


# BMJ Open Association between spinal and non-spinal health conditions reported in epidemiological studies: a scoping review protocol

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## ABSTRACT

**Introduction** The increasing prevalence of coexisting health conditions poses a challenge to healthcare providers and healthcare systems. Spinal pain (eg, neck and back pain) and spinal pathologies (eg, osteoporotic fractures and degenerative spinal disease) exist concurrently with other non-spinal health conditions (NSHC). However, the scope of what associations may exist among these co-occurring conditions is unclear. Therefore, this scoping review aims to map the epidemiological literature that reports associations between spine-related pain and pathologies (SPPs) and NSHCs.

**Methods and analysis** This scoping review will follow the JBI protocol and Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews. We will systematically search the literature using key words and MeSH terms for SPPs and NSHCs. Terminology/vocabulary for NSHCs will include those for communicable and non-communicable diseases as reported by WHO Global Burden of Disease reports. Five databases will be searched from inception: MEDLINE, EMBASE, APA PsycInfo, Scopus and Web of Science Core Collection. Papers published in English, in peer-reviewed journals, including measures of association between SPPs and NSHCs and using observational epidemiologic study designs will be included. Excluded will be studies of cadaveric, animal or health behaviours; studies with no measures of association and non-observational epidemiologic studies. Results will include the number of studies, the studies that have evaluated the measures of association and the frequency of the studied associations between SPPs and NSHCs. Results will be reported in tables and diagrams. Themes of comorbidities will be synthesised into a descriptive report.

**Ethics and dissemination** This scoping review was deemed exempt from ethics review. This review will provide a comprehensive overview of the literature that reports associations between SPPs and NSHCs to inform future research initiatives and practices. Results will be disseminated through publication in peer-reviewed journals and research conferences.

**Registration details** <https://osf.io/w49u3>.

## INTRODUCTION

Spine-related pain and pathologies (SPPs) represent a heterogeneous range of problems affecting the spinal column and associated structures.<sup>1</sup> Combined, SPPs are

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This scoping review will study the most common and highly burdensome conditions, as listed in the WHO Global Burden of Disease studies.
- ⇒ This review will use a rigorous search strategy designed by an information specialist and health sciences librarian.
- ⇒ All observational epidemiologic study designs will be included to provide a comprehensive overview of the corpus of the literature on associations of spine-related pain and pathologies and non-spinal health conditions.
- ⇒ A limitation is that exclusion of non-English studies and grey literature may result in missing some relevant material.

some of the most debilitating and costly problems affecting humankind. Among the most common patient concerns, neck and back pain are the primary cause of years lived with disability globally for the past two decades (2000–2019).<sup>2,3</sup> Spine pain, mainly low back and neck pain, accounts for the highest amounts of spending; estimated to be \$134.5 billion per year in the USA as of 2016.<sup>4</sup> Yet, pain is not the only spinal concern for which people seek the services of healthcare providers.<sup>5</sup> Healthcare may be sought for spinal conditions such as osteoarthritis, osteoporosis, deformity and other disorders that may or may not be painful. As well, some asymptomatic people seek advice on how to prevent spinal concerns, such as prevention of spinal osteoporosis, work injuries or reoccurrence of back pain.<sup>6</sup>

Common non-spinal health conditions (NSHCs), such as cardiovascular diseases, cancers, diabetes and respiratory disorders, are leading causes of mortality, disability, disability adjusted life years and morbidity.<sup>2,3</sup> These diseases account for 80% of all premature non-communicable disease deaths,

estimated at 33.3 million people annually.<sup>7</sup> SPPs and NSHCs are concurrently listed in the global top 20 leading causes of years lived with disability, inflicting enormous health and financial tolls on individuals and society.<sup>2,3</sup>

Associations have been reported between SPPs and NSHCs, including mental health disorders,<sup>8–11</sup> diabetes,<sup>11–14</sup> obesity<sup>15</sup> and various musculoskeletal conditions.<sup>16,17</sup> Such associations are important to consider because they may complicate the clinical management of patients and they are related to lower quality of life, poorer functional status and increased utilisation of healthcare.<sup>18</sup> Healthcare providers and policy makers must consider these complex relationships, as the presence of two or more conditions may impact delivery and effectiveness of clinical care and disease management.<sup>19</sup> Currently, it is largely unknown if co-occurrence manifests because SPPs and NSHCs are common or if they may be risk factors or causal for one another or if they have common underlying etiological pathways.

Understanding the epidemiological relationships between SPPs and NSHCs may inform directions for future research. Whether NSHCs concurrent with SPPs have the potential to influence each other is not well understood. It could be hypothesised that treatment of symptoms or disability of either SPPs or NSHCs might influence the status of the other condition, for better or for worse. Additional influences between SPPs and NSHCs may include health behaviours, biopsychosocial inputs, politics, ecosystem and other social factors.<sup>20</sup> Thus, information about these relationships at a population level may help to inform future research that is relevant for healthcare providers, healthcare systems, and public health efforts.

At present, there are no studies that have assessed the over-arching associations of SPPs and NSHCs. Initial explorations of biopsychosocial risk factors for co-occurring SPPs and NSHCs have been reported.<sup>9,18,21</sup> However, the breadth of conditions reported to co-occur with SPPs, how they may be associated and the ecosocial context within which they occur is understudied. To the best of our knowledge, there has been no study of associations of SPPs with NSHCs that report the quantity of studies, designs reported, populations studied, knowledge clusters, research activity, use of measures of association and evidence gaps. In summary, the corpus of the literature on associations of SPPs and NSHCs has not been established, which represents uncharted territory in spine research.

Therefore, the purpose of this scoping review protocol is to describe how we will chart the characteristics of the epidemiological literature that reports associations between SPPs and NSHCs. Our aim is to provide a comprehensive overview of the literature that reports associations between SPPs and NSHCs, to describe the research knowledge base, identify gaps and report evidence that may inform future research and practices.

The research questions will be:

RQ1: What studies have evaluated measures of association between SPPs and NSHCs?

RQ2: What are the most frequently studied SPPs and NSHCs associations?

RQ3: What are the bibliometric properties and characteristics of these papers?

## METHODS AND ANALYSIS

We report our protocol using the Preferred Reporting Items for Systematic reviews and Meta-analysis Protocols (PRISMA-P).<sup>22,23</sup> The completed review will be reported using the PRISMA extension for scoping reviews (PRISMA-ScR).<sup>24,25</sup> This protocol is registered in the Open Science Framework registry (<https://osf.io/w49u3>). Preliminary searches of PubMed, EMBASE, APA PsycInfo, Scopus and Web of Science Core Collection, International Prospective Register of Systematic Reviews (PROSPERO) and Open Science Framework did not identify any similar reviews on the associations between SPPs and NSHCs.

### Conceptual and theoretical frameworks

This scoping review will rely on elements of ecosocial theory. Approaching complex associations with simple biomedical theories and biopsychosocial models<sup>26</sup> has been criticised.<sup>27–31</sup> Instead, models that include additional factors that contribute to complex pragmatic models have been suggested.<sup>30</sup> A social epidemiological theoretic approach may be more useful for understanding the complexities involved in SPPs and co-occurring NSHCs.<sup>32</sup> Multifactorial social epidemiological theories and models may be helpful to frame research questions to better study complex relationships.<sup>33,34</sup> The ecosocial theory of disease distribution, first proposed in 1994 by Krieger,<sup>35</sup> recognises that humans are simultaneously social beings and biological organisms.<sup>36</sup> It contextualises associations between illnesses, causes, mechanisms and the biological embodiment of social and ecological influences, the combination of which may create population patterns of health and disease.<sup>30</sup> Ecosocial theory suggests that people shape their environments and do not merely respond passively to them.<sup>36</sup> For research to contribute to recommendations, models should include ‘socio-political, environmental, and structural determinants of health’,<sup>37</sup> as these are the environments and structures on which the recommendations would be made.<sup>37</sup> Despite the seemingly good fit of ecosocial theory as a lens through which to view musculoskeletal research, we have not seen this theory applied in the literature on SPPs. Thus, due to the complex nature of these relationships, we chose ecosocial theory as a lens through which to view this study.

### Operational definitions

We define co-occurrence as the presence of two or more health concerns.<sup>38</sup> Co-occurrence does not imply an underlying relationship, whether it be causal, complicating or reciprocal.<sup>39</sup> Unlike comorbidity, with co-occurrence, there is no directionality of potential relationships between disorders; the disorders merely are concurrent.<sup>38,39</sup>

We define SPPs as a range of problems affecting the spinal column and associated structures, including the vertebrae, intervertebral discs, facet joints, sacroiliac joints, tendons and ligaments, muscles, spinal cord and nerve roots.<sup>1,40</sup> We use a previously published taxonomy<sup>9</sup> to operationally define SPPs for this scoping review (online supplemental file 1).

We define NSHCs as any disease or disorder that is not a SPP that is listed in the Global Health Estimates cause categories from the WHO Global Burden of Disease 2000–2019 data.<sup>2</sup> All Global Health Estimates cause names (categories of diseases) are provided in online supplemental file 2. All specific diseases within the Global Health Estimates are listed in Annex Table B of the Global Health Estimates Technical Paper.<sup>2</sup> We also include the top 10 leading causes of death (according to WHO) in the search terms.<sup>41</sup>

### Study design

We will follow guidelines for designing, conducting and reporting scoping reviews, as described in the JBI (formerly Joanna Briggs Institute) Manual for Evidence Synthesis and supporting literature.<sup>42–44</sup> We will incorporate guidance provided by authors in the fields of library science, medicine, epidemiology and environmental sciences.<sup>45–51</sup> We will use the Preferred Reporting Items for Systematic reviews and Meta-analyses for Reporting Literature Searches (PRISMA-S) extension to verify that each component of each search is completely reported and reproducible.<sup>52</sup>

Studies will be included that are observational epidemiologic designs and examine disease prevalence, association with other disorders, influence of multiple inputs, social determinants and relationships to health outcomes.<sup>53</sup> We will use the Population, Concept, Context and Types of Evidence framework for scoping reviews, as published by the JBI, to determine eligibility, as represented in table 1.<sup>54</sup> We will include papers published from the inception of the databases searched to the search date of execution.

### Information sources and search

We will search: MEDLINE (Ovid), EMBASE (Ovid), APA PsycInfo (Ovid), Scopus and Web of Science Core Collection from inception through the search date. Searches will be repeated as necessary to update the evidence table until data extraction are complete, at which time we will not further update the search.

To develop the initial search strategy, four authors, including an evidence synthesis methodologist and a health sciences research librarian (BNG, CDJ, CC and KM), developed the main search syntax for MEDLINE using primarily National Library of Medicine Medical Subject Headings (MeSH). To create syntax that would lead to a cross-tabulation of SPPs and NSHCs, we searched the MeSH database for each type of SPP and each Global Health Estimates cause name. A pilot search was performed to assess the feasibility of the scope of the project and to identify other terms for developing a final search strategy in MEDLINE. A health sciences librarian peer-reviewed the search strategy using the Peer Review of Electronic Search Strategies process to improve the quality and comprehensiveness of the search and reduce errors.<sup>55</sup>

In alignment with PRISMA-P,<sup>29</sup> we present the initial search strategy for the first database (MEDLINE) in online supplemental file 3. Syntaxes for other databases will be created by a health sciences librarian by modifying the MEDLINE syntax to meet the specifications of the additional databases. These syntaxes will also undergo the Peer Review of Electronic Search Strategies process. References will be imported from EndNote V.20 into the Covidence evidence synthesis platform. Duplicate citations will be removed using Covidence.

Screening and data extraction will be done using Covidence and all processes will be piloted in advance to make necessary corrections to processes prior to screening. A screening, coding and data extraction manual will be written, and screeners and data extractors will be trained by the lead author and methodologist prior to screening.

**Table 1** Population, concept, context and types of evidence framework for eligibility criteria

JBI topic	Inclusion criteria	Exclusion criteria
Population	<ul style="list-style-type: none"> <li>▶ Humans</li> <li>▶ Any age</li> </ul>	<ul style="list-style-type: none"> <li>▶ Animals or cadaver studies</li> </ul>
Concept	<ul style="list-style-type: none"> <li>▶ Measures of association between SPP and NSHC (eg, ORs and risk ratios)</li> </ul>	<ul style="list-style-type: none"> <li>▶ Intervention or treatments (eg, clinical trials, systematic reviews of interventions)</li> <li>▶ Self-care or health behaviours (eg, exercise, smoking cessation, as these are not conditions)</li> </ul>
Context	<ul style="list-style-type: none"> <li>▶ Global</li> </ul>	<ul style="list-style-type: none"> <li>▶ Treatment settings</li> </ul>
Type of evidence	<ul style="list-style-type: none"> <li>▶ Published in indexed peer-reviewed journals</li> <li>▶ Observational epidemiological studies (eg, cross-sectional, cohort, case-control, ecologic designs)</li> <li>▶ English language</li> </ul>	<ul style="list-style-type: none"> <li>▶ Grey literature</li> </ul>

NSHC, non-spinal health conditions; SPPs, spinal pain and pathologies.



Screeners will possess, at the minimum, a clinical doctorate or equivalent degree. A team of international, interprofessional and independent reviewers will participate in study selection, data extraction and synthesis. Independent pairs of reviewers will screen titles and abstracts to identify eligible studies, based on the selection criteria. In the event there is no consensus on eligibility, a third reviewer with a clinical doctorate and a PhD in public health/epidemiology will serve as a mediator. A lead author will verify accurate selection of eligibility on randomly selected references.

Eligible citations will be retrieved electronically in full text or manually scanned from periodicals in our libraries, or through interlibrary loan. Independent pairs of reviewers will read the full text to confirm study eligibility and will independently extract the relevant data, entering it into Covidence. All review and extraction will be done by two reviewers to ensure accuracy. The evidence table will be constructed and will be tested by the team prior to use. Data items for the extraction tables will include the following.

- ▶ SPP studied.
- ▶ NSHC studied.
- ▶ Relationship studied.
- ▶ Geographic location of population.
- ▶ Sample size.
- ▶ Study population/participants/age/race.
- ▶ Research design.
- ▶ Title of the paper, title of the periodical year of publication.
- ▶ Funding sources.
- ▶ Author(s), country of author(s)

The process for reaching consensus and verifying selection will be the same one used in the prior stage. Two lead authors will verify the accuracy of data extraction on randomly selected papers. We will mine the references of the final selected studies to look for additional relevant papers to screen and to potentially include in the review. We will attempt to contact authors of studies for which we have questions during data extraction.

### Synthesis of results and quality assessment

A PRISMA flowchart will report the study selection process and the flow of included studies. Data entered into Covidence will be saved as a Microsoft Excel workbook for conducting data analyses. A table will report frequencies of associations reported in the included studies. Primary categories of SPPs will be listed along the y-axis and NSHC will be listed along the x-axis. Each cell will represent the number of studies reporting measures of association for each cross-tabbed association. To contextualise the reported associations between SPPs and NSHCs within ecosocial theory, we will include the geographic location, age and race of each population studied. We will also include the country of the author of each paper, providing information on whether the study is performed by researchers from within or outside of the population studied. To capture socioeconomic

information, a component of ecosocial theory, we will use globe graphs to map high-income, middle-income and low-income regions of study and those of the authors of papers reviewed. Results from the data extraction will be summarised in a report. We will focus on providing a high-level overview of the literature and will not assess for risk of bias or quality of individual studies; such summaries and quality assessment of results are not requirements for scoping reviews designed to map the extent of the literature on a topic.<sup>43 47 50 51 54</sup> For face validity, we will report demographic data of the authoring team to show representativeness of the authors across countries, income regions, professions and experience.

### Patient and public involvement

There will be no patient or public involvement in this review.

### DISCUSSION

The purpose of this a priori protocol is to report and guide the scoping review process and increase transparency of our methods. The report will provide a map of the current literature and discuss gaps and future research considerations. The results of this study will inform patients, healthcare providers, researchers and policy makers about the extent of the literature that reports associations between SPPs and NSHCs. To the best of our knowledge, this is the first study to scope the literature on the association between SPPs and NSHCs.

This scoping review will characterise the evidence by systematically collating and cataloguing the characteristics and extent of the available literature.<sup>43 48</sup> Such a catalogue may then become a comprehensive database of literature.<sup>45</sup> Establishing an evidence map of SPP and NSHC associations can help set priorities for future epidemiological studies and systematic reviews and the development of specific research questions.<sup>43 45 46 48–50</sup> Based on the knowledge afforded by a scoping review, forthcoming projects could investigate directionality of associations, the potential influence of the severity and chronicity of a SPPs and the number and types of SPPs an individual has on NSHCs. Furthermore, the map can reveal where there is so little research that conducting a systematic review would be a waste of resources, or even futile.<sup>46 47</sup>

### ETHICS AND DISSEMINATION

This is a review of published literature. Thus, the institutional review board of the National University of Health Sciences determined that the project does not involve human participants and deemed the project exempt from ethics review (RS2203). Results of the project will be disseminated through publication in peer-reviewed, scientific journals and research conference presentations.

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**Supplementary File 1. Taxonomy involved in operational definition of spinal pain and pathologies.**

Group	Type	Examples of Included Symptoms and Conditions
<b>I. Spinal pain of unknown origin:</b> Spinal disorder with history and exam findings not leading to a clinical diagnosis. Diagnostic imaging, laboratory, or neurodiagnostic findings are non-contributory.	Spinal pain of unknown origin	Idiopathic neck pain, thoracic back pain, low back pain, pelvic/coccygeal pain
	Psychogenic spinal pain	Pain disorders primarily of psychological origin
<b>II. Spinal syndromes:</b> Spinal disorder with history and exam findings leading to a likely clinical diagnosis. Diagnostic imaging, laboratory, or neurodiagnostic findings typically do not confirm such disorders. Syndrome usually improves with treatment targeted at primary pain generator.	Spinal syndromes	Spinal neurogenic pain, Spinal joint pain syndromes, Spinal myofascial pain, Spinal soft tissue injury/sprains/strains, Torticollis
<b>III. Spinal pathology:</b> Spinal disorder with history and exam findings leading to a likely clinical diagnosis confirmed by diagnostic imaging, laboratory, or neurodiagnostic findings.	Arthritis	Osteoarthritis, ankylosing spondylitis, juvenile rheumatoid arthritis, psoriatic arthritis, reactive arthritis, rheumatoid arthritis, seronegative spondyloarthropathy
	Trauma	Dislocation, Subluxation, Fractures, Traumatic spinal cord injury, Myelopathy
	Non-traumatic spinal cord disorders	Myelopathy, Spinal dural arteriovenous fistulas, Spinal hematoma, Multiple sclerosis, Amyotrophic lateral sclerosis, Spinal muscular atrophy
	Infectious	Tuberculosis, Arachnoiditis, Epineural fibrosis, Other spinal infectious organisms
	Neoplastic	Bone tumors (benign, malignant, metastatic), Intradural and epidural tumors, Meningeal carcinomatosis, Multiple myeloma
	Metabolic	Osteopenia, Osteochondrosis (Scheurmann's disease), Osteitis fibrosa cystica, Ochronotic spondylosis, Paget's disease
	Congenital or developmental	Scoliosis, Spina bifida, Spondylolisthesis, Vertebral osteochondrosis, Interspinous pseudoarthrosis, Vertebral epiphysitis
	Spinal referred pain	Sickle cell anemia, Lymphoma, Abdominal abscess, Bacterial endocarditis, Carcinomatous

		lymphadenopathy, Lymphosarcoma, Hodgkin disease, Aortic aneurysm, Embolism of renal artery, Myocardial ischemia, Myocardial infarction, Visceral referred pain
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**Supplementary File 2. Classification of Other Health Conditions from the Global Health Estimates.**

<b>Global Health Estimates Cause Group</b>	<b>Global Health Estimates Cause Names</b>
I. Communicable, maternal, perinatal and nutritional conditions	Infectious and parasitic diseases
	Respiratory infectious
	Maternal conditions
	Neonatal conditions
	Nutritional deficiencies
II. Noncommunicable diseases	Malignant neoplasms
	Other neoplasms
	Diabetes mellitus
	Endocrine, blood, immune disorders
	Mental and substance abuse disorders
	Neurological conditions
	Sense organ diseases
	Cardiovascular diseases
	Respiratory diseases
	Digestive diseases
	Genitourinary diseases
	Skin diseases
	Musculoskeletal diseases
	Congenital anomalies
	Oral conditions
	Sudden infant death syndrome
III. Injuries	Unintentional injuries
	Intentional injuries

**Supplementary File 3. Database(s): Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions 1946 to April 27, 2023**

Search Strategy:

#	Searches	Results
1	exp Spinal Diseases/ or exp Spinal Cord Diseases/ or Spinal Injuries/ or Spinal Fractures/ or Spinal Stenosis/ or Osteoarthritis, Spine/ or Intervertebral Disc Displacement/ or Intervertebral Disc Degeneration/ or Intervertebral Disc/in or Zygapophyseal Joint/in or Radiculopathy/ or Polyradiculopathy/ or Spondylolysis/ or Synovial Cyst/ or Spinal Curvatures/ or exp Spinal Dysraphism/ or exp Neural Tube Defects/ or Cauda Equina Syndrome/ or Neck Pain/ or Neck Injuries/ or Neck Muscles/in or exp Cervical Vertebrae/in or Whiplash Injuries/ or exp Brachial Plexus Neuropathies/ or Brachial Plexus/in or Cervical Plexus/in or exp Torticollis/ or Thoracic Injuries/ or Thoracic Vertebrae/in or Low Back Pain/ or exp Back Pain/ or exp Back Injuries/ or Piriformis Muscle Syndrome/ or Sciatica/ or Lumbar Vertebrae/in or Lumbosacral region/in or exp Back Muscles/in or Coccyx/in or Lumbosacral Plexus/in or Sacroiliac Joint/in or Pelvic Girdle Pain/	404548
2	((spine* or spinal* or vertebr*) adj2 (condition* or diseas* or pathol* or pain* or injur* or fractur* or degener* or disabil* or disorder* or impair* or instabil* or symptom* or syndrome* or discomfort* or sore* or ach* or dysfunction* or dysraph* or tear* or imping* or myalg* or complaint* or ischem* or infect* or neoplas* or cancer* or tumour* or tumor* or malignan* or metast* or oncol* or mening* or metabol* or congenital* or abnormal* or osteochond* or osteophyt* or osteoscleros* or osteomyelit* or osteitis* or atroph* or compress* or idiopath* or neurogen* or arthrit* or osteoarthritis* or trauma* or developmental* or torticollis* or tuberculosis* or sprain* or strain*)).ti.	69065
3	(stenos?s* adj2 (spine* or spinal* or vertebr* or lumbar* or lumbo* or (low* adj2 back) or low-back* or lower-back* or intervertebr* or sacrum* or sacral* or sacroiliac* or sacroiliac* or neck* or cervic* or thorac*)).ti.	4905
4	((disc or discs or disk*) adj2 (pain* or extru* or degenerat* or displac* or herniat* or prolaps* or sequestered or slipped or protru* or avuls* or bulg*)).ti.	11835
5	((discogen* or intervertebr* or vertebr*) adj2 (pain* or injur* or ach* or myalg* or symptom* or syndrome* or discomfort* or sore* or impairment* or disorder* or dysfunction* or tear* or imping* or sprain* or strain* or trauma* or extru* or degenerat* or displac* or herniat* or prolaps* or sequestered or slipped or protru* or avuls* or bulg)).ti.	5754
6	(radiculopath* or radiating* or radicular* or polyradicul* or poly-radicul*).ti.	6762

7	((neuropath* or pathol*) adj2 (spine* or spinal* or vertebr* or lumbar* or (low* adj2 back) or low-back* or lower-back* or thorac* or intervertebr* or lumbo* or sacrum* or sacral* or sacro-iliac* or sacroiliac* or neck* or cervic*)).ti.	1698
8	((facet* or zygapophys*) adj2 (pain* or injur* or ach* or myalg* or symptom* or syndrome* or discomfort* or sore* or impairment* or disorder* or dysfunction* or tear* or imping* or sprain* or strain* or trauma* or extru* or degenerat* or displac* or herniat* or prolaps* or sequestered or slipped or protru* or avuls* or bulg* or arthros* or arthrit* or hypertroph*)).ti.	571
9	(segmental* adj2 (pain* or injur* or ach* or myalg* or symptom* or syndrome* or discomfort* or sore* or impairment* or disorder* or dysfunction* or tear* or imping* or sprain* or strain* or trauma* or extru* or degenerat* or displac* or herniat* or prolaps* or sequestered or slipped or protru* or avuls* or bulg* or arthros* or arthrit* or hypertroph*)).ti.	311
10	spondyl*.ti.	29151
11	((spine* or spinal*) adj2 curvatur*) or kyphos* or lordos* or scolios* or hyperkyphos*).ti.	19215
12	((subacute* or combined*) adj2 degener*) or (somatic* adj2 dysfunction*) or (skeletal* adj2 hyperostos*)).ti.	1251
13	(discit* or (synovial* adj2 cyst*) or platybas* or (neurone* adj2 disease*) or (Gehrig* adj2 disease*) or (Scheuermann* adj2 disease*) or (cauda* adj2 (equina adj1 syndrom*)) or (ossif* adj2 (longitud* adj2 ligament*)) or (posterior* adj2 (cervical* adj2 sympath*)) or (spinocerebellar* adj2 (degen* or atax*)) or myelit* or myelopath* or (lateral* adj2 scleros*) or polio* or postpoliomyelit* or pneumorrhach* or (epidural* adj2 neoplasm*) or (stiff-person* adj2 syndrome*) or syringomyel* or (tabes* adj2 dorsalis*) or (neural tube adj2 defect*) or (spin* adj2 bifida*) or arnold-chiari* or anencephal* or encephalocele* or meningocele* or meningomyelocele* or (catrell* adj1 pentalog*)).ti.	68007
14	((subluxation* or osteitis*) adj2 (spine* or spinal* or vertebr* or lumbar* or lumbo* or (low* adj2 back) or low-back* or lower-back* or neck* or sacrum* or sacral* or sacroiliac* or sacro-iliac* or cervic* or thorac*)).ti.	173
15	((neck* or cervic*) adj2 (pain* or injur* or fractur* or ach* or myalg* or symptom* or syndrome* or discomfort* or sore* or impairment* or disorder* or dysfunction* or tear* or imping* or sprain* or strain*)).ti.	15029
16	((cervicogen* or cervico-gen*) adj2 (pain* or injur* or ach* or myalg* or symptom* or syndrome* or discomfort* or sore* or impairment* or disorder* or dysfunction* or tear* or imping* or sprain* or strain* or headach*)).ti.	428

17	(whiplash* or torticollis* or cervicalg* or cervicodyn* or neckach* or ((neck* or cervical*) adj2 tender*)).ti.	4280
18	((brachial* adj2 (neuropath* or neurit*)) or brachioplexopath*).ti.	279
19	((c-spine* or "c spine") adj2 (pain* or injur* or ach* or myalg* or symptom* or syndrome* or discomfort* or sore* or impairment* or disorder* or dysfunction* or tear* or imping* or sprain* or strain*)).ti.	17
20	(brachial* adj2 (plexus* adj2 (pain* or injur* or ach* or myalg* or symptom* or syndrome* or discomfort* or sore* or impairment* or disorder* or dysfunction* or tear* or imping* or sprain* or strain*))).ti.	1638
21	((thorac* or t-spine* or mid-back* or midback* or costotransvers*) adj2 (pain* or injur* or fractur* or ach* or myalg* or symptom* or syndrome* or discomfort* or sore* or impairment* or disorder* or dysfunction* or sprain* or strain*)).ti.	6538
22	(low* adj2 (back or trunk*) adj2 (pain* or (nerve adj2 root*) or osteoarth* or radicul* or stenosis* or injur* or fractur* or discomfort* or dysfunction* or sore* or herniat* or trauma* or sprain* or strain* or ach*)).ti.	17790
23	((lumbar* or lumbo*) adj2 (pain* or (nerve adj2 root*) or osteoarth* or radicul* or stenosis* or injur* or discomfort* or dysfunction* or sore* or herniat* or trauma* or sprain* or strain* or ach*)).ti.	9369
24	(back adj2 (pain* or (nerve adj2 root*) or osteoarth* or radicul* or stenosis* or injur* or fractur* or discomfort* or dysfunction* or sore* or herniat* or trauma* or sprain* or strain* or ach*)).ti.	23677
25	(backach* or back-ach* or dorsalg* or lumbago* or lumboischialg* or coccydyn* or coccygodyn* or coccalg* or coccygalg* or (piriformis* adj2 syndrome*)).ti.	2308
26	((coccyx* or coccygeal* or tailbone*) adj2 (pain* or (nerve adj2 root*) or osteoarth* or radicul* or stenosis* or injur* or discomfort* or dysfunction* or sore* or herniat* or sprain* or strain*)).ti.	35
27	((sacral* or sacro* or sacrum*) adj2 (pain* or (nerve adj2 root*) or osteoarth* or radicul* or stenosis* or injur* or discomfort* or dysfunction* or sore* or herniat* or sprain* or strain* or trauma* or ach*)).ti.	907
28	(SI adj2 joint* adj2 (pain* or (nerve adj2 root*) or osteoarth* or radicul* or stenosis* or injur* or discomfort* or dysfunction* or sore* or herniat* or sprain* or strain* or ach*)).ti.	2
29	(sciatica* or (sciat* adj2 (pain* or (nerve adj2 root*) or osteoarth* or radicul* or stenosis* or injur* or discomfort* or dysfunction* or sore* or herniat* or sprain* or strain* or trauma* or ach*))).ti.	3625



30	(pelvic* adj girdle* adj2 (pain* or injur* or ach* or myalg* or symptom* or syndrome* or discomfort* or sore* or impairment* or disorder* or dysfunction* or tear* or imping* or sprain* or strain*)).ti.	236
31	or/2-30	260128
32	exp Infections/ or exp Neoplasms/ or exp Musculoskeletal Diseases/ or exp Digestive System Diseases/ or exp Stomatognathic Diseases/ or exp Respiratory Tract Diseases/ or exp Otorhinolaryngologic Diseases/ or exp Nervous System Diseases/ or exp Eye Diseases/ or exp Urogenital Diseases/ or exp Cardiovascular Diseases/ or exp Lymphatic Diseases/ or exp Hematologic Diseases/ or exp Connective Tissue Diseases/ or exp Skin Diseases/ or exp Nutrition Diseases/ or exp Metabolic Diseases/ or exp Endocrine System Diseases/ or exp Immune System Diseases/ or exp Occupational Diseases/	14965495
33	exp "Congenital, Hereditary, and Neonatal Diseases and Abnormalities"/	1360071
34	exp "Wounds and Injuries"/	1003222
35	exp Mental Disorders/ or Mental Health/ or Anxiety/ or Depression/ or Stress, Psychological/ or exp Self-Injurious Behavior/ or exp Substance-Related Disorders/	1708713
36	or/32-35	16297990
37	(diabet* or cardiovascular* or (heart* adj2 diseas*) or hypertens* or (myocard* adj2 infarc*) or stroke* or (respirat* adj2 infect*) or asthma* or (chronic* adj2 pulmonary*) or COPD or diarrh* or kidney* or vitamin*).ti.	1533509
38	(tuberculos* or mening* or osteoporos* or osteopen* or osteochond* or osteoarthritis* arthrit* or cancer* or neoplas* or tumour* or tumor* or metast* or malignan* or oncol* or headach*).ti.	2334790
39	((((spine* or spinal* or vertebr*) adj2 (tuberculos* or mening* or osteoporos* or osteopen* or osteochond* or osteoarthritis* or arthrit* or cancer* or neoplas* or tumour* or tumor* or metast* or malignan* or oncol*)) or (cervicog* adj2 headache*)).ti.	9614
40	38 not 39	2325307
41	(mental* or psycholog* or psychiat* or anxiety* or depression* or depressed* or neurotic* or neurosis* or neuroses* or neurocognit* or neurodevelop* or panic or obsessive-compuls* or schizophren* or phobia or phobic* or dissociativ* or bipolar* or ((mood* or personality* or sexual* or cognit*) adj2 (disorder* or dysfunct*)) or (cognit* adj2 declin*) or amnesia* or dement* or alzhaim* or dyslex* or aphasia* or paranoi* or (sleep adj wake) or (sleep* adj2 disorder*) or ((substance* or alcohol* or drug* or narcotic* or opioid*) adj2 (abuse* or use*)) or self-injur* or self-harm* or ptsd or ((post-traum** or trauma*) adj2 stress*) or (stress* adj2 psycholog*)).ti.	943959

42	37 or 40 or 41	4729818
43	exp Cohort Studies/	2473198
44	Cross-Sectional Studies/	464113
45	Case-Control Studies/	327386
46	Epidemiologic Studies/	9307
47	"Surveys and Questionnaires"/	558535
48	((cohort* adj2 (study or studies or analy*)) or cross-section* or (cross* adj1 section*) or (observational* adj2 (study or studies or analy*)) or (ecologic* adj2 (study or studies or analy*)) or case-control* or follow-up* or prospective* or retrospectiv* or longitudinal* or survey* or questionnair*).ti,ab,kw.	4417957
49	observational study.pt.	140959
50	or/43-49	5484477
51	(associ* or correlat* or co-relat* or co-occur* or relation* or related*).ti.	2068396
52	1 and 36 and 50 and 51	11311
53	1 and 42 and 50	7508
54	31 and 36 and 50 and 51	7644
55	31 and 42 and 50	4257
56	52 or 53 or 54 or 55	19154
57	exp Animals/	26322020
58	exp Humans/	21206368
59	57 not 58	5115652
60	(surgery* or surgeries* or surgical* or post-surg* or fusion* or fixation* or screw* or discectom* or perioperative* or peri-operative* or postoperative* or post-operative* or laminectom* or arthroplast* or vertebroplast* or resection* or reconstruction* or decompression* or repair* or augmentation* or instrumentation* or transection* or thoracotomy or microdiscectom*).ti.	1325578
61	su.fs.	2239229

62	(comment or clinical conference or congress or consensus development conference or editorial or letter or review or systematic review or guideline or practice guideline or case reports or study guide).pt.	7438229
63	56 not (59 or 60 or 61 or 62)	12116
64	limit 63 to English language	11101