Accepted author's manuscript. Published in final edited form as: The Journal of Spinal Cord Medicine 2023 Sep 8 (in press).
Publisher DOI: 10.1080/10790268.2023.2251205

Systematic review and meta-analysis use in the field of spinal cord injury research: a bibliometric analysis

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Word count: Abstract 289, Manuscript without references: 3'069
No. of figures: 4
No. of tables: 2
No. of references: 34

Abstract

Objective: To subvert issues of low sample sizes and high attrition rates and generate epidemiologically-sound evidence, collaborative research—through international consortia and multi-centric studies—and meta-analysis approaches are encouraged in spinal cord injury (SCI) research. We investigated the use of systematic reviews and meta-analyses (SRMA) methodology in SCI research and evaluated the quality of evidence across publications we identified.

Methods: We searched the Web of Science Core Collection database by topic without time or language restrictions through 16 December 2022. We identified additional relevant articles through Embase.com. SRMA including human and animal SCI populations were eligible for inclusion. We analyzed data using Bibliometrix and VOSviewer. We used JBI tool (former Joanna Briggs Institute) to assess methodological quality of a subset of 50 randomly selected articles.

Results: We based our analysis on data from 1'224 documents authored by 5'237 scholars published in 424 sources between 1985–2022. The use of SRMA methodology in the field gained momentum in 2009 and a steady increase followed with an annual growth rate of ≈15%. Our findings indicate major research themes in the field include recovery, SCI management, rehabilitation, and quality of life. Over the past 30 years there has been a shift from SRMA concerning functional recovery, secondary health complications, and quality of life toward biomarkers and neuro-regeneration. The major methodological issues across articles we evaluated included opaquely described search strategies, poorly reported critical appraisals, and insufficiently addressing publication bias. In addition, only one-fifth of articles reported review protocol registration.

Conclusions: Our bibliometric analysis clearly shows a rapid increase of SRMA applications in SCI research. We discuss the most important methodological concerns we identified among a randomly selected set of articles and provide guidance for improving adherence to methodological and reporting SRMA guidelines.

Key words: research trends; bibliometric analysis; spinal cord injury; systematic review and meta-analysis

Introduction

As a result of high clinical heterogeneity of underlying populations with spinal cord injury (SCI) characterized by injury severity and accompanying health condition variations, research is challenging.[1-3] To make study populations more homogenous, some studies purposively exclude individuals with tetraplegia or women, resulting in women and individuals with severe injuries as largely underrepresented in human SCI research.[1] Further, most evidence in the field is observational with cross-sectional study design and few available interventional studies. In addition, researchers experience difficulties recruiting study participants and attrition rates are often high which results in insufficiently powered studies for testing scientific hypotheses.[4] Collaborative research through international consortia, such as the European Multicenter Study about Spinal Cord Injury or the North American Clinical Trials Network, and multi-centric observational and interventional studies are increasingly utilized to generate epidemiologically-sound evidence in the field.[5-9] Yet rigorous systematic reviews and meta-analyses (SRMA) remain essential for informing evidence-based guidelines and recommendations for SCI-care.

In recent decades, SRMA studies have grown exponentially. PubMed showed 435 SRMA published in 1995 compared with 20'774 in 2017—an approximated growth rate of 4'676%.[10] Such growth led to increasing overlap and redundancy among research topics with only around 3% of SRMA estimated as methodologically-sound and non-redundant or providing useful clinical information.[11-13] We suggest such findings of interest for SCI research when considering limited methodological quality of underlying evidence in original SCI studies. To date, there are no published bibliometric reports of SCI research analyzing available scientific literature with SRMA methodology. Thus, our primary aim was to perform a bibliometric analysis of publications applying SRMA methodology in SCI research indexed in the Web of Science (WoS) database. We sought to understand the extent SRMA methodology is applied in practice. In addition, we aimed to evaluate the methodological quality of 50 randomly selected articles by exploring the extent inherent methodological issues of underlying evidence is addressed when interpreting evidence gathered through SRMA.

Materials and Methods

Study Protocol, Data Source and Search Strategy

We registered our study protocol in the Open Science Framework registry.[14] The primary data source was the WoS Core Collection database. We developed the search strategy in collaboration with medical information specialists (BM and TR) and combined terms relevant to SCI and SRMA methodology (**Supplemental Table 1**). We conducted the search by topic, which searches title, abstract, and keyword fields of WoS records. We did not apply language or date restrictions. We excluded meeting abstracts, proceedings papers, editorials, and letters from the search strategy. We set the last searched date as 16 December 2022. To identify

additional relevant articles, we searched the database Embase.com (searched on 16 January 2023); which offers a thesaurus search and ensures articles about the same topics are indexed under the same standardized terms, providing greater search accuracy for SCI articles (search strategy provided in **Supplemental Table 2**). We downloaded the complete set of bibliographic data in .ris and .ciw formats.

Inclusion and Exclusion Criteria and Reference Screening

SRMA including solely SCI populations (adult and paediatric), mixed populations, such as SCI and able-bodied individuals or SCI and other types of neurotrauma, or animal models of SCI were eligible for inclusion. Two reviewers independently screened titles and abstracts via EndNote (SS, MG) and included articles forming the final reference set. We transformed the final reference set back into the WoS using included SRMA accession number fields, DOIs, and PMIDs.

Data Analysis and Visualization

We analyzed data analysis using Bibliometrix (Version 3.0) operated under the web interface, Biblioshiny.[15] We used the software to (i) provide a general overview of the dataset; (ii) detect temporal trends of annual scientific production to identify important running points in the field; and (iii) identify the most productive entities (authors, institutions, and sources) and the most influential articles. We used visualization tools to generate the distribution map of top 50 highest frequency author keywords over time and provide an overview of author keyword trends using the trend topics function (minimum word frequency=5, number of words per year=3). We performed a thematic analysis to provide clusters of author keywords and their interconnections grouped as specific themes. Themes showed two major properties: density (vertical axis) and centrality (horizontal axis). Centrality is the degree of correlation among different topics, while density measures the cohesiveness among the nodes. Centrality and importance increase with the increasing number of relations a node has with others in the thematic network. Cohesiveness among a node—which represents the density of a research field—delineates its capability to develop and sustain itself. In thematic evolution analysis, we provided an overview of the evolution of themes across the years using 250 author keywords with minimum cluster frequency of 5 per thousand documents and applying Walktrap clustering algorithm. We selected slices two times (2012 and 2020) and compared three time periods: 1985–2012; 2013–2020; and 2020–2022. We removed terms relevant to SRMA and the SCI population from our visualization analyses.

Further, we used the VOSviewer (version 1.6.18) to perform author keyword co-occurrence analysis and visualize bibliometric network graphs, such as the order of co-occurrence keywords with high frequencies.[16] The author keyword co-occurrence analysis was based on words co-occurring in >0.5% of publications (≥6 times). We removed words related to SCI and SRMA terminology and descriptive words, such as neurology, outcome, and

humans, from our analysis. For co-authorship analysis based on institutions, we included a maximum of 25 organizations per document, with a minimum of 12 or 1% of total number of documents per organization, which left 40 entities to be included in the analysis.

Methodological Quality of Selected Articles

We used the JBI tool (former Joanna Briggs Institute)[17] to assess the methodological quality of 50 randomly selected SRMA. We randomized using the random number generation function in Excel. The JBI tool comprises 11 questions to guide the appraisal of systematic reviews (SR) or meta-analyses (MA). Each question should be answered as “yes,” “no,” or “unclear.” Not applicable—“NA”—is also provided as an option and appropriate in rare instances. Two independent reviewers completed the assessment. In cases of disagreement, they consulted a senior reviewer to reach consensus. We descriptively summarized and visually presented major methodological concerns among selected articles.

Results

After applying the search strategy, we retrieved 3'805 references from the WoS Core Collection. After title and abstract screening, we included 1'137 references based on our inclusion and exclusion criteria. We additionally found 2'305 references within Embase.com. Among those, we identified 334 as potentially eligible for inclusion after title and abstract screening. From 334, we identified 161 references previously not found by our initial WoS search; we transferred those 161 references back to WoS for a total of 1'298 references. We exported 1’298 references to Biblioshiny. After further filtering, we excluded 74 references from analyses. Thus, we analyzed 1'224 publications (**Figure 1**).

General Overview of the Findings

Between 1985 and 2022, 1'224 documents were published across 424 different sources, such as journals and book chapters. Documents were authored by 5'237 scholars. The average number of co-authors per document was 5.65 with 8.9% of documents engaging international collaborations (**Table 1**). Compared with 2008 (18 articles) and 2007 (7), SRMA methodology gained momentum in 2009 (30) and steadily increased—with an annual growth rate of 15%—in 2020 (136), 2021 (131), and 2022 (179), which represents the historic maximum (**Supplemental Figure 1**). The average number of citations per document was 30.05. Included documents comprised 2'370 author keywords and 3'456 keywords plus, which we used in our current analyses (**Table 1**). The metadata we used in our analysis were good quality (**Supplemental Table 3**).

Most Productive Entities and Influential Documents

Almost one-fifth of documents were published in *Spinal Cord* (n=138, 11.3%); the *Journal of Neurotrauma* (n=46, 3.8%); and the *Journal of Spinal Cord Medicine* (n=46, 3.8%). Contributions to the literature were globally distributed with most from the United States (n=347, 28.3%), Canada (n = 333, 27.2%), and China (n = 215, 17.6%). The top 3 most productive universities were the University of British Columbia, Canada (n=192, 15.7%); University of Toronto, Canada (n=155, 12.7%); and Tehran University of Medical Sciences, Iran (n =87, 7.1%). Dr. MG Fehlings (n=49, 4.0%); Dr. V Rahimi-Movaghar (n=25, 2.0%); and Dr. AR Vaccaro (n=22, 1.8%) were among the most productive authors (**Table 1**). Based on our analysis, Canada, the United States, and the United Kingdom had the highest proportions of multiple country publications (**Supplemental Figure 2**). **Supplemental Figure 3** depicts the collaboration network among the top 40 universities. North American institutions placed nearly equal emphasis on global cooperation and collaborated most closely with each other. We identified a cluster of collaborating European institutions originating from Switzerland, The Netherlands, and the United Kingdom. **Table 2** provides an overview of the 10 most cited papers that applied an SRMA approach.[18-27] The most common topics covered among these articles include (i) prevalence and incidence of SCI and common conditions requiring rehabilitation; (ii) psychosocial aspects of SCI, as well as (iv) medication use and regenerative therapies for health maintenance and recovery post-injury.

Popular Research Themes and Topic Trends

Figure 2 provides an overview of the top 50 most frequent author keywords. "Rehabilitation" (n=101) was the most frequent keyword used across the 1'244 documents, followed by "neuropathic pain" (n=37), "quality of life" (n=32), and "exercise" (n=26). **Figure 3a** shows author keyword co-occurrence mapping (co-occurring in >0.5% of publications) in SRMA among an SCI population. Overall, 95 keywords were grouped into 10 clusters among which rehabilitation, functional recovery, neuropathic pain, quality of life and epidemiology were the largest. The emerging research topic trend over the past 5 years include stroke, inflammation, stem cells, and neuropathic pain (**Figure 3b**). In thematic map analysis (**Figure 3c**), themes in the upper-right quadrant—motor or driving themes—are characterized by both high density and centrality, meaning that they are developed, relevant, and popular for the research field. Those include functional recovery, neuroprotection, stem cells, regeneration, and safety. The lower right quadrant depicts the basic themes characterized by high centrality or relevance and low density. Among others, themes include rehabilitation, pain, quality of life, and depression, which are foundational and critical for the field's development. The upper left quadrant depicts highly specialized themes, such as neuroimaging and frozen elephant trunk, which remain marginal contributors to the developing use of SRMA in SCI. With relatively little research

output or not highly cited publications compared with other quadrants, the lower left quadrant represents emerging or disappearing themes. However, the lower left quadrant possibly foregrounds research in the field by highlighting the areas possibly demanding more attention or investment. (**Figure 3c**). **Figure 3d** and **Supplemental Figures 4a–c** provide an overview of the evolution of themes across time. Over the past 30 years, SRMA concerning neurological recovery, assistive technologies, secondary health complications, such as spasticity, pain, and pressure ulcers, and quality of life shifted focus toward functioning, neuro-regeneration, and biomarkers. Themes most recently driving research (2020–2022) include cardiovascular diseases, such as venous thromboembolism and stroke; nutrition; pregnancy; and magnetic resonance imaging. Rehabilitation remains an important theme over the whole period of observation.

Methodological Quality of Random Publications

Among 50 randomly selected articles, only six (12%) registered their SR protocols. Most articles clearly stated review questions (94%) and provided appropriate inclusion criteria (80%). Although 82% of studies used appropriate sources to search for relevant articles, only 36% provided transparent search strategies. Around half (n=29, 58%) of the studies transparently reported criteria applied to evaluate methodological quality of individual studies. We have noted that SRMA including either animal only or mixed animal and human studies did not perform the quality assessment despite the existing tools designed specifically for assessing the methodological quality of experimental, in vivo, or in vitro studies. The most commonly applied tools for the assessment of risk of bias in individual studies were: Cochrane Collaboration's tools (n=8), Physiotherapy Evidence Database (PEDro) tool (n=7) and the Newcastle-Ottawa Scale (n=6). Only 36% clearly stated two independent reviewers completed quality assessments. A large proportion of studies (42%) did not clearly state if precautions were taken to minimize errors. Since most studies were SR without MA (n=35, 70%), it appears most studies (70%) used appropriate methods to combine results from individual studies (through narrative synthesis). Around two-thirds (64%) of studies appear to provide conclusions or recommendations supported by underlying evidence and clear directives for future research. Finally, 40% of articles we evaluated provided clear information about whether appropriate methods were applied to explore the likelihood of publication bias. To note the other reporting concerns: (i) among those randomly selected articles, the two thirds focused on SCI population only, and the rest included SCI and other health conditions (e.g. neurogenerative diseases, brain trauma, etc.) and sometimes results were not clearly disaggregated per population; and (ii) the most of the SRMA focused on humans (95%), yet, many missed to summarize the basic characteristics of included population (e.g. total number of individuals included in SRMA was reported only in 15 studies, whereas, the mean age, or

age range was summarized in only 6 SRMA). A result summary appears in **Figure 4** with details in **Supplemental Table 5 and Supplemental table 5**.

Discussion

Our present study provides a comprehensive overview of research hotspots and thematic focus shifts and emphasizes methodological limitations of published SRMA in SCI research. Contributions to the literature were globally distributed with the largest contributions from the United States, Canada, and China. Similarly, Canada, the United States, and the United Kingdom were the top three countries engaged in international collaborative efforts. Rehabilitation, functional recovery, neuropathic pain, quality of life, and epidemiology were the largest author keywords clusters. Over the past 30 years, we found a shift from SRMA concerning neurological recovery, assistive technologies, secondary health complications, such as spasticity, pain and pressure ulcers, and quality of life toward functioning, neuro-regeneration, and biomarkers. Next, we discuss the most important findings and provide direction for improving SRMA use in SCI research in the future.

With a substantial number of articles published in 2021 and 2022, we observed an evident increase in SRMA use in SCI research starting from 2009. The former at least partially explained by COVID-19 pandemic-driven hyperproduction, which resulted in widespread disruption of applied clinical research activities and provided an opportunity to focus on SRMA.[13] Hyperproduction influences the methodological quality of published articles and possibly leads to publication of overlapping or repetitive SRMA. Overlapping SRMA may yield substantial diversity in final results from variations in research question framing, inclusion and exclusion criteria—which influence the choice of eligible studies—and statistical methods used to pool evidence.[13] For instance, one major methodological issues across evaluated articles included a lack of transparency in the search strategy, which makes the update of existing SRMA challenging if not impossible. Further, we support recommendations for registering SR protocols to provide transparency in research—allowing readers to identify deviations from planned methods and analyses—and avoid overlap and redundancy in research efforts.[28] We observed only 12% of evaluated articles with registered SR protocols. The literature observes similarly: only a small fraction of SR (10–20%) are registered in PROSPERO.[29, 30] The top three sources in the field (*Spinal Cord*, *Journal of Neurotrauma*, *Journal of Spinal Cord Medicine*) currently do not require SR protocol registration. Although protocol registration does not guarantee SR quality, such as applying correct methods to conduct analyses, we recommend leading journals implement protocol registration as a prerequisite for submission to promote high quality research output.

Other methodological issues we uncovered include poor reporting on critical appraisal and insufficient attention to publication bias. It is difficult to understand whether those methodological limitations are inherent or a consequence of poor adherence to reporting guidelines, such as the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). Despite general[28, 31] and SCI-specific[32] guidelines for conducting SRMA, we noted some authors still rely on PRISMA as a methodological guideline rather than a reporting checklist. PRISMA provides an orientation for completely reporting SRMA and improving SR transparency; thus, conducting SR remains outside PRISMA's scope.[33] It is important to emphasize such misuse is a rather common misappropriation in biomedical research as well.[34]

Finally, 18 SRMA (36%) frequently provided vague conclusions—a common practice, since many published SRMA claim existing evidence insufficient for drawing clear conclusions.[13] Often the absence of high quality evidence is truly the case; however, we observed one-third of SRMA did not provide clear directives for improving future research in the field or filling existing gaps in the literature, which is worrisome.

Strengths and Limitations

Our bibliometric study is the first of its kind—to our knowledge—to characterize the landscape of SRMA use in SCI research. Besides inherent limitations of bibliometric analyses writ large, we emphasize limitations relevant for our current study: essential differences in database design, curatorial policies, and journal indexing, which possibly influence the quality of documents retrieved by systematic search. Since WoS shows high overlap with Scopus and provides the highest quality metadata, also shown true in our case, we selected WoS to identify relevant articles. Experienced information specialists developed a sensitive search strategy; our title and abstract search removed irrelevant documents and avoided documents retrieved from inappropriate database indexing. In addition, we searched Embase.com and managed to find an additional 161 documents in WoS. Although we minimized the possibility of missing relevant documents, some journals were not indexed in WoS; therefore, it is inevitable we missed some documents. Further, a bibliometric analysis, which focuses on bibliometric data such as authors' names, academic affiliations, reference lists, abstract or keywords, limits our ability to conduct in-depth analyses of the characteristics of populations, demographics, and temporal trends within individual studies. To delve into such details, a comprehensive analysis of the full texts of the identified SRMA would be necessary. For instance, an umbrella review would be informative when multiple SRMAs have already been published on a specific research topic or in the case of inconsistent or conflicting results of the existing meta-analyses. Finally, we evaluated the methodological quality of 50 (4%) randomly selected articles. Although our findings on methodological limitations align with the general literature, we suggest interpreting them with caution.

Conclusions

We present a comprehensive overview of research hotspots and shifts in thematic focus and emphasize methodological limitations of published SRMA. When developing clinical guidelines, SRMA must focus on the best available evidence. Individual-level data MA possibly provides more influential results and higher generalizability when compared with summary-level data analysis. We suggest the SCI research community invest in collaborative efforts to facilitate data sharing.

Disclaimer statements

Conflict of Interest: Authors declare no conflict of interest.

Funding: None.

Acknowledgments: We thank Kristin Marie Bivens for her editorial work and guidance on our manuscript.

Data Availability Statement: The datasets generated during the current study are available upon reasonable request from corresponding author.

Author statement

Stevan Stojic: conceptualization, methodology, data curation, formal analysis, writing-original draft preparation, visualization. **Beatrice Minder**: conceptualization, methodology, data curation; writing-original draft preparation. **Gabriela Boehl**: conceptualization, methodology, Writing- Reviewing and Editing. **Tania Rivero:** conceptualization, methodology, Writing- Reviewing and Editing. **Marcel Zwahlen:** conceptualization, methodology, Writing- Reviewing and Editing. **Armin Gemperli:** supervision, conceptualization, methodology, Writing- Reviewing and Editing**. Marija Glisic**: supervision, project administration, conceptualization, methodology, Writing- Reviewing and Editing.

Table 1. The main information about the data.

Description	Results
Time span	1985:2022
Sources (journals, book chapters, etc.)	424
Documents	1224
Annual growth rate %	15.05
Document average age	6.2
Average citations per doc	30.05
DOCUMENT CONTENTS	
Keywords plus (ID)	3459
Author's keywords (DE)	2370
AUTHORS	
Authors	5237
Authors of single-authored documents	21
AUTHORS COLLABORATION	
Single-authored documents	22
Co-authors per document	5.65
International co-authorships %	8.91
DOCUMENT TYPES	
Article	232
Review	992

375
376 **Table 2**. Top 10 most cited documents.
377
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Document title, authors, and journal	Total citations (TC)	TC/ Year	Normalized TC[1]
Whiting, P. F.; Wolff, R. F.; Deshpande, S.; Di Nisio, M.; Duffy, S.; Hernandez, A. V.; Keurentjes, J. C.; Lang, S.; Misso, K.; Ryder, S.; Schmidlkofer, S.; Westwood, M.; Kleijnen, J., Cannabinoids for Medical Use: A Systematic Review and Meta-analysis. JAMA 2015, 313 (24), 2456–73.[27]	1207	134.11	22.83
Singh, A.; Tetreault, L.; Kalsi-Ryan, S.; Nouri, A.; Fehlings, M. G., Global prevalence and incidence of traumatic spinal cord injury. Clin Epidemiol 2014, 6, 309–31[23]	569	56.90	10.95
Ma, V. Y.; Chan, L.; Carruthers, K. J., Incidence, prevalence, costs, and impact on disability of common conditions requiring rehabilitation in the United States: stroke, spinal cord injury, traumatic brain injury, multiple sclerosis, osteoarthritis, rheumatoid arthritis, limb loss, and back pain. Arch Phys Med Rehabil 2014, 95 (5), 986–995.e1.[21]	514	51.40	9.89
Tetzlaff, W.; Okon, E. B.; Karimi-Abdolrezaee, S.; Hill, C. E.; Sparling, J. S.; Plemel, J. R.; Plunet, W. T.; Tsai, E. C.; Baptiste, D.; Smithson, L. J.; Kawaja, M. D.; Fehlings, M. G.; Kwon, B. K., A systematic review of cellular transplantation therapies for spinal cord injury. J Neurotrauma 2011, 28 (8), 1611–82.[24]	395	30.38	5.93
Westerveld, L. A.; Verlaan, J. J.; Oner, F. C., Spinal fractures in patients with ankylosing spinal disorders: a systematic review of the literature on treatment, neurological status and complications. Eur Spine J 2009, 18 (2), 145–56[26]	336	22.40	4.11
Ben Amar, M., Cannabinoids in medicine: A review of their therapeutic potential. J Ethnopharmacol 2006, 105 (1-2), 1–25.[18]	329	18.28	3.35
Simpson, L. A.; Eng, J. J.; Hsieh, J. T.; Wolfe, D. L.; Spinal Cord Injury Rehabilitation Evidence Scire Research, T., The health and life priorities of individuals with spinal cord injury: a systematic review. J Neurotrauma 2012, 29 (8), 1548–55.[22]	312	26.00	5.07
Kubler, A.; Birbaumer, N., Brain-computer interfaces and communication in paralysis: extinction of goal directed thinking in completely paralysed patients? Clin Neurophysiol 2008, 119 (11), 2658–66.[20]	305	19.06	4.75
van den Berg, M. E.; Castellote, J. M.; Mahillo-Fernandez, I.; de Pedro-Cuesta, J., Incidence of spinal cord injury worldwide: a systematic review. Neuroepidemiology 2010, 34 (3), 184–92; discussion 192.[25]	295	21.07	4.33
Kairy, D.; Lehoux, P.; Vincent, C.; Visintin, M., A systematic review of clinical outcomes, clinical process, healthcare utilization and costs associated with telerehabilitation. Disabil Rehabil 2009, 31 (6), 427–47.[19]	292	19.47	3.57

[1]Calculated by dividing the actual count of citing items by the expected citation rate for documents with the same year of publication.

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