuhara.mp.	32
31	unverricht.mp.	357
32	lundborg.mp.	355
33	petit mal.mp.	1003
34	grand mal.mp.	1494
35	jme.mp.	738
36	jmes.mp.	8
37	janz.mp.	71
38	Jacksonian Seizure/ [1966-1976]	53931
39	bcects.mp.	58
40	bects.mp.	258
41	convuls*.mp.	35190
42	pyknolep*.mp.	49
43	tonic-clonic.mp.	9934
44	(nodding adj4 syndrome*).mp.	126
45	(lightning adj4 attack*).mp.	4

46	(salaam adj4 attack*).mp.	2
47	(cryptogenic adj4 spasm*).mp.	71
48	hypsarrhythmi*.mp.	816
49	(infant* adj4 spasm*).mp.	4694
50	(nodding adj4 spasm*).mp.	29
51	(spasm* adj4 nutan*).mp.	110
52	(symptom* adj4 west).mp.	144
53	(west adj4 syndrom*).mp.	1427
54	landau-kleffner.mp.	516
55	lennox gastaut.mp.	1477
56	(febrile adj4 fit?).mp.	25
57	absence status.mp.	243
58	kozhevniko???.mp.	54
59	kojewniko???.mp.	29
60	kojevniko???.mp.	16
61	kozhewniko???.mp.	1
62	or/14-61 [epilepsy or seizures]	265264
63	exp Stroke/	134958
64	stroke\$.mp.	301266
65	(cerebr??vascular adj4 accident*).mp.	7319
66	(cereb* adj4 infarct*).mp.	45490
67	(cerebr??vascular adj4 disease?).mp.	23786
68	(cva or cvas).mp.	3034
69	(tia or tias).mp.	9254
70	transient isch?emic attack?.mp.	14294
71	poststroke.mp.	5250
72	(brain* adj4 vascular adj4 accident*).mp.	63
73	(brain* adj4 infarct*).mp.	12245
74	brain* attack*.mp.	308
75	appoplex*.mp.	3
76	apoplex*.mp.	3353

77	Stroke Rehabilitation/	13332
78	claudication syndrome*.mp.	8
79	foveate syndrome*.mp.	21
80	millard gubler syndrome*.mp.	1
81	"top of the basilar syndrome*".mp.	42
82	weber syndrome*.mp.	3118
83	(choroidal adj4 infarct*).mp.	159
84	(hemisphere* adj4 infarct*).mp.	746
85	medullary syndrome*.mp.	904
86	(cereb* adj4 syndrome*).mp.	7569
87	viesteaux-wallenberg syndrome*.mp.	0
88	wallenberg syndrome*.mp.	197
89	cadasil?.mp.	1393
90	(subcort* adj4 infarct*).mp.	1941
91	(multi?infarct* adj4 dement*).mp.	92
92	(lacun* adj4 dement*).mp.	87
93	aca infarct*.mp.	31
94	(heubner adj4 infarct*).mp.	8
95	mca infarct*.mp.	377
96	(cereb* adj4 occlu*).mp.	17700
97	(cereb* adj4 thrombo*).mp.	10018
98	(lacun* adj4 syndrome*).mp.	366
99	pca infarct*.mp.	57
100	or/63-99 [stroke]	379170
101	exp Multiple Sclerosis/	58886
102	(multiple adj3 sclero*).mp.	84306
103	(disseminat* adj3 sclero*).mp.	911
104	exp Demyelinating Diseases/	100524
105	demyelinat*.mp.	36735
106	(neuromyelit* adj4 optica*).mp.	4466
107	(myelin oligodendrocyte glycoprotein* adj4 disorder*).mp.	55

108	(myelin oligodendrocyte glycoprotein* adj4 disease*).mp.	136
109	or/101-108 [MS or demyelinating]	131940
110	exp Headache/	27767
111	exp Headache Disorders/	34486
112	headache*.mp.	94648
113	head-ache*.mp.	115
114	migraine*.mp.	39847
115	exp head/ and exp pain/	3125
116	(head* adj4 pain*).mp.	10408
117	cephalalgi*.mp.	890
118	or/110-117 [headache]	119078
119	13 and 62 [sex differences and epilepsy or seizures]	3238
120	13 and 100 [sex differences and stroke]	9603
121	13 and 109 [sex differences and MS or demyelinating]	1839
122	13 and 118 [sex differences and headache]	2637
123	exp animals/ not (exp animals/ and exp humans/)	4725904
124	119 not 123 [sex differences and epilepsy or seizures NOT animal studies]	2976
125	120 not 123 [sex differences and stroke NOT animal studies]	9423
126	121 not 123 [sex differences and MS or demyelinating NOT animal studies]	1756
127	122 not 123 [sex differences and headache NOT animal studies]	2620
128	limit 124 to "all adult (19 plus years)"	1869
129	limit 124 to "all child (0 to 18 years)"	1809
130	124 not 129	1167
131	128 or 130 [sex differences and epilepsy or seizures NOT animal studies NOT child studies]	2254
132	limit 125 to "all adult (19 plus years)"	7936
133	limit 125 to "all child (0 to 18 years)"	1339
134	125 not 133	8084
135	132 or 134 [sex differences and stroke NOT animal studies NOT child studies]	9267
136	limit 126 to "all adult (19 plus years)"	1352
137	limit 126 to "all child (0 to 18 years)"	651
138	126 not 137	1105

139	136 or 138 [sex differences and MS or demyelinating NOT animal studies NOT child studies]	1672
140	limit 127 to "all adult (19 plus years)"	1885
141	limit 127 to "all child (0 to 18 years)"	1266
142	127 not 141	1354
143	140 or 142 [sex differences and headache NOT animals studies NOT child studies]	2244
144	limit 131 to yr="2009 -Current" [sex differences and epilepsy or seizures NOT animal studies NOT child studies, from 2009 to present]	831
145	limit 135 to yr="2009 -Current" [sex differences and stroke NOT animal studies NOT child studies, from 2009 to present]	5143
146	limit 139 to yr="2009 -Current" [sex differences and MS or demyelinating NOT animal studies NOT child studies, from 2009 to present]	763
147	limit 143 to yr="2009 -Current" [sex differences and headache NOT animal studies NOT child studies, from 2009 to present]	898
148	144 or 145 or 146 or 147	7274

Database(s): **Embase Classic+Embase** 1947 to 2020 August 17

Search Strategy:

#	Searches	Results
1	exp *sex difference/	46982
2	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 differenc*).ti,kw,hw.	403552
3	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 factor*).ti,kw,hw.	18935
4	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 compar*).ti,kw,hw.	7263
5	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 impact*).ti,kw,hw.	4054
6	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 influen*).ti,kw,hw.	8678
7	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 confound*).ti,kw,hw.	53
8	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 associat*).ti,kw,hw.	10047
9	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 link????).ti,kw,hw.	3349
10	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 contribut*).ti,kw,hw.	1070
11	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 specific*).ti,kw,hw.	12683
12	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 distribut*).ti,kw,hw.	2163

13	or/1-12	451578
14	exp "seizure, epilepsy and convulsion"/	404444
15	epilep*.mp.	266828
16	seizur*.mp.	255688
17	seizing.mp.	766
18	aura?.mp.	19710
19	(dravet adj4 syndrom*).mp.	1756
20	myoclon*.mp.	32360
21	(atroph* adj4 dentatorubral-pallidoluvsian).mp.	0
22	atypical inclusion body disease*.mp.	0
23	(biotin adj4 encephalopath*).mp.	9
24	naito-oyanagi.mp.	3
25	(haw river adj4 syndrome*).mp.	9
26	(may white adj4 syndrome*).mp.	4
27	lafora.mp.	926
28	merrf.mp.	1001
29	fukuhara.mp.	45
30	unverricht.mp.	517
31	lundborg.mp.	495
32	petit mal.mp.	2852
33	grand mal.mp.	11839
34	jme.mp.	1254
35	jmes.mp.	8
36	janz.mp.	148
37	bcects.mp.	99
38	bects.mp.	378
39	convuls*.mp.	72117
40	pyknolep*.mp.	153
41	tonic-clonic.mp.	24226
42	(nodding adj4 syndrome*).mp.	212
43	(lightning adj4 attack*).mp.	7

44	(salaam adj4 attack*).mp.	15
45	(cryptogenic adj4 spasm*).mp.	119
46	hypsarrhythmi*.mp.	2023
47	(infant* adj4 spasm*).mp.	8136
48	(nodding adj4 spasm*).mp.	51
49	(spasm* adj4 nutan*).mp.	178
50	(symptom* adj4 west).mp.	219
51	landau-kleffner.mp.	1053
52	lennox gastaut.mp.	4304
53	(febrile adj4 fit?).mp.	53
54	absence status.mp.	399
55	kozhevniko???.mp.	79
56	kojewniko???.mp.	45
57	kojevniko???.mp.	29
58	kozhewniko???.mp.	1
59	or/14-58 [epilepsy or seizures]	478503
60	exp cerebrovascular accident/	216527
61	stroke\$.mp.	463137
62	(cerebr??vascular adj4 accident*).mp.	216000
63	(cereb* adj4 infarct*).mp.	39944
64	(cerebr??vascular adj4 disease?).mp.	90665
65	(cva or cvas).mp.	6993
66	(tia or tias).mp.	20150
67	transient isch?emic attack?.mp.	43401
68	poststroke.mp.	7093
69	(brain* adj4 vascular adj4 accident*).mp.	112
70	(brain* adj4 infarct*).mp.	65851
71	brain* attack*.mp.	554
72	appoplex*.mp.	3
73	apoplex*.mp.	5101
74	stroke rehabilitation/	3586

75	claudes syndrome*.mp.	37
76	foville syndrome*.mp.	48
77	millard gublar syndrome*.mp.	0
78	"top of the basilar syndrome*".mp.	78
79	weber syndrome*.mp.	3886
80	(choroidal adj4 infarct*).mp.	191
81	(hemisphere* adj4 infarct*).mp.	1142
82	medullary syndrome*.mp.	457
83	(cereb* adj4 syndrome*).mp.	12377
84	vieseaux-wallenberg syndrome*.mp.	0
85	wallenberg syndrome*.mp.	1091
86	cadasil?.mp.	2584
87	(subcort* adj4 infarct*).mp.	2778
88	(multi?infarct* adj4 dement*).mp.	12411
89	(lacun* adj4 dement*).mp.	132
90	aca infarct*.mp.	59
91	(heubner adj4 infarct*).mp.	10
92	mca infarct*.mp.	785
93	(cereb* adj4 occlu*).mp.	38802
94	(cereb* adj4 thrombo*).mp.	17668
95	(lacun* adj4 syndrome*).mp.	529
96	pca infarct*.mp.	93
97	or/60-96 [stroke]	672976
98	exp demyelinating disease/	184579
99	(multiple adj3 sclero*).mp.	149447
100	(disseminat* adj3 sclero*).mp.	1353
101	demyelinat*.mp.	64947
102	(neuromyelit* adj4 optica*).mp.	8095
103	(myelin oligodendrocyte glycoprotein* adj4 disorder*).mp.	103
104	(myelin oligodendrocyte glycoprotein* adj4 disease*).mp.	200
105	or/98-104 [MS or demyelinating]	211317

106	exp "headache and facial pain"/	319885
107	headache*.mp.	290313
108	head-ache*.mp.	330
109	migraine*.mp.	74416
110	exp head/ and exp pain/	34096
111	(head* adj4 pain*).mp.	19430
112	cephalalgi*.mp.	2015
113	or/106-112 [headache]	365211
114	13 and 59 [sex differences and epilepsy or seizures]	4842
115	13 and 97 [sex differences and stroke]	15006
116	13 and 105 [sex differences and MS or demyelinating]	2644
117	13 and 113 [sex differences and headache]	5536
118	(exp animals/ or exp animal experimentation/ or nonhuman/) not ((exp animals/ or exp animal experimentation/ or nonhuman/) and exp human/)	7309464
119	114 not 118 [sex differences and epilepsy or seizures NOT animal studies]	4392
120	115 not 118 [sex differences and stroke NOT animal studies]	14598
121	116 not 118 [sex differences and MS or demyelinating NOT animal studies]	2490
122	117 not 118 [sex differences and headache NOT animal studies]	5449
123	limit 119 to (adult <18 to 64 years> or aged <65+ years>)	2226
124	limit 119 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	1580
125	119 not 124	2812
126	123 or 125 [sex differences and epilepsy or seizures NOT animal studies NOT child studies]	3667
127	limit 120 to (adult <18 to 64 years> or aged <65+ years>)	10061
128	limit 120 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	993
129	120 not 128	13605
130	127 or 129 [sex differences and stroke NOT animal studies NOT child studies]	14420
131	limit 121 to (adult <18 to 64 years> or aged <65+ years>)	1466
132	limit 121 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	425
133	121 not 132	2065

134	131 or 133 [sex differences and MS or demyelinating NOT animal studies NOT child studies]	2402
135	limit 122 to (adult <18 to 64 years> or aged <65+ years>)	3280
136	limit 122 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	1402
137	122 not 136	4047
138	135 or 137 [sex differences and headache NOT animal studies NOT child studies]	4924
139	limit 126 to yr="2009 -Current" [sex differences and epilepsy or seizures NOT animal studies NOT child studies, 2009 to present]	2135
140	limit 130 to yr="2009 -Current" [sex differences and stroke NOT animal studies NOT child studies, 2009 to present]	9979
141	limit 134 to yr="2009 -Current" [sex differences and MS or demyelinating NOT animal studies NOT child studies, 2009 to present]	1565
142	limit 138 to yr="2009 -Current" [sex differences and headache NOT animal studies NOT child studies, 2009 to present]	2855
143	limit 139 to conference abstracts	197
144	139 not 143 [sex differences and epilepsy or seizures NOT animal studies NOT child studies, 2009 to present NOT conference abstracts]	1938
145	limit 140 to conference abstracts	1482
146	140 not 145 [sex differences and stroke NOT animal studies NOT child studies, 2009 to present NOT conference abstracts]	8497
147	limit 141 to conference abstracts	173
148	141 not 147 [sex differences and MS or demyelinating NOT animal studies NOT child studies, 2009 to present NOT conference abstracts]	1392
149	limit 142 to conference abstracts	260
150	142 not 149 [sex differences and headache NOT animal studies NOT child studies, 2009 to present NOT conference abstracts]	2595
151	144 or 146 or 148 or 150	13275

August 19, 2020

Database(s): **Cochrane Central Register of Controlled Trials** 2014 to Present

Search Strategy:

#	Searches	Results
1	exp Sex Characteristics/ or sex factors/	7149
2	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 differenc*).ti,kw,hw.	6653
3	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 factor*).ti,kw,hw.	10468
4	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 compar*).ti,kw,hw.	11541
5	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 impact*).ti,kw,hw.	901
6	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 influen*).ti,kw,hw.	1390
7	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 confound*).ti,kw,hw.	48
8	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 associat*).ti,kw,hw.	4879
9	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 link????).ti,kw,hw.	3341
10	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 contribut*).ti,kw,hw.	35
11	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 specific*).ti,kw,hw.	854
12	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 distribut*).ti,kw,hw.	1405
13	or/1-12	39488
14	exp "seizure, epilepsy and convulsion"/ or exp Epilepsy/ or myoclonus/ or Jacksonian Seizure/	3014
15	epilep*.mp.	8517
16	seizur*.mp.	8878
17	seizing.mp.	18
18	aura?.mp.	1670
19	(dravet adj4 syndrom*).mp.	102
20	myoclon*.mp.	692
21	(atroph* adj4 dentatorubral-pallidoluvsian).mp.	0
22	atypical inclusion body disease*.mp.	0
23	(biotin adj4 encephalopath*).mp.	0
24	naito-oyanagi.mp.	0
25	(haw river adj4 syndrome*).mp.	0
26	(may white adj4 syndrome*).mp.	158
27	lafora.mp.	4
28	merrf.mp.	4

29	fukuhara.mp.	0
30	unverricht.mp.	12
31	lundborg.mp.	14
32	petit mal.mp.	16
33	grand mal.mp.	88
34	jme.mp.	24
35	jmes.mp.	0
36	janz.mp.	4
37	bcects.mp.	3
38	bects.mp.	21
39	convuls*.mp.	1709
40	pyknolep*.mp.	1
41	tonic-clonic.mp.	697
42	(nodding adj4 syndrome*).mp.	10
43	(lightning adj4 attack*).mp.	0
44	(salaam adj4 attack*).mp.	1
45	(cryptogenic adj4 spasm*).mp.	3
46	hypsarrhythmi*.mp.	64
47	(infant* adj4 spasm*).mp.	297
48	(nodding adj4 spasm*).mp.	1
49	(spasm* adj4 nutan*).mp.	0
50	(symptom* adj4 west).mp.	14
51	landau-kleffner.mp.	7
52	lennox gastaut.mp.	278
53	(febrile adj4 fit?).mp.	3
54	absence status.mp.	6
55	kozhevniko???.mp.	2
56	kojewniko???.mp.	0
57	kojevniko???.mp.	0
58	kozhewniko???.mp.	0
59	or/14-58 [epilepsy or seizures]	16048

60	exp Stroke/ or exp Stroke/ or Stroke Rehabilitation/	10049
61	stroke\$.mp.	57629
62	(cerebr??vascular adj4 accident*).mp.	14423
63	(cereb* adj4 infarct*).mp.	4889
64	(cerebr??vascular adj4 disease?).mp.	4243
65	(cva or cvas).mp.	566
66	(tia or tias).mp.	1863
67	transient isch?emic attack?.mp.	3121
68	poststroke.mp.	1376
69	(brain* adj4 vascular adj4 accident*).mp.	11
70	(brain* adj4 infarct*).mp.	1912
71	brain* attack*.mp.	31
72	apoplex*.mp.	0
73	apoplex*.mp.	350
74	stroke rehabilitation/	2365
75	claudication syndrome*.mp.	0
76	fovea syndrome*.mp.	0
77	millard gublar syndrome*.mp.	0
78	"top of the basilar syndrome*".mp.	0
79	weber syndrome*.mp.	16
80	(choroidal adj4 infarct*).mp.	1
81	(hemisphere* adj4 infarct*).mp.	52
82	medullary syndrome*.mp.	10
83	(cereb* adj4 syndrome*).mp.	503
84	viesteaux-wallenberg syndrome*.mp.	0
85	wallenberg syndrome*.mp.	4
86	cadASIL?.mp.	28
87	(subcort* adj4 infarct*).mp.	82
88	(multi?infarct* adj4 dement*).mp.	326
89	(lacun* adj4 dement*).mp.	10
90	aca infarct*.mp.	1

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4	91	(heubner adj4 infarct*).mp.
5	92	mca infarct*.mp.
6	93	(cereb* adj4 occlu*).mp.
7	94	(cereb* adj4 thrombo*).mp.
8	95	(lacun* adj4 syndrome*).mp.
9	96	pca infarct*.mp.
10	97	or/60-96 [stroke]
11	98	exp Demyelinating Diseases/ or exp Demyelinating Diseases/ or exp Multiple Sclerosis/
12	99	(multiple adj3 sclero*).mp.
13	100	(disseminat* adj3 sclero*).mp.
14	101	demyelinat*.mp.
15	102	(neuromyelit* adj4 optica*).mp.
16	103	(myelin oligodendrocyte glycoprotein* adj4 disorder*).mp.
17	104	(myelin oligodendrocyte glycoprotein* adj4 disease*).mp.
18	105	or/98-104 [MS or demyelinating]
19	106	exp "headache and facial pain"/ or exp Headache/ or exp Headache Disorders/
20	107	headache*.mp.
21	108	head-ache*.mp.
22	109	migraine*.mp.
23	110	exp head/ and exp pain/
24	111	(head* adj4 pain*).mp.
25	112	cephalalgi*.mp.
26	113	or/106-112 [headache]
27	114	13 and 59 [sex differences and epilepsy or seizures]
28	115	13 and 97 [sex differences and stroke]
29	116	13 and 105 [sex differences and MS or demyelinating]
30	117	13 and 113 [sex differences and headache]
31	118	limit 114 to yr="2009 -Current" [sex differences and epilepsy or seizures, 2009 to present]
32	119	limit 115 to yr="2009 -Current" [sex differences and stroke, 2009 to present]
33	120	limit 116 to yr="2009 -Current" [sex differences and MS or demyelinating, 2009 to present]
34	121	limit 117 to yr="2009 -Current" [sex differences and headache, 2009 to present]
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122	118 or 119 or 120 or 121	2357
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Database(s): **Ovid Emcare Nursing** 1995 to Present

Search Strategy:

#	Searches	Results
1	exp *sex difference/	17673
2	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 differenc*).ti,kw,hw.	108237
3	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 factor*).ti,kw,hw.	3462
4	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 compar*).ti,kw,hw.	2113
5	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 impact*).ti,kw,hw.	1334
6	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 influen*).ti,kw,hw.	2202
7	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 confound*).ti,kw,hw.	24
8	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 associat*).ti,kw,hw.	3095
9	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 link????).ti,kw,hw.	394
10	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 contribut*).ti,kw,hw.	261
11	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 specific*).ti,kw,hw.	2760
12	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 distribut*).ti,kw,hw.	353
13	or/1-12	118662
14	exp "seizure, epilepsy and convulsion"/	61035
15	epilep*.mp.	32137
16	seizur*.mp.	39304
17	seizing.mp.	222
18	aura?.mp.	4694
19	(dravet adj4 syndrom*).mp.	206
20	myoclon*.mp.	4709
21	(atroph* adj4 dentatorubral-pallidoluvsian).mp.	0
22	atypical inclusion body disease*.mp.	0
23	(biotin adj4 encephalopath*).mp.	0
24	naito-oyanagi.mp.	0
25	(haw river adj4 syndrome*).mp.	1

26	(may white adj4 syndrome*).mp.	0
27	lafora.mp.	50
28	merrf.mp.	101
29	fukuhara.mp.	11
30	unverricht.mp.	38
31	lundborg.mp.	47
32	petit mal.mp.	58
33	grand mal.mp.	1513
34	jme.mp.	98
35	jmes.mp.	3
36	janz.mp.	20
37	bcects.mp.	5
38	bects.mp.	31
39	convuls*.mp.	7175
40	pyknolep*.mp.	3
41	tonic-clonic.mp.	4238
42	(nodding adj4 syndrome*).mp.	49
43	(lightning adj4 attack*).mp.	1
44	(salaam adj4 attack*).mp.	0
45	(cryptogenic adj4 spasm*).mp.	8
46	hypsarrhythmi*.mp.	158
47	(infant* adj4 spasm*).mp.	1060
48	(nodding adj4 spasm*).mp.	2
49	(spasm* adj4 nutan*).mp.	13
50	(symptom* adj4 west).mp.	39
51	landau-kleffner.mp.	200
52	lennox gastaut.mp.	618
53	(febrile adj4 fit?).mp.	6
54	absence status.mp.	38
55	kozhevniko???.mp.	7
56	kojewniko???.mp.	0

57	kojevniko???.mp.	0
58	kozhewniko???.mp.	0
59	or/14-58 [epilepsy or seizures]	70654
60	exp cerebrovascular accident/	59614
61	stroke\$.mp.	119669
62	(cerebr??vascular adj4 accident*).mp.	58780
63	(cereb* adj4 infarct*).mp.	7229
64	(cerebr??vascular adj4 disease?).mp.	18586
65	(cva or cvas).mp.	1030
66	(tia or tias).mp.	2850
67	transient isch?emic attack?.mp.	11666
68	poststroke.mp.	3605
69	(brain* adj4 vascular adj4 accident*).mp.	12
70	(brain* adj4 infarct*).mp.	15250
71	brain* attack*.mp.	172
72	apoplex*.mp.	0
73	apoplex*.mp.	585
74	stroke rehabilitation/	1152
75	claudication syndrome*.mp.	4
76	foveate syndrome*.mp.	8
77	millard gublar syndrome*.mp.	0
78	"top of the basilar syndrome*".mp.	12
79	weber syndrome*.mp.	548
80	(choroidal adj4 infarct*).mp.	23
81	(hemisphere* adj4 infarct*).mp.	194
82	medullary syndrome*.mp.	63
83	(cereb* adj4 syndrome*).mp.	1806
84	viesteaux-wallenberg syndrome*.mp.	0
85	wallenberg syndrome*.mp.	185
86	cadasil?.mp.	635
87	(subcort* adj4 infarct*).mp.	673

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4	88	(multi?infarct* adj4 dement*).mp. 4341
5	89	(lacun* adj4 dement*).mp. 27
6	90	aca infarct*.mp. 3
7	91	(heubner adj4 infarct*).mp. 4
8		
9	92	mca infarct*.mp. 145
10	93	(cereb* adj4 occlu*).mp. 7407
11	94	(cereb* adj4 thrombo*).mp. 3169
12	95	(lacun* adj4 syndrome*).mp. 97
13	96	pca infarct*.mp. 14
14	97	or/60-96 [stroke] 166160
15	98	exp demyelinating disease/ 29756
16	99	(multiple adj3 sclero*).mp. 24666
17	100	(disseminat* adj3 sclero*).mp. 42
18	101	demyelinat*.mp. 8283
19	102	(neuromyelit* adj4 optica*).mp. 1087
20	103	(myelin oligodendrocyte glycoprotein* adj4 disorder*).mp. 24
21	104	(myelin oligodendrocyte glycoprotein* adj4 disease*).mp. 45
22	105	or/98-104 [MS or demyelinating] 32839
23	106	exp "headache and facial pain"/ 80703
24	107	headache*.mp. 71279
25	108	head-ache*.mp. 41
26	109	migraine*.mp. 18750
27	110	exp head/ and exp pain/ 9069
28	111	(head* adj4 pain*).mp. 4946
29	112	cephalalgi*.mp. 412
30	113	or/106-112 [headache] 89106
31	114	13 and 59 [sex differences and epilepsy or seizures] 963
32	115	13 and 97 [sex differences and stroke] 5088
33	116	13 and 105 [sex differences and MS or demyelinating] 605
34	117	13 and 113 [sex differences and headache] 1803
35	118	(exp animals/ or exp animal experimentation/ or nonhuman/) not ((exp animals/ or exp animal experimentation/ or nonhuman/) and exp human/) 461862
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119	114 not 118 [sex differences and epilepsy or seizures NOT animal studies]	917
120	115 not 118 [sex differences and stroke NOT animal studies]	5040
121	116 not 118 [sex differences and MS or demyelinating NOT animal studies]	585
122	117 not 118 [sex differences and headache NOT animal studies]	1786
123	limit 119 to (adult <18 to 64 years> or aged <65+ years>)	508
124	limit 119 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	302
125	119 not 124	615
126	123 or 125 [sex differences and epilepsy or seizures NOT animal studies NOT child studies]	788
127	limit 120 to (adult <18 to 64 years> or aged <65+ years>)	3730
128	limit 120 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	265
129	120 not 128	4775
130	127 or 129 [sex differences and stroke NOT animal studies NOT child studies]	4992
131	limit 121 to (adult <18 to 64 years> or aged <65+ years>)	402
132	limit 121 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	78
133	121 not 132	507
134	131 or 133 [sex differences and MS or demyelinating NOT animal studies NOT child studies]	572
135	limit 122 to (adult <18 to 64 years> or aged <65+ years>)	1050
136	limit 122 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	419
137	122 not 136	1367
138	135 or 137 [sex differences and headache NOT animal studies NOT child studies]	1624
139	limit 126 to yr="2009 -Current" [sex differences and epilepsy or seizures NOT animal studies NOT child studies, 2009 to present]	545
140	limit 130 to yr="2009 -Current" [sex differences and stroke NOT animal studies NOT child studies, 2009 to present]	3750
141	limit 134 to yr="2009 -Current" [sex differences and MS or demyelinating NOT animal studies NOT child studies, 2009 to present]	454
142	limit 138 to yr="2009 -Current" [sex differences and headache NOT animal studies NOT child studies, 2009 to present]	1055

143	139 or 140 or 141 or 142	5407
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Database(s): **APA PsycInfo** 1806 to August Week 3 2020

Search Strategy:

#	Searches	Results
1	exp human sex differences/	113766
2	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 differenc*).mp.	160431
3	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 factor*).mp.	34887
4	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 compar*).mp.	38823
5	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 impact*).mp.	8784
6	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 influen*).mp.	19926
7	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 confound*).mp.	2051
8	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 associat*).mp.	33724
9	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 link????).mp.	5784
10	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 contribut*).mp.	6265
11	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 specific*).mp.	22091
12	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 distribut*).mp.	3832
13	or/1-12	268972
14	exp epilepsy/ or exp seizures/	35420
15	epilep*.mp.	44883
16	seizur*.mp.	34374
17	seizing.mp.	383
18	aura?.mp.	5466
19	(dravet adj4 syndrom*).mp.	290
20	myoclon*.mp.	3153
21	(atroph* adj4 dentatorubral-pallidoluvsian).mp.	0
22	atypical inclusion body disease*.mp.	0
23	(biotin adj4 encephalopath*).mp.	1
24	naito-oyanagi.mp.	0

25	(haw river adj4 syndrome*).mp.	0
26	(may white adj4 syndrome*).mp.	0
27	lafora.mp.	89
28	merrf.mp.	46
29	fukuhara.mp.	10
30	unverricht.mp.	54
31	lundborg.mp.	55
32	petit mal.mp.	375
33	grand mal.mp.	593
34	jme.mp.	310
35	jmes.mp.	8
36	janz.mp.	37
37	bcects.mp.	32
38	bects.mp.	109
39	convuls*.mp.	6938
40	pyknolep*.mp.	20
41	tonic-clonic.mp.	1539
42	(nodding adj4 syndrome*).mp.	19
43	(lightning adj4 attack*).mp.	1
44	(salaam adj4 attack*).mp.	1
45	(cryptogenic adj4 spasm*).mp.	18
46	hypsarrhythmi*.mp.	125
47	(infant* adj4 spasm*).mp.	619
48	(nodding adj4 spasm*).mp.	5
49	(spasm* adj4 nutan*).mp.	8
50	(symptom* adj4 west).mp.	47
51	landau-kleffner.mp.	214
52	lennox gastaut.mp.	317
53	(febrile adj4 fit?).mp.	2
54	absence status.mp.	54
55	kozhevniko???.mp.	25

56	kojewniko???.mp.	3
57	kojevniko???.mp.	4
58	kozhewniko???.mp.	0
59	or/14-58 [epilepsy or seizures]	66146
60	cerebrovascular accidents/	21013
61	stroke\$.mp.	36733
62	(cerebr??vascular adj4 accident*).mp.	21344
63	(cereb* adj4 infarct*).mp.	2559
64	(cerebr??vascular adj4 disease?).mp.	3030
65	(cva or cvas).mp.	470
66	(tia or tias).mp.	1015
67	transient isch?emic attack?.mp.	1142
68	poststroke.mp.	1811
69	(brain* adj4 vascular adj4 accident*).mp.	30
70	(brain* adj4 infarct*).mp.	1704
71	brain* attack*.mp.	43
72	appoplex*.mp.	0
73	apoplex*.mp.	151
74	stroke rehabilitation/	0
75	claudicatio syndrome*.mp.	0
76	foveate syndrome*.mp.	0
77	millard gublar syndrome*.mp.	0
78	"top of the basilar syndrome*".mp.	3
79	weber syndrome*.mp.	128
80	(choroidal adj4 infarct*).mp.	13
81	(hemisphere* adj4 infarct*).mp.	190
82	medullary syndrome*.mp.	22
83	(cereb* adj4 syndrome*).mp.	1675
84	viesteaux-wallenberg syndrome*.mp.	0
85	wallenberg syndrome*.mp.	19
86	cadasil?.mp.	327

1		
2		
3		
4	87	(subcort* adj4 infarct*).mp. 500
5	88	(multi?infarct* adj4 dement*).mp. 79
6	89	(lacun* adj4 dement*).mp. 29
7		
8		
9	90	aca infarct*.mp. 7
10		
11	91	(heubner adj4 infarct*).mp. 0
12	92	mca infarct*.mp. 50
13		
14	93	(cereb* adj4 occlu*).mp. 1916
15	94	(cereb* adj4 thrombo*).mp. 686
16		
17	95	(lacun* adj4 syndrome*).mp. 38
18		
19	96	pca infarct*.mp. 15
20		
21	97	or/60-96 [stroke] 44738
22	98	demyelination/ or multiple sclerosis/ 13968
23		
24	99	(multiple adj3 sclero*).mp. 16209
25		
26	100	(disseminat* adj3 sclero*).mp. 65
27		
28	101	demyelinat*.mp. 5561
29		
30	102	(neuromyelit* adj4 optica*).mp. 963
31		
32	103	(myelin oligodendrocyte glycoprotein* adj4 disorder*).mp. 9
33		
34	104	(myelin oligodendrocyte glycoprotein* adj4 disease*).mp. 171
35		
36	105	or/98-104 [MS or demyelinating] 19667
37		
38	106	exp headache/ 15324
39		
40	107	headache*.mp. 22630
41		
42	108	head-ache*.mp. 18
43		
44	109	migraine*.mp. 12940
45		
46	110	(head* adj4 pain*).mp. 3372
47		
48	111	cephalalgi*.mp. 408
49		
50	112	or/106-111 [headache] 24602
51		
52	113	13 and 59 [sex differences and epilepsy or seizures] 1731
53		
54	114	13 and 97 [sex differences and stroke] 1696
55		
56	115	13 and 105 [sex differences and MS or demyelinating] 644
57		
58	116	13 and 112 [sex differences and headache] 1072
59		
60	117	limit 113 to yr="2009 -Current" [sex differences and epilepsy or seizures, 2009 to present] 864

118	limit 114 to yr="2009 -Current" [sex differences and stroke, 2009 to present]	1111
119	limit 115 to yr="2009 -Current" [sex differences and MS or demyelinating, 2009 to present]	468
120	limit 116 to yr="2009 -Current" [sex differences and headache, 2009 to present]	546
121	117 or 118 or 119 or 120	2772

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Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	



SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	
Limitations	20	Discuss the limitations of the scoping review process.	
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med.* 2018;169:467–473. doi: [10.7326/M18-0850](https://doi.org/10.7326/M18-0850).



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Sex Differences in Neurology: A scoping review protocol

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Sex Differences in Neurology: A scoping review protocol

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Abstract

Introduction: Sex and gender are independently important in health and disease but have been incompletely explored in neurology. This is in part contributed to by the pre-existing male bias in scientific literature that results in fewer females being included in clinical research and the often interchangeable use of sex and gender in the literature.

This scoping review intends to identify the advances as well as under-explored aspects of this field to provide a road map for future research. This paper outlines the methods for a scoping review of published, peer-reviewed literature on sex and gender differences in four subspecialty areas of neurology: demyelination, stroke, epilepsy, and headache.

Methods and Analysis: A detailed search strategy will be used to search 5 databases pertaining only to sex differences. Specific inclusion and exclusion criteria will be applied to capture relevant literature published from 2014-2020. Data will be collected and synthesized to provide an overview of information retrieved, a narrative synthesis of each subspecialty area, and map of results.

Ethics and Dissemination: Research ethics board approval was not required for this study. This study will aid in mapping recent trends in sex differences in four major neurological conditions and will help identify areas for further research. A manuscript will be compiled for publication and presentations of findings.

Registration Details: The final protocol is registered with the Open Science Framework (<https://osf.io/n937x/>).

Keywords: Sex, Gender, Neurology, Women's Issues, Scoping Review

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This will be one of the most comprehensive studies to date to summarize the available literature on sex and gender differences in four of the largest neurology subspecialties across diverse periods of hormonal changes
- Both quantitative and qualitative studies will be assessed.
- The review will cover five databases (Ovid MEDLINE, PsychINFO, Embase, Central Registry of Controlled Trials, Ovid Emcare).
- Grey literature, commentaries, cases, and pilot studies will not be included in the literature search.
- Due to the vast literature and broad topic, only studies published within the past 5 years will be included.

INTRODUCTION

Medicine has moved away from a ‘one size fits all’ model of care in favor of a targeted, precision-based medicine approach that recognizes the importance of population variables in health and disease. Of particular note are sex and gender, which have historically been used interchangeably or omitted as a variable in research design.[1] With the National Institute of Health’s (NIH) policy change requiring sex to be defined as a biological variable, research is moving towards an increasing understanding of how sex influences neurological illness and treatment.

The interchangeable use of sex and gender in medical literature disregards distinctions between biological factors and sociocultural norms. Sex refers to biological differences between male and females (e.g., hormonal and genetic differences).[2] Sex differences play an important role in disease prevalence, presentation and outcomes, as well as in treatment efficacy and tolerability.[3,4] Gender refers to socially constructed roles, behaviours, expressions, and identities of individuals (e.g., risk-taking behaviour, treatment by others).[2] Gender differences have been implicated in health behaviours and disease outcomes.[3] Both sex and gender are independently important in health and disease, interacting through an individual’s life course and resulting in different health and disease outcomes.

The extent of sex and gender differences in neurology is incompletely explored. There has historically been a male bias in scientific literature, particularly in neuroscience, with females excluded from clinical trials or fewer females than males recruited to clinical trials.[1] Although this discrepancy has been reduced in recent years, gaps in studies examining sex and gender differences remain in the literature. Despite recent research indicating that 85.5% of human neuroscience studies include both male and female participants, 73.5% of these studies did not analyze data by sex.[1] As well, males are exclusively studied 4 times as often as females.[1] To optimize care for patients with neurological conditions, it is important to understand how sex and gender each impact health and disease outcomes.

Therefore, this protocol is appropriately set for a scoping review of sex and gender differences across 4 neurology subspecialties: demyelination, stroke, headache, and epilepsy. These four subspecialty areas were chosen as they are among the largest

1
2
3 subspecialties in neurology. Furthermore, these conditions commonly affect younger
4 adults, allowing for further evaluation of sex differences during periods of hormonal
5 changes (i.e., menstruation, pregnancy, menopause). The aims of the scoping are: a) to
6 systematically map the research conducted in these areas, and b) to identify any existing
7 gaps in knowledge. These findings may inform future research and ultimately enable
8 implementation of sex- and gender-specific strategies in clinical practice.
9

10 11 **METHODS**

12 **Scoping Review Aim**

13 The aim is to conduct a scoping review of sex differences in neurologic conditions, using
14 the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocols
15 (PRISMA-P) guidelines.[5] The final protocol is registered with the Open Science
16 Framework (<https://osf.io/n937x/>).
17
18

19 **Research Objectives**

20 This scoping review will explore how sex differences affect different aspects of patient
21 experiences in four subspecialty areas in neurology: demyelination, stroke, headache, and
22 epilepsy. The findings will be used to summarize research conducted in these areas and
23 identify any existing gaps of knowledge.
24
25

26 The broad research question for this review is: How does sex impact the epidemiology,
27 pathophysiology, clinical presentation, response to intervention, and disease outcomes in
28 neurologic conditions?
29
30

31 **Identifying Relevant Studies**

32 **Participants**

33 Studies of participants with primary neurologic conditions in one of the four neurology
34 subspecialties (i.e., demyelination, stroke, headache, epilepsy) will be included. Primary
35 demyelination conditions will be considered as multiple sclerosis, neuromyelitis optica
36 spectrum disorders, and acute disseminated encephalomyelitis. Primary stroke conditions
37 will be considered as ischemic strokes, hemorrhagic strokes, and cerebral venous sinus
38 thrombosis (CVST). Primary headache conditions will be considered as migraines,
39 tension-type headaches, cluster headaches, paroxysmal hemicrania, hemicrania continua,
40 or short-lasting unilateral neuralgiform (SUNCT) headaches/short-lasting unilateral
41 neuralgiform headaches with autonomic symptoms (SUNA). Primary epilepsy conditions
42 will be considered as any epileptic seizures (i.e., non-epileptic events will not be
43 included). Studies of participants with primary diagnoses of neuromuscular conditions,
44 movement disorders, sleep disorders, neuro-infectious diseases, neuro-ophthalmology, or
45 neuro-oncologic conditions will not be included.
46
47
48

49 **Interventions**

50 Studies that explore sex or gender differences in neurology will be included in initial
51 review due to their often-interchangeable use in research. Ultimately, only studies
52 exploring true sex differences will be included. Sex will be defined as the biological
53 differences between males and females (e.g., hormonal, genetic). Gender will be defined
54 as social norms for men and women, including social constructs and attitudes.
55
56
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60

Inclusion and Exclusion Criteria

The scoping review will include (must meet all of the following):

1. Reviews, primary research (i.e., qualitative, quantitative, mixed methods)
2. Human adults ≥ 18 years
3. Sex- or gender-specific data as a primary objective of the study
4. At least one of the four neurologic subspecialties of interest (i.e., demyelination, stroke, headache, epilepsy)
5. Published in English language

The scoping review will exclude (must meet 1 of the following):

1. Abstracts, commentaries, editorials, letters to the editor, case reports, case series, animal studies, phase 1 and 2 studies, pilot studies
2. Duplicate studies, irrelevant studies, those with a wrong aim, availability in abstract form only, and multiple articles from the same study
3. Humans < 18 years
4. Primary objective is not sex-specific endpoint
5. Condition is not in one of the four neurologic subspecialties of interest (i.e., demyelination, stroke, headache, epilepsy)
6. Not published in English language

Search Strategy

The search strategy will be designed and conducted by an information specialist using terms for each of the main concepts found within the review's research questions. The search strategy will include broad terms related to each neurologic condition, their synonyms, sex or gender. The search strategy will first be validated in MEDLINE (Ovid) and subsequently translated in Cochrane Central Registry of Controlled Trials (Ovid), EMBASE (Ovid), Emcare (Ovid), and PsychINFO (Ovid). See supplementary file 1 for the search strategy syntax that will be used in MEDLINE (Ovid).

Free text terms will be run to identify additional relevant studies that were not identified with the controlled classifying terminology. Reference lists of relevant systematic reviews and all included articles will be reviewed to identify additional studies of relevance. Lastly, articles from authors of included studies will be sought for inclusion. Grey literature will not be searched. Given the rapidly evolving field and recent advances in sex and gender differences in person-centered medicine, studies will be limited to those published between 2014-2020. This time frame was chosen as in 2015/2016, the US National Institutes of Health designed awards to promote the integration of sex and gender into clinical studies.[6] These policies highlighted the importance of considering sex in study design and analysis and subsequently led to a new generation of research. This scoping review focuses on the aftermath of this historical change to provide a review of recent work in this field.

Data Collection and Study Selection

Searches will be exported into EndNote software, with duplicates identified and removed. Study selection will involve a two-stage process:

- 1
- 2
- 3 1. Title and abstract review
- 4 2. Full-text review
- 5
- 6

7 For the first stage, two reviewers with the aid of Covidence software will screen the titles
8 and abstracts of articles identified in the search and additional sources described. The
9 inclusion/exclusion criteria will be tested on sample abstraction prior to beginning full
10 abstract review. At the second stage, full-text articles will be obtained and assessed again
11 by two reviewers to determine if they meet inclusion and exclusion criteria. Reasons for
12 exclusion will be documented for all articles at both stages. In the case of disagreement
13 not resolved by discussion, a third reviewer will be consulted. A complete PRISMA flow
14 chart and table of all included studies will be prepared for the final review.[5]
15

16 **Data Charting Process**

17 Reviewers will independently extract data using a standardized data collection form
18 designed for this study. Prior to implementation, the research team will review this form
19 to ensure all relevant information is accurately captured. Data charted will include, but
20 not be limited to: study citation, study methods (e.g., aim, design, population, “n” sample
21 size), key findings, patient characteristics (e.g., pregnancy, menopause), neurologic
22 condition, and sex- and gender-specific information relevant to the patient experience
23 (e.g., epidemiology, pathophysiology, risk factors, clinical features, diagnostics, medical
24 and surgical treatments, disease outcomes, psychosocial outcomes, and comorbidities).
25 All study outcomes will be reviewed, including both qualitative and quantitative results.
26 Data abstraction will occur concurrently by two independent reviewers. To ensure
27 accuracy, extracted information by each reviewer will be compared and discrepancies
28 will be discussed to ensure consistency between reviewers. Authors of eligible studies
29 will be contacted, if necessary, to obtain further information. The data will be compiled
30 into a single Microsoft Excel spreadsheet.
31

32 The methodological quality of studies included for in-depth review will be examined, as
33 applicable, using a modified version of the Critical Appraisal Skills Program (CASP)
34 quality assessment tool for qualitative studies.[7] The Confidence in the Evidence from
35 Reviews of Qualitative research (CERQual) approach will be used to determine how
36 much certainty should be placed on findings from the review’s synthesis.[8]
37

38 **Results Synthesis**

39 The neurology subspecialty areas previously identified will be used as a foundation to
40 organize results as an overview of all of the information retrieved and to establish the
41 extent and nature of the literature. The following presentation strategies will be used for
42 each subspecialty area:

- 43 1. Basic overview of amount, type, and distribution of included studies
- 44 2. Narrative synthesis and mapping of results
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A meta-analysis of quantitative results will not be performed as that is not part of scoping
review methodology.

Patient and Public Involvement

No patient involvement.

ETHICS AND DISSEMINATION

No ethical approval was required for this study as it is literature-based.

Given that sex and gender differences are not studied with consistent methods, the overview presented by this scoping review may provide clarity regarding what is currently known about sex differences in neurology. This scoping review will map the recent trends observed in sex difference research in neurology and identify subspecialty areas in need of further research. An understanding of sex-differences in neurology is necessary for implementation of sex-specific strategies to optimize patient care.

Knowledge translation will occur through presentation of results at relevant national and international conferences, and publication in a peer-reviewed journal. The study team will use their individual networks to encourage broad dissemination of results.

CONTRIBUTORSHIP STATEMENT

AP, EB, and GM initiated the project. AP and EB advised on study methods and revised the draft paper. EW and GM wrote the first drafts of the paper. All authors were involved in the response to reviewers and approved the final version of the paper.

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COMPETING INTERESTS

No authors have any competing interests to declare.

REFERENCES

1. Mamlouk GM, Dorris DM, Barrett LR, *et al.* Sex bias and omission in neuroscience research is influenced by research model and journal, but not reported NIH funding. *Front Neuroendocrinol* 2020;**57**. doi:10.1016/j.yfrne.2020.100835
2. What is gender? What is sex? Can. Institutes Heal. Res. 2020. <https://cihr-irsc.gc.ca/e/48642.html> (accessed 3 May 2021).
3. Connelly PJ, Azizi Z, Alipour P, *et al.* The Importance of Gender to Understand Sex Differences in Cardiovascular Disease. *Can J Cardiol* 2021;**37**:699–710. doi:10.1016/j.cjca.2021.02.005
4. Zucker I, Prendergast BJ. Sex differences in pharmacokinetics predict adverse drug reactions in women. *Biol Sex Differ* 2020;**11**:32. doi:10.1186/s13293-020-00308-5
5. Tricco AC, Lillie E, Zarin W, *et al.* PRISMA extension for scoping reviews (PRISMA-ScR): Checklist and explanation. *Ann. Intern. Med.* 2018;**169**:467–73. doi:10.7326/M18-0850
6. Consideration of Sex as a Biological Variable in NIH-funded Research . NIH website. Updated June 9, 2015. Accessed July 1, 2021. https://orwh.od.nih.gov/sites/orwh/files/docs/NOT-OD-15-102_Guidance.pdf.
7. Critical Appraisal Skills Programme. CASP Qualitative Checklist. *CASP Online* 2018.
8. Lewin S, Glenton C, Munthe-Kaas H, *et al.* Using Qualitative Evidence in Decision Making for Health and Social Interventions: An Approach to Assess Confidence in Findings from Qualitative Evidence Syntheses (GRADE-CERQual). *PLoS Med* 2015;**12**. doi:10.1371/journal.pmed.1001895

August 18, 2020 Searches

Databases:

- Ovid Medline ALL
- Ovid Embase

August 19, 2020 Searches

Databases:

- Ovid Cochrane Central Register of Controlled Trials
- Ovid Emcare
- Ovid PsycINFO

August 18, 2020

Database(s): **Ovid MEDLINE(R) ALL** 1946 to August 17, 2020

Search Strategy:

#	Searches	Results
1	*sex factors/	5525
2	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 differenc*).ti,kf,hw.	33981
3	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 factor*).ti,kf,hw.	271950
4	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 compar*).ti,kf,hw.	5519
5	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 impact*).ti,kf,hw.	2812
6	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 influen*).ti,kf,hw.	6758
7	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 confound*).ti,kf,hw.	43
8	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 associat*).ti,kf,hw.	7924
9	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 link????).ti,kf,hw.	2182
10	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 contribut*).ti,kf,hw.	892
11	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 specific*).ti,kf,hw.	9851
12	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 distribut*).ti,kf,hw.	56980
13	or/1-12	365404
14	exp Epilepsy/	111569

15	epilep*.mp.	163872
16	seizur*.mp.	142544
17	seizing.mp.	554
18	aura?.mp.	11568
19	myoclonus/ [1966-1976]	5154
20	(dravet adj4 syndrom*).mp.	1003
21	myoclon*.mp.	17146
22	(atroph* adj4 dentatorubral-pallidoluisian).mp.	400
23	atypical inclusion body disease*.mp.	0
24	(biotin adj4 encephalopath*).mp.	8
25	naito-oyanagi.mp.	3
26	(haw river adj4 syndrome*).mp.	5
27	(may white adj4 syndrome*).mp.	2
28	lafora.mp.	644
29	merrf.mp.	642
30	fukuhara.mp.	32
31	unverricht.mp.	357
32	lundborg.mp.	355
33	petit mal.mp.	1003
34	grand mal.mp.	1494
35	jme.mp.	738
36	jmes.mp.	8
37	janz.mp.	71
38	Jacksonian Seizure/ [1966-1976]	53931
39	bcects.mp.	58
40	bects.mp.	258
41	convuls*.mp.	35190
42	pyknolep*.mp.	49
43	tonic-clonic.mp.	9934
44	(nodding adj4 syndrome*).mp.	126
45	(lightning adj4 attack*).mp.	4

46	(salaam adj4 attack*).mp.	2
47	(cryptogenic adj4 spasm*).mp.	71
48	hyparrhythmi*.mp.	816
49	(infant* adj4 spasm*).mp.	4694
50	(nodding adj4 spasm*).mp.	29
51	(spasm* adj4 nutan*).mp.	110
52	(symptom* adj4 west).mp.	144
53	(west adj4 syndrom*).mp.	1427
54	landau-kleffner.mp.	516
55	lennox gastaut.mp.	1477
56	(febrile adj4 fit?).mp.	25
57	absence status.mp.	243
58	kozhevniko???.mp.	54
59	kojewniko???.mp.	29
60	kojevniko???.mp.	16
61	kozhevniko???.mp.	1
62	or/14-61 [epilepsy or seizures]	265264
63	exp Stroke/	134958
64	stroke\$.mp.	301266
65	(cerebr??vascular adj4 accident*).mp.	7319
66	(cereb* adj4 infarct*).mp.	45490
67	(cerebr??vascular adj4 disease?).mp.	23786
68	(cva or cvas).mp.	3034
69	(tia or tias).mp.	9254
70	transient isch?emic attack?.mp.	14294
71	poststroke.mp.	5250
72	(brain* adj4 vascular adj4 accident*).mp.	63
73	(brain* adj4 infarct*).mp.	12245
74	brain* attack*.mp.	308
75	appoplex*.mp.	3
76	apoplex*.mp.	3353

77	Stroke Rehabilitation/	13332
78	claude syndrome*.mp.	8
79	foville syndrome*.mp.	21
80	millard gublar syndrome*.mp.	1
81	"top of the basilar syndrome*".mp.	42
82	weber syndrome*.mp.	3118
83	(choroidal adj4 infarct*).mp.	159
84	(hemisphere* adj4 infarct*).mp.	746
85	medullary syndrome*.mp.	904
86	(cereb* adj4 syndrome*).mp.	7569
87	vieseaux-wallenberg syndrome*.mp.	0
88	wallenberg syndrome*.mp.	197
89	cadasil?.mp.	1393
90	(subcort* adj4 infarct*).mp.	1941
91	(multi?infarct* adj4 dement*).mp.	92
92	(lacun* adj4 dement*).mp.	87
93	aca infarct*.mp.	31
94	(heubner adj4 infarct*).mp.	8
95	mca infarct*.mp.	377
96	(cereb* adj4 occlu*).mp.	17700
97	(cereb* adj4 thrombo*).mp.	10018
98	(lacun* adj4 syndrome*).mp.	366
99	pca infarct*.mp.	57
100	or/63-99 [stroke]	379170
101	exp Multiple Sclerosis/	58886
102	(multiple adj3 sclero*).mp.	84306
103	(disseminat* adj3 sclero*).mp.	911
104	exp Demyelinating Diseases/	100524
105	demyelinat*.mp.	36735
106	(neuromyelit* adj4 optica*).mp.	4466
107	(myelin oligodendrocyte glycoprotein* adj4 disorder*).mp.	55

108	(myelin oligodendrocyte glycoprotein* adj4 disease*).mp.	136
109	or/101-108 [MS or demyelinating]	131940
110	exp Headache/	27767
111	exp Headache Disorders/	34486
112	headache*.mp.	94648
113	head-ache*.mp.	115
114	migraine*.mp.	39847
115	exp head/ and exp pain/	3125
116	(head* adj4 pain*).mp.	10408
117	cephalalgi*.mp.	890
118	or/110-117 [headache]	119078
119	13 and 62 [sex differences and epilepsy or seizures]	3238
120	13 and 100 [sex differences and stroke]	9603
121	13 and 109 [sex differences and MS or demyelinating]	1839
122	13 and 118 [sex differences and headache]	2637
123	exp animals/ not (exp animals/ and exp humans/)	4725904
124	119 not 123 [sex differences and epilepsy or seizures NOT animal studies]	2976
125	120 not 123 [sex differences and stroke NOT animal studies]	9423
126	121 not 123 [sex differences and MS or demyelinating NOT animal studies]	1756
127	122 not 123 [sex differences and headache NOT animal studies]	2620
128	limit 124 to "all adult (19 plus years)"	1869
129	limit 124 to "all child (0 to 18 years)"	1809
130	124 not 129	1167
131	128 or 130 [sex differences and epilepsy or seizures NOT animal studies NOT child studies]	2254
132	limit 125 to "all adult (19 plus years)"	7936
133	limit 125 to "all child (0 to 18 years)"	1339
134	125 not 133	8084
135	132 or 134 [sex differences and stroke NOT animal studies NOT child studies]	9267
136	limit 126 to "all adult (19 plus years)"	1352
137	limit 126 to "all child (0 to 18 years)"	651
138	126 not 137	1105

139	136 or 138 [sex differences and MS or demyelinating NOT animal studies NOT child studies]	1672
140	limit 127 to "all adult (19 plus years)"	1885
141	limit 127 to "all child (0 to 18 years)"	1266
142	127 not 141	1354
143	140 or 142 [sex differences and headache NOT animals studies NOT child studies]	2244
144	limit 131 to yr="2009 -Current" [sex differences and epilepsy or seizures NOT animal studies NOT child studies, from 2009 to present]	831
145	limit 135 to yr="2009 -Current" [sex differences and stroke NOT animal studies NOT child studies, from 2009 to present]	5143
146	limit 139 to yr="2009 -Current" [sex differences and MS or demyelinating NOT animal studies NOT child studies, from 2009 to present]	763
147	limit 143 to yr="2009 -Current" [sex differences and headache NOT animal studies NOT child studies, from 2009 to present]	898
148	144 or 145 or 146 or 147	7274

Database(s): **Embase Classic+Embase** 1947 to 2020 August 17

Search Strategy:

#	Searches	Results
1	exp *sex difference/	46982
2	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 differenc*).ti,kw,hw.	403552
3	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 factor*).ti,kw,hw.	18935
4	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 compar*).ti,kw,hw.	7263
5	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 impact*).ti,kw,hw.	4054
6	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 influen*).ti,kw,hw.	8678
7	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 confound*).ti,kw,hw.	53
8	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 associat*).ti,kw,hw.	10047
9	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 link????).ti,kw,hw.	3349
10	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 contribut*).ti,kw,hw.	1070
11	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 specific*).ti,kw,hw.	12683
12	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 distribut*).ti,kw,hw.	2163

13	or/1-12	451578
14	exp "seizure, epilepsy and convulsion"/	404444
15	epilep*.mp.	266828
16	seizur*.mp.	255688
17	seizing.mp.	766
18	aura?.mp.	19710
19	(dravet adj4 syndrom*).mp.	1756
20	myoclon*.mp.	32360
21	(atroph* adj4 dentatorubral-pallidoluvsian).mp.	0
22	atypical inclusion body disease*.mp.	0
23	(biotin adj4 encephalopath*).mp.	9
24	naito-oyanagi.mp.	3
25	(haw river adj4 syndrome*).mp.	9
26	(may white adj4 syndrome*).mp.	4
27	lafora.mp.	926
28	merrf.mp.	1001
29	fukuhara.mp.	45
30	unverricht.mp.	517
31	lundborg.mp.	495
32	petit mal.mp.	2852
33	grand mal.mp.	11839
34	jme.mp.	1254
35	jmes.mp.	8
36	janz.mp.	148
37	bcects.mp.	99
38	bects.mp.	378
39	convuls*.mp.	72117
40	pyknolep*.mp.	153
41	tonic-clonic.mp.	24226
42	(nodding adj4 syndrome*).mp.	212
43	(lightning adj4 attack*).mp.	7

44	(salaam adj4 attack*).mp.	15
45	(cryptogenic adj4 spasm*).mp.	119
46	hyparrhythmi*.mp.	2023
47	(infant* adj4 spasm*).mp.	8136
48	(nodding adj4 spasm*).mp.	51
49	(spasm* adj4 nutan*).mp.	178
50	(symptom* adj4 west).mp.	219
51	landau-kleffner.mp.	1053
52	lennox gastaut.mp.	4304
53	(febrile adj4 fit?).mp.	53
54	absence status.mp.	399
55	kozhevniko???.mp.	79
56	kojewniko???.mp.	45
57	kojevniko???.mp.	29
58	kozhewniko???.mp.	1
59	or/14-58 [epilepsy or seizures]	478503
60	exp cerebrovascular accident/	216527
61	stroke\$.mp.	463137
62	(cerebr??vascular adj4 accident*).mp.	216000
63	(cereb* adj4 infarct*).mp.	39944
64	(cerebr??vascular adj4 disease?).mp.	90665
65	(cva or cvas).mp.	6993
66	(tia or tias).mp.	20150
67	transient isch?emic attack?.mp.	43401
68	poststroke.mp.	7093
69	(brain* adj4 vascular adj4 accident*).mp.	112
70	(brain* adj4 infarct*).mp.	65851
71	brain* attack*.mp.	554
72	apoplex*.mp.	3
73	apoplex*.mp.	5101
74	stroke rehabilitation/	3586

75	claudie syndrome*.mp.	37
76	foville syndrome*.mp.	48
77	millard gublar syndrome*.mp.	0
78	"top of the basilar syndrome*".mp.	78
79	weber syndrome*.mp.	3886
80	(choroidal adj4 infarct*).mp.	191
81	(hemisphere* adj4 infarct*).mp.	1142
82	medullary syndrome*.mp.	457
83	(cereb* adj4 syndrome*).mp.	12377
84	vieseaux-wallenberg syndrome*.mp.	0
85	wallenberg syndrome*.mp.	1091
86	cadasil?.mp.	2584
87	(subcort* adj4 infarct*).mp.	2778
88	(multi?infarct* adj4 dement*).mp.	12411
89	(lacun* adj4 dement*).mp.	132
90	aca infarct*.mp.	59
91	(heubner adj4 infarct*).mp.	10
92	mca infarct*.mp.	785
93	(cereb* adj4 occlu*).mp.	38802
94	(cereb* adj4 thrombo*).mp.	17668
95	(lacun* adj4 syndrome*).mp.	529
96	pca infarct*.mp.	93
97	or/60-96 [stroke]	672976
98	exp demyelinating disease/	184579
99	(multiple adj3 sclero*).mp.	149447
100	(disseminat* adj3 sclero*).mp.	1353
101	demyelinat*.mp.	64947
102	(neuromyelit* adj4 optica*).mp.	8095
103	(myelin oligodendrocyte glycoprotein* adj4 disorder*).mp.	103
104	(myelin oligodendrocyte glycoprotein* adj4 disease*).mp.	200
105	or/98-104 [MS or demyelinating]	211317

106	exp "headache and facial pain"/	319885
107	headache*.mp.	290313
108	head-ache*.mp.	330
109	migraine*.mp.	74416
110	exp head/ and exp pain/	34096
111	(head* adj4 pain*).mp.	19430
112	cephalalg*.mp.	2015
113	or/106-112 [headache]	365211
114	13 and 59 [sex differences and epilepsy or seizures]	4842
115	13 and 97 [sex differences and stroke]	15006
116	13 and 105 [sex differences and MS or demyelinating]	2644
117	13 and 113 [sex differences and headache]	5536
118	(exp animals/ or exp animal experimentation/ or nonhuman/) not ((exp animals/ or exp animal experimentation/ or nonhuman/) and exp human/)	7309464
119	114 not 118 [sex differences and epilepsy or seizures NOT animal studies]	4392
120	115 not 118 [sex differences and stroke NOT animal studies]	14598
121	116 not 118 [sex differences and MS or demyelinating NOT animal studies]	2490
122	117 not 118 [sex differences and headache NOT animal studies]	5449
123	limit 119 to (adult <18 to 64 years> or aged <65+ years>)	2226
124	limit 119 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	1580
125	119 not 124	2812
126	123 or 125 [sex differences and epilepsy or seizures NOT animal studies NOT child studies]	3667
127	limit 120 to (adult <18 to 64 years> or aged <65+ years>)	10061
128	limit 120 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	993
129	120 not 128	13605
130	127 or 129 [sex differences and stroke NOT animal studies NOT child studies]	14420
131	limit 121 to (adult <18 to 64 years> or aged <65+ years>)	1466
132	limit 121 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	425
133	121 not 132	2065

134	131 or 133 [sex differences and MS or demyelinating NOT animal studies NOT child studies]	2402
135	limit 122 to (adult <18 to 64 years> or aged <65+ years>)	3280
136	limit 122 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	1402
137	122 not 136	4047
138	135 or 137 [sex differences and headache NOT animal studies NOT child studies]	4924
139	limit 126 to yr="2009 -Current" [sex differences and epilepsy or seizures NOT animal studies NOT child studies, 2009 to present]	2135
140	limit 130 to yr="2009 -Current" [sex differences and stroke NOT animal studies NOT child studies, 2009 to present]	9979
141	limit 134 to yr="2009 -Current" [sex differences and MS or demyelinating NOT animal studies NOT child studies, 2009 to present]	1565
142	limit 138 to yr="2009 -Current" [sex differences and headache NOT animal studies NOT child studies, 2009 to present]	2855
143	limit 139 to conference abstracts	197
144	139 not 143 [sex differences and epilepsy or seizures NOT animal studies NOT child studies, 2009 to present NOT conference abstracts]	1938
145	limit 140 to conference abstracts	1482
146	140 not 145 [sex differences and stroke NOT animal studies NOT child studies, 2009 to present NOT conference abstracts]	8497
147	limit 141 to conference abstracts	173
148	141 not 147 [sex differences and MS or demyelinating NOT animal studies NOT child studies, 2009 to present NOT conference abstracts]	1392
149	limit 142 to conference abstracts	260
150	142 not 149 [sex differences and headache NOT animal studies NOT child studies, 2009 to present NOT conference abstracts]	2595
151	144 or 146 or 148 or 150	13275

August 19, 2020

Database(s): **Cochrane Central Register of Controlled Trials** 2014 to Present
 Search Strategy:

#	Searches	Results
1	exp Sex Characteristics/ or sex factors/	7149
2	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 differenc*).ti,kw,hw.	6653
3	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 factor*).ti,kw,hw.	10468
4	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 compar*).ti,kw,hw.	11541
5	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 impact*).ti,kw,hw.	901
6	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 influen*).ti,kw,hw.	1390
7	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 confound*).ti,kw,hw.	48
8	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 associat*).ti,kw,hw.	4879
9	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 link????).ti,kw,hw.	3341
10	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 contribut*).ti,kw,hw.	35
11	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 specific*).ti,kw,hw.	854
12	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 distribut*).ti,kw,hw.	1405
13	or/1-12	39488
14	exp "seizure, epilepsy and convulsion"/ or exp Epilepsy/ or myoclonus/ or Jacksonian Seizure/	3014
15	epilep*.mp.	8517
16	seizur*.mp.	8878
17	seizing.mp.	18
18	aura?.mp.	1670
19	(dravet adj4 syndrom*).mp.	102
20	myoclon*.mp.	692
21	(atroph* adj4 dentatorubral-pallidoluvnsian).mp.	0
22	atypical inclusion body disease*.mp.	0
23	(biotin adj4 encephalopath*).mp.	0
24	naito-oyanagi.mp.	0
25	(haw river adj4 syndrome*).mp.	0
26	(may white adj4 syndrome*).mp.	158
27	lafora.mp.	4
28	merrf.mp.	4
29	fukuhara.mp.	0
30	unverricht.mp.	12

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3		
4	31	lundborg.mp.
5	32	petit mal.mp.
6	33	grand mal.mp.
7	34	jme.mp.
8	35	jmes.mp.
9	36	janz.mp.
10	37	bcects.mp.
11	38	bects.mp.
12	39	convuls*.mp.
13	40	pyknolep*.mp.
14	41	tonic-clonic.mp.
15	42	(nodding adj4 syndrome*).mp.
16	43	(lightning adj4 attack*).mp.
17	44	(salaam adj4 attack*).mp.
18	45	(cryptogenic adj4 spasm*).mp.
19	46	hyparrhythmi*.mp.
20	47	(infant* adj4 spasm*).mp.
21	48	(nodding adj4 spasm*).mp.
22	49	(spasm* adj4 nutan*).mp.
23	50	(symptom* adj4 west).mp.
24	51	landau-kleffner.mp.
25	52	lennox gastaut.mp.
26	53	(febrile adj4 fit?).mp.
27	54	absence status.mp.
28	55	kozhevniko???.mp.
29	56	kojewniko???.mp.
30	57	kojevniko???.mp.
31	58	kozhevniko???.mp.
32	59	or/14-58 [epilepsy or seizures]
33	60	exp Stroke/ or exp Stroke/ or Stroke Rehabilitation/
34	61	stroke\$.mp.
35		
36		
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62	(cerebr??vascular adj4 accident*).mp.	14423
63	(cereb* adj4 infarct*).mp.	4889
64	(cerebr??vascular adj4 disease?).mp.	4243
65	(cva or cvas).mp.	566
66	(tia or tias).mp.	1863
67	transient isch?emic attack?.mp.	3121
68	poststroke.mp.	1376
69	(brain* adj4 vascular adj4 accident*).mp.	11
70	(brain* adj4 infarct*).mp.	1912
71	brain* attack*.mp.	31
72	appoplex*.mp.	0
73	apoplex*.mp.	350
74	stroke rehabilitation/	2365
75	claudicatio syndrome*.mp.	0
76	foveate syndrome*.mp.	0
77	millard gubler syndrome*.mp.	0
78	"top of the basilar syndrome*".mp.	0
79	weber syndrome*.mp.	16
80	(choroidal adj4 infarct*).mp.	1
81	(hemisphere* adj4 infarct*).mp.	52
82	medullary syndrome*.mp.	10
83	(cereb* adj4 syndrome*).mp.	503
84	viesteaux-wallenberg syndrome*.mp.	0
85	wallenberg syndrome*.mp.	4
86	cadasil?.mp.	28
87	(subcort* adj4 infarct*).mp.	82
88	(multi?infarct* adj4 dement*).mp.	326
89	(lacun* adj4 dement*).mp.	10
90	aca infarct*.mp.	1
91	(heubner adj4 infarct*).mp.	0
92	mca infarct*.mp.	58

93	(cereb* adj4 occlu*).mp.	778
94	(cereb* adj4 thrombo*).mp.	1351
95	(lacun* adj4 syndrome*).mp.	43
96	pca infarct*.mp.	2
97	or/60-96 [stroke]	67382
98	exp Demyelinating Diseases/ or exp Demyelinating Diseases/ or exp Multiple Sclerosis/	3721
99	(multiple adj3 sclero*).mp.	10544
100	(disseminat* adj3 sclero*).mp.	15
101	demyelinat*.mp.	1290
102	(neuromyelit* adj4 optica*).mp.	196
103	(myelin oligodendrocyte glycoprotein* adj4 disorder*).mp.	2
104	(myelin oligodendrocyte glycoprotein* adj4 disease*).mp.	5
105	or/98-104 [MS or demyelinating]	11495
106	exp "headache and facial pain"/ or exp Headache/ or exp Headache Disorders/	5085
107	headache*.mp.	32810
108	head-ache*.mp.	21
109	migraine*.mp.	7454
110	exp head/ and exp pain/	319
111	(head* adj4 pain*).mp.	3720
112	cephalalgi*.mp.	54
113	or/106-112 [headache]	36541
114	13 and 59 [sex differences and epilepsy or seizures]	279
115	13 and 97 [sex differences and stroke]	1780
116	13 and 105 [sex differences and MS or demyelinating]	288
117	13 and 113 [sex differences and headache]	913
118	limit 114 to yr="2009 -Current" [sex differences and epilepsy or seizures, 2009 to present]	200
119	limit 115 to yr="2009 -Current" [sex differences and stroke, 2009 to present]	1401
120	limit 116 to yr="2009 -Current" [sex differences and MS or demyelinating, 2009 to present]	251
121	limit 117 to yr="2009 -Current" [sex differences and headache, 2009 to present]	617
122	118 or 119 or 120 or 121	2357

Database(s): **Ovid Emcare Nursing** 1995 to Present
 Search Strategy:

#	Searches	Results
1	exp *sex difference/	17673
2	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 differenc*).ti,kw,hw.	108237
3	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 factor*).ti,kw,hw.	3462
4	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 compar*).ti,kw,hw.	2113
5	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 impact*).ti,kw,hw.	1334
6	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 influen*).ti,kw,hw.	2202
7	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 confound*).ti,kw,hw.	24
8	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 associat*).ti,kw,hw.	3095
9	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 link????).ti,kw,hw.	394
10	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 contribut*).ti,kw,hw.	261
11	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 specific*).ti,kw,hw.	2760
12	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 distribut*).ti,kw,hw.	353
13	or/1-12	118662
14	exp "seizure, epilepsy and convulsion"/	61035
15	epilep*.mp.	32137
16	seizur*.mp.	39304
17	seizing.mp.	222
18	aura?.mp.	4694
19	(dravet adj4 syndrom*).mp.	206
20	myoclon*.mp.	4709
21	(atroph* adj4 dentatorubral-pallidoluvsian).mp.	0
22	atypical inclusion body disease*.mp.	0
23	(biotin adj4 encephalopath*).mp.	0
24	naito-oyanagi.mp.	0
25	(haw river adj4 syndrome*).mp.	1
26	(may white adj4 syndrome*).mp.	0
27	lafora.mp.	50
28	merrf.mp.	101
29	fukuhara.mp.	11

30	unverricht.mp.	38
31	lundborg.mp.	47
32	petit mal.mp.	58
33	grand mal.mp.	1513
34	jme.mp.	98
35	jmes.mp.	3
36	janz.mp.	20
37	bcects.mp.	5
38	bects.mp.	31
39	convuls*.mp.	7175
40	pyknolep*.mp.	3
41	tonic-clonic.mp.	4238
42	(nodding adj4 syndrome*).mp.	49
43	(lightning adj4 attack*).mp.	1
44	(salaam adj4 attack*).mp.	0
45	(cryptogenic adj4 spasm*).mp.	8
46	hypsarrhythmi*.mp.	158
47	(infant* adj4 spasm*).mp.	1060
48	(nodding adj4 spasm*).mp.	2
49	(spasm* adj4 nutan*).mp.	13
50	(symptom* adj4 west).mp.	39
51	landau-kleffner.mp.	200
52	lennox gastaut.mp.	618
53	(febrile adj4 fit?).mp.	6
54	absence status.mp.	38
55	kozhevniko???.mp.	7
56	kojewniko???.mp.	0
57	kojevniko???.mp.	0
58	kozhevniko???.mp.	0
59	or/14-58 [epilepsy or seizures]	70654
60	exp cerebrovascular accident/	59614

61	stroke\$.mp.	119669
62	(cerebr??vascular adj4 accident*).mp.	58780
63	(cereb* adj4 infarct*).mp.	7229
64	(cerebr??vascular adj4 disease?).mp.	18586
65	(cva or cvas).mp.	1030
66	(tia or tias).mp.	2850
67	transient isch?emic attack?.mp.	11666
68	poststroke.mp.	3605
69	(brain* adj4 vascular adj4 accident*).mp.	12
70	(brain* adj4 infarct*).mp.	15250
71	brain* attack*.mp.	172
72	appoplex*.mp.	0
73	apoplex*.mp.	585
74	stroke rehabilitation/	1152
75	claudication syndrome*.mp.	4
76	fovea syndrome*.mp.	8
77	millard gublar syndrome*.mp.	0
78	"top of the basilar syndrome*".mp.	12
79	weber syndrome*.mp.	548
80	(choroidal adj4 infarct*).mp.	23
81	(hemisphere* adj4 infarct*).mp.	194
82	medullary syndrome*.mp.	63
83	(cereb* adj4 syndrome*).mp.	1806
84	viesteaux-wallenberg syndrome*.mp.	0
85	wallenberg syndrome*.mp.	185
86	cadASIL?.mp.	635
87	(subcort* adj4 infarct*).mp.	673
88	(multi?infarct* adj4 dement*).mp.	4341
89	(lacun* adj4 dement*).mp.	27
90	aca infarct*.mp.	3
91	(heubner adj4 infarct*).mp.	4

92	mca infarct*.mp.	145
93	(cereb* adj4 occlu*).mp.	7407
94	(cereb* adj4 thrombo*).mp.	3169
95	(lacun* adj4 syndrome*).mp.	97
96	pca infarct*.mp.	14
97	or/60-96 [stroke]	166160
98	exp demyelinating disease/	29756
99	(multiple adj3 sclero*).mp.	24666
100	(disseminat* adj3 sclero*).mp.	42
101	demyelinat*.mp.	8283
102	(neuromyelit* adj4 optica*).mp.	1087
103	(myelin oligodendrocyte glycoprotein* adj4 disorder*).mp.	24
104	(myelin oligodendrocyte glycoprotein* adj4 disease*).mp.	45
105	or/98-104 [MS or demyelinating]	32839
106	exp "headache and facial pain"/	80703
107	headache*.mp.	71279
108	head-ache*.mp.	41
109	migraine*.mp.	18750
110	exp head/ and exp pain/	9069
111	(head* adj4 pain*).mp.	4946
112	cephalalgi*.mp.	412
113	or/106-112 [headache]	89106
114	13 and 59 [sex differences and epilepsy or seizures]	963
115	13 and 97 [sex differences and stroke]	5088
116	13 and 105 [sex differences and MS or demyelinating]	605
117	13 and 113 [sex differences and headache]	1803
118	(exp animals/ or exp animal experimentation/ or nonhuman/) not ((exp animals/ or exp animal experimentation/ or nonhuman/) and exp human/)	461862
119	114 not 118 [sex differences and epilepsy or seizures NOT animal studies]	917
120	115 not 118 [sex differences and stroke NOT animal studies]	5040
121	116 not 118 [sex differences and MS or demyelinating NOT animal studies]	585
122	117 not 118 [sex differences and headache NOT animal studies]	1786

123	limit 119 to (adult <18 to 64 years> or aged <65+ years>)	508
124	limit 119 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	302
125	119 not 124	615
126	123 or 125 [sex differences and epilepsy or seizures NOT animal studies NOT child studies]	788
127	limit 120 to (adult <18 to 64 years> or aged <65+ years>)	3730
128	limit 120 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	265
129	120 not 128	4775
130	127 or 129 [sex differences and stroke NOT animal studies NOT child studies]	4992
131	limit 121 to (adult <18 to 64 years> or aged <65+ years>)	402
132	limit 121 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	78
133	121 not 132	507
134	131 or 133 [sex differences and MS or demyelinating NOT animal studies NOT child studies]	572
135	limit 122 to (adult <18 to 64 years> or aged <65+ years>)	1050
136	limit 122 to (embryo or infant or child or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	419
137	122 not 136	1367
138	135 or 137 [sex differences and headache NOT animal studies NOT child studies]	1624
139	limit 126 to yr="2009 -Current" [sex differences and epilepsy or seizures NOT animal studies NOT child studies, 2009 to present]	545
140	limit 130 to yr="2009 -Current" [sex differences and stroke NOT animal studies NOT child studies, 2009 to present]	3750
141	limit 134 to yr="2009 -Current" [sex differences and MS or demyelinating NOT animal studies NOT child studies, 2009 to present]	454
142	limit 138 to yr="2009 -Current" [sex differences and headache NOT animal studies NOT child studies, 2009 to present]	1055
143	139 or 140 or 141 or 142	5407

Database(s): **APA PsycInfo** 1806 to August Week 3 2020

Search Strategy:

#	Searches	Results
1	exp human sex differences/	113766
2	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 differenc*).mp.	160431
3	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 factor*).mp.	34887
4	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 compar*).mp.	38823
5	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 impact*).mp.	8784
6	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 influen*).mp.	19926
7	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 confound*).mp.	2051
8	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 associat*).mp.	33724
9	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 link????).mp.	5784
10	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 contribut*).mp.	6265
11	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 specific*).mp.	22091
12	((sex?? or gender* or male* or female* or m#n or wom#n) adj4 distribut*).mp.	3832
13	or/1-12	268972
14	exp epilepsy/ or exp seizures/	35420
15	epilep*.mp.	44883
16	seizur*.mp.	34374
17	seizing.mp.	383
18	aura?.mp.	5466
19	(dravet adj4 syndrom*).mp.	290
20	myoclon*.mp.	3153
21	(atroph* adj4 dentatorubral-pallidoluvsian).mp.	0
22	atypical inclusion body disease*.mp.	0
23	(biotin adj4 encephalopath*).mp.	1
24	naito-oyanagi.mp.	0
25	(haw river adj4 syndrome*).mp.	0
26	(may white adj4 syndrome*).mp.	0
27	lafora.mp.	89
28	merrf.mp.	46
29	fukuhara.mp.	10

30	unverricht.mp.	54
31	lundborg.mp.	55
32	petit mal.mp.	375
33	grand mal.mp.	593
34	jme.mp.	310
35	jmes.mp.	8
36	janz.mp.	37
37	bcects.mp.	32
38	bects.mp.	109
39	convuls*.mp.	6938
40	pyknolep*.mp.	20
41	tonic-clonic.mp.	1539
42	(nodding adj4 syndrome*).mp.	19
43	(lightning adj4 attack*).mp.	1
44	(salaam adj4 attack*).mp.	1
45	(cryptogenic adj4 spasm*).mp.	18
46	hypsarrhythmi*.mp.	125
47	(infant* adj4 spasm*).mp.	619
48	(nodding adj4 spasm*).mp.	5
49	(spasm* adj4 nutan*).mp.	8
50	(symptom* adj4 west).mp.	47
51	landau-kleffner.mp.	214
52	lennox gastaut.mp.	317
53	(febrile adj4 fit?).mp.	2
54	absence status.mp.	54
55	kozhevniko???.mp.	25
56	kojewniko???.mp.	3
57	kojevniko???.mp.	4
58	kozhevniko???.mp.	0
59	or/14-58 [epilepsy or seizures]	66146
60	cerebrovascular accidents/	21013

61	stroke\$.mp.	36733
62	(cerebr??vascular adj4 accident*).mp.	21344
63	(cereb* adj4 infarct*).mp.	2559
64	(cerebr??vascular adj4 disease?).mp.	3030
65	(cva or cvas).mp.	470
66	(tia or tias).mp.	1015
67	transient isch?emic attack?.mp.	1142
68	poststroke.mp.	1811
69	(brain* adj4 vascular adj4 accident*).mp.	30
70	(brain* adj4 infarct*).mp.	1704
71	brain* attack*.mp.	43
72	appoplex*.mp.	0
73	apoplex*.mp.	151
74	stroke rehabilitation/	0
75	claudicatio syndrome*.mp.	0
76	foveate syndrome*.mp.	0
77	millard gublar syndrome*.mp.	0
78	"top of the basilar syndrome*".mp.	3
79	weber syndrome*.mp.	128
80	(choroidal adj4 infarct*).mp.	13
81	(hemisphere* adj4 infarct*).mp.	190
82	medullary syndrome*.mp.	22
83	(cereb* adj4 syndrome*).mp.	1675
84	viesteaux-wallenberg syndrome*.mp.	0
85	wallenberg syndrome*.mp.	19
86	cadasil?.mp.	327
87	(subcort* adj4 infarct*).mp.	500
88	(multi?infarct* adj4 dement*).mp.	79
89	(lacun* adj4 dement*).mp.	29
90	aca infarct*.mp.	7
91	(heubner adj4 infarct*).mp.	0

92	mca infarct*.mp.	50
93	(cereb* adj4 occlu*).mp.	1916
94	(cereb* adj4 thrombo*).mp.	686
95	(lacun* adj4 syndrome*).mp.	38
96	pca infarct*.mp.	15
97	or/60-96 [stroke]	44738
98	demyelination/ or multiple sclerosis/	13968
99	(multiple adj3 sclero*).mp.	16209
100	(disseminat* adj3 sclero*).mp.	65
101	demyelinat*.mp.	5561
102	(neuromyelit* adj4 optica*).mp.	963
103	(myelin oligodendrocyte glycoprotein* adj4 disorder*).mp.	9
104	(myelin oligodendrocyte glycoprotein* adj4 disease*).mp.	171
105	or/98-104 [MS or demyelinating]	19667
106	exp headache/	15324
107	headache*.mp.	22630
108	head-ache*.mp.	18
109	migraine*.mp.	12940
110	(head* adj4 pain*).mp.	3372
111	cephalalgi*.mp.	408
112	or/106-111 [headache]	24602
113	13 and 59 [sex differences and epilepsy or seizures]	1731
114	13 and 97 [sex differences and stroke]	1696
115	13 and 105 [sex differences and MS or demyelinating]	644
116	13 and 112 [sex differences and headache]	1072
117	limit 113 to yr="2009 -Current" [sex differences and epilepsy or seizures, 2009 to present]	864
118	limit 114 to yr="2009 -Current" [sex differences and stroke, 2009 to present]	1111
119	limit 115 to yr="2009 -Current" [sex differences and MS or demyelinating, 2009 to present]	468
120	limit 116 to yr="2009 -Current" [sex differences and headache, 2009 to present]	546
121	117 or 118 or 119 or 120	2772

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Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	



SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	
Limitations	20	Discuss the limitations of the scoping review process.	
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. *Ann Intern Med.* 2018;169:467–473. doi: [10.7326/M18-0850](https://doi.org/10.7326/M18-0850).



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