

REVIEW ARTICLE

Overview of Cochrane Systematic Reviews for Rehabilitation Interventions in Persons With Spinal Cord Injury: A Mapping Synthesis



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Abstract

Objective: This article aims to describe the evidence on rehabilitation interventions for persons with spinal cord injury (SCI) identified in Cochrane Systematic Reviews (CSRs) selected for inclusion in the World Health Organization Rehabilitation Programme—Package of Interventions for Rehabilitation.

Data Sources: The CSRs search was led by the Cochrane Rehabilitation team, using the tagging process, using the terms “spinal cord injury” and “rehabilitation” in the Cochrane Library.

Study Selection: We performed an overview of all the CSRs according to the inclusion criteria defined with the World Health Organization: rehabilitation interventions in persons with SCI.

Data Extraction: The CSRs identified after the screening process were summarized using an evidence map, grouping outcomes, and comparisons of included CSRs indicating the effect and the quality of evidence to provide a comprehensive view of what is known.

Data Synthesis: Out of 248 CSRs from the past 10 years tagged in the Cochrane Rehabilitation database, 3 were related to SCI. They provide data on 13 outcomes analyzed within 11 comparisons for a total of 64 primary studies, including 2024 participants with SCI. Of these, 7 outcomes and 1 comparison focused on people with cervical SCI. Rehabilitation interventions might improve respiratory outcomes and pain relief in people with SCI. There is uncertainty whether bodyweight-supported treadmill training, robotic-assisted training, and functional electrostimulation affect walking speed and capacity.

Conclusions: The current evidence needs to be confirmed by better quality research. Therefore, future priorities are the improvement of methodological quality of the studies in people with SCI, particularly considering the complexity of this health condition. Further, there is a need for more CSRs in the field.

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In 2017 the World Health Organization (WHO) launched the “Rehabilitation 2030: A Call for Action” initiative to globally improve rehabilitation management into health services.¹ Within this framework, the WHO Rehabilitation Programme is developing a Package of Interventions for Rehabilitation (WHO PIR) for 20 health conditions.² This package will provide a prioritized set of evidence-based interventions to support ministries of health in integrating rehabilitation services into health systems.³ They will respond to the global needs for rehabilitation services that should be integrated inside primary health care to reach more people in need.⁴ The development of the PIR is following a stepwise

approach³; the second step, here referred to as “best evidence for rehabilitation,” aims to identify high-quality evidence relating to the effectiveness of interventions for rehabilitation for several key health conditions, including spinal cord injury (SCI).

SCI may result in impairments of the motor, sensory, and autonomous nervous system. Worldwide, the prevalence of SCI is 1:1000, and the incidence is between 4 and 9 new cases per 100,000 people per year.⁵ Although this is a relatively low number, the effect on an individual is substantial in terms of functioning, quality of life, and costs.⁶ Epidemiological studies have indicated that there has been no appreciable change in the incidence of SCI over the past 25 years, though there were changes in demographic characteristics.^{6–10} The mean age at onset of SCI increased from 29 to 42 years because of a

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higher number of older people who sustain injury from falls. In addition, more injuries in the elderly result in incomplete tetraplegia. The changes in demographics affect the rehabilitation needs of people with SCI and the outcomes that they value. Further, the trends toward higher injury levels, older age at onset, and an increasing proportion of nontraumatic etiology provide significant challenges for research.^{11,12} Because of the growing likelihood of preexisting medical conditions and secondary medical complications, a higher percentage of persons do not meet eligibility criteria for research studies, and overall treatment outcomes can be less favorable in the future owing to trends in age and injury severity.¹³

Systematic reviews of randomized controlled trials (RCTs) remain the best form of evidence to inform treatment decisions,¹⁴ even considering the methodological complexities related to the synthesis of SCI rehabilitation research¹³ and the low production of primary studies that can justify their scarcity. Cochrane Reviews are the reference standard among systematic reviews for their methodological rigor and quality.¹⁵ The evidence gathered from these reviews is the strongest available and was consequently considered by WHO as highly relevant for PIR development. Cochrane Rehabilitation has been charged with finding this evidence, and this article aims to describe the research performed and the Cochrane evidence found on rehabilitation interventions for persons with SCI. The results provide an overall description of all the available evidence in the field through a specific methodology still not widely used in medicine: an evidence map.¹⁶

Methods

The methods for developing the content of the WHO PIR have been established and published collaboratively by the WHO Rehabilitation Programme and Cochrane Rehabilitation, under the guidance of the WHO's guideline review committee.³ We performed an overview of the Cochrane Systematic Reviews (CSRs) relevant to the WHO PIR for SCI development, summarizing and quantifying high-quality research on the effectiveness of rehabilitation interventions in persons with SCI. The overview was reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis¹⁷ and it was registered on OSF Registries (10.17605/OSF.IO/KQ4GC).

List of abbreviations:

BWSTT	bodyweight-supported treadmill training
CSR	Cochrane Systematic Reviews
CES	cranial electrotherapy stimulation
FES	functional electrical stimulation
GRADE	Grading of Recommendations, Assessment, Development, and Evaluations
QoL	quality of life
rTMS	repetitive transcranial magnetic stimulation
RAT	robotic-assisted training
SCI	spinal cord injury
tDCS	transcranial direct current stimulation
TENS	transcutaneous electrical nerve stimulation
WHO	World Health Organization
WHO PIR	WHO Rehabilitation Programme—Package of Interventions for Rehabilitation

Search strategy

The search strategy was based on the methodology developed by WHO and Cochrane Rehabilitation for WHO PIR.^{2,3} The selection of health conditions was conducted by the WHO Rehabilitation Programme Advisory Board in the summer of 2018 and based on the disability statistics of the Global Burden of Disease Study 2016¹⁸ and expert opinion. It was performed according to the following 2 criteria: (1) to be amenable to rehabilitation and (2) to cover different disease areas (eg, musculoskeletal, cardiovascular, nervous system). In addition, the level of disability associated with these health conditions and prevalence estimates were considered.³

The CSRs search was led by Cochrane Rehabilitation team using the tagging process.¹⁹ The search strings were composed of terms defining the health condition, in this case, “spinal cord injury” and “rehabilitation,” and run in the Cochrane Library. A Cochrane Rehabilitation team extracted the full citations, including abstracts, of all CSRs and protocols published from the inception of the Cochrane Library (1996) to August 31, 2019, importing these into Knack database to be tagged by tagging reviewers. They selected the CSRs relevant to rehabilitation using the following criteria: all reviews on interventions provided or prescribed by rehabilitation professionals.¹⁹ Searches were limited to the most recent 10 years (2009–2019), because the guide for the conducting of an overview indicates that imposing a date restriction could be appropriate to include current best evidence.²⁰ The CSRs relevant to rehabilitation are constantly being updated in an online database²¹ <https://rehabilitation.cochrane.org/evidence>. The search for the WHO was run in August 2019, with an update for this paper in September 2021.

Assessment of methodological quality of included reviews

We used the AMSTAR 2 tool to assess the methodological quality of the included SRs that contains 16 items. The AMSTAR 2 is not designed to generate an overall score and it is important to note that a high score may disguise critical weaknesses in 7 specific items.²² We used a process of considered judgment to interpret weaknesses detected by these critical items and to reach consensus on the methodological quality of the included reviews. Two independent assessors applied this instrument to all included systematic reviews, with any disagreements resolved through discussion with a third assessor.

Data extraction and quality of evidence appraisal

Starting from the table of findings of each identified CSR, we identified and extracted data on each reported outcome related to an intervention relevant for rehabilitation. These data included type of outcome and its measure, number of primary studies and participants, population, comparison (experimental and control interventions), effect (in favor of experimental or control intervention or no effect), and, lastly, the judgment of the quality of evidence for each comparison and outcome.

We extracted Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) judgments present within each CSR; where these were not reported, 2 authors independently, with a consensus reached through discussion, used the standard GRADE approach^{23,24} to achieve a judgment on the quality of evidence for the review primary outcomes; a third author was consulted when no consensus was possible. This post hoc GRADE-ing process required retrieving the original primary

Table 1 Characteristics of the studies included

Authors	Title	Total No. of Included Studies (No. of Participants)	Population	Setting	Intervention	Control	Outcome	Outcome Measurements	N° Studies (No. of Participants)	Effect	Grade
Berlowitz 2013 ²⁵	RMT for cervical SCI	11 (212)	Patients with cervical SCI	Hospital and community	RMT	Control	Dyspnea: Follow-up: 6-8 weeks	Borg scale, modified Borg scale and VAS	3 (58)	No effect	Low
Berlowitz 2013 ²⁵	RMT for cervical SCI	11 (212)	Patients with cervical SCI	Hospital and community	RMT	Control	Vital capacity: Follow-up: 6-12 weeks	Spirometry	4 (108)	Favor intervention	Low
Berlowitz 2013 ²⁵	RMT for cervical SCI	11 (212)	Patients with cervical SCI	Hospital and community	RMT	Control	Maximum inspiratory pressure: Follow-up: 6-12 weeks	Spirometry	8 (147)	Favor intervention	Low
Berlowitz 2013 ²⁵	RMT for cervical SCI	11 (212)	Patients with cervical SCI	Hospital and community	RMT	Control	Maximum expiratory pressure: Follow-up: 6-12 weeks	Spirometry	6 (151)	Favor intervention	Low
Berlowitz 2013 ²⁵	RMT for cervical SCI	11 (212)	Patients with cervical SCI	Hospital and community	RMT	Control	Forced expiratory volume in 1 second: Follow-up: 6-12 weeks	Spirometry	4 (97)	No effect	Low
Berlowitz 2013 ²⁵	RMT for cervical SCI	11 (212)	Patients with cervical SCI	Hospital and community	RMT	Control	Quality of life: Follow-up: 6-12 weeks	SF-36 questionnaire	4 (78)	Not estimable	Very low
Berlowitz 2013 ²⁵	RMT for cervical SCI	11 (212)	Patients with cervical SCI	Hospital and community	RMT	Control	Respiratory complications: Follow-up: 8 weeks	Numbers of complications	1 (14)	Not estimable	Very low
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	tDCS	Sham tDCS	Chronic pain	VAS or NRS 0-10 (short-term outcome)	2 (57)	Favor intervention	Low
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	tDCS	Sham tDCS	Chronic pain	VAS or NRS 0-10 (mid-term outcome)	2 (57)	Favor intervention	Low
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	tDCS	Sham tDCS	Chronic pain	NRS 0-10 (long-term outcome)	1 (39)	No effect	Low
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	rTMS	Sham rTMS	Chronic pain	NRS 0-10 (short-term outcome)	3 (71)	Not estimable	Very low
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	CES	Sham CES	Chronic pain	Short-term outcome NRS/BPI pain intensity subscale	2 (138)	No effect	Low
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	Exercise program	Waitlist control or no intervention	Chronic pain	SF-36 and VAS (short-term outcomes, standardized mean difference)	2 (101)	Favor intervention	Low
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	Exercise program	Waitlist control or no intervention	Chronic pain	WUSPI and VAS (short-term outcomes, standardized mean difference)	2 (101)	Favor intervention	Low
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	Acupuncture	Sham acupuncture and Trager treatment intervention	Chronic pain	WUSPI (short-term outcome)	2 (35)	No effect	Low
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	Acupuncture	Sham acupuncture and Trager treatment intervention	Chronic pain	WUSPI (mid-term outcome)	2 (35)	No effect	Low

(continued on next page)

Table 1 (Continued)

Authors	Title	Total No. of Included Studies (No. of Participants)	Population	Setting	Intervention	Control	Outcome	Outcome Measurements	N° Studies (No. of Participants)	Effect	Grade
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	TENS	Sham TENS	Chronic pain	DDS neurogenic pain intensity (short-term outcomes)	1 (20)	No effect	Low
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	TENS	Sham TENS	Chronic pain	DDS neurogenic pain intensity (short-term outcomes): Neutral expectation	NA	NA	NA
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	TENS	Sham TENS	Chronic pain	DDS neurogenic pain intensity (short-term outcomes): Positive expectation	NA	NA	NA
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	TENS	Sham TENS	Chronic pain	DDS musculoskeletal pain intensity (short-term outcomes)	NA	NA	NA
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	TENS	Sham TENS	Chronic pain	DDS musculoskeletal pain intensity (short-term outcomes): Neutral expectation	NA	NA	NA
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	TENS	Sham TENS	Chronic pain	DDS musculoskeletal pain intensity (short-term outcomes): Positive expectation	NA	NA	NA
Boldt 2014 ²⁶	Nonpharmacologic interventions for chronic pain in people with SCI	16 (616)	People living with SCI	Inpatient and outpatient	MCBP	Waitlist	Chronic pain	CPG, pain intensity (short-term outcomes)	1 (61)	Not estimable	Very low
Mehrholtz 2012 ²⁷	Locomotor training for walking after SCI	5 (309)	Participants of any age and sex with a traumatic SCI	NR	BWSTT	All other	Walking	Speed of walking (m/s)	4 (274)	No effect	Moderate
Mehrholtz 2012 ²⁷	Locomotor training for walking after SCI	5 (309)	Participants of any age and sex with a traumatic SCI	NR	BWSTT	All other	Walking	Walking capacity (meters walked in 6 min)	3 (234)	No effect	Low
Mehrholtz 2012 ²⁷	Locomotor training for walking after SCI	5 (309)	Participants of any age and sex with a traumatic SCI	NR	FES AND BWSTT	All other	Walking	Speed of walking (at final follow-up, m/s)	2 (88)	No effect	Low
Mehrholtz 2012 ²⁷	Locomotor training for walking after SCI	5 (309)	Participants of any age and sex with a traumatic SCI	NR	FES AND BWSTT	All other	Walking	Walking capacity (in meters walked in 6 min)	1 (74)	No effect	Low
Mehrholtz 2012 ²⁷	Locomotor training for walking after SCI	5 (309)	Participants of any age and sex with a traumatic SCI	NR	RAT	All other	Walking	Speed of walking (at final follow-up, m/s)	1 (74)	No effect	Low
Mehrholtz 2012 ²⁷	Locomotor training for walking after SCI	5 (309)	Participants of any age and sex with a traumatic SCI	NR	RAT	All other	Walking	Walking capacity (in meters walked in 6 min)	1 (74)	Favor control	Low

Abbreviations: CPG, chronic pain grade; DDS, descriptor differential scale; MCBP, multidisciplinary cognitive-behavioral program; NA, not applicable; NR, not reported; NRS, numeric rating scale; SF-36, 36-item short form; VAS, visual analog scale; WUSPI, wheelchair user's shoulder pain index.

studies included in each CSR. The GRADE judgments were tabulated within standard Summary of Findings tables, using GRADE-Pro software. During this process, no update to the searches or evidence in the original CSR was performed. Furthermore, the authors of this article provided GRADE judgments for reported primary outcomes only.

Summarizing evidence within a map

We summarized the results using an evidence map, a specific methodology used to identify the literature within a research field to provide a comprehensive view of what is known and where evidence gaps exist.¹⁶ An Excel sheet was used to map the evidence, grouping outcomes and comparison of included CSRs indicating the effect (no, in favor of intervention, in favor of control) and the quality of evidence (very low, low, moderate, and high).

Results

Of the 248 CSRs from the past 10 years tagged by Cochrane Rehabilitation, 3 were related to SCI. The characteristics of the CSRs included are reported in [table 1](#).

The results of AMSTAR 2 assessment indicated high methodological quality of CSRs included, even if often they did not report any information about funding sources (see [table 2](#)).

One review²⁵ evaluated the quality of evidence using the GRADE approach, whereas the other 2^{26,27} did not report GRADE judgment, which the authors consequently assessed. The CSRs provide information on the effectiveness of rehabilitation interventions on respiratory and quality of life (QoL) outcomes in patients with cervical SCI in hospital and community settings²⁵ and on chronic pain and walking in patients with SCI in inpatient and outpatient settings.^{26,27} They provide data on 13 outcomes analyzed within 11 comparisons for a total of 64 primary studies, including 2024 participants with SCI. Of these, 7 outcomes were analyzed within 1 comparison for people with a cervical SCI. The evidence map findings are reported in [table 3](#).

Findings in spinal cord injury

One comparison provided moderate-quality evidence of no effect of bodyweight-supported treadmill training (BWSTT) on walking speed (10%). Two comparisons provided low-quality evidence on the effects of transcranial direct current stimulation (tDCS) and exercise programs on pain relief in the short and medium term, in

Table 2 AMSTAR 2 assessment

AMSTAR 2	Berlowitz 2013 ²⁵	Boldt 2014 ²⁶	Mehrholz 2012 ²⁷
Did the research questions and inclusion criteria for the review include the components of PICO?	Y	Y	Y
Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?	Y	Y	Y
Did the review authors explain their selection of the study designs for inclusion in the review?	Y	Y	Y
Did the review authors use a comprehensive literature search strategy?	Y	Y	Y
Did the review authors perform study selection in duplicate?	Y	Y	Y
Did the review authors perform data extraction in duplicate?	Y	Y	Y
Did the review authors provide a list of excluded studies and justify the exclusions?	Y	Y	Y
Did the review authors describe the included studies in adequate detail?	Y	Y	Y
Did the review authors use a satisfactory technique for assessing the RoB in individual studies that were included in the review?	Y	Y	Y
Did the review authors report on the sources of funding for the studies included in the review?	N	N	N
If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	Y	Y	Y
If meta-analysis was performed, did the review authors assess the potential effect of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	Y	Y	Y
Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?	Y	Y	Y
Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Y	Y	Y
If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely effect on the results of the review?	Y	Y	Y
Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	Y	Y	Y
Total	15	15	15

Abbreviations: PICO, population, intervention, comparison and outcome; RoB, risk of bias.

Table 3 Evidence map on people with SCI

Treatment	RMT*	tDCS**	rTMS**	CES**	Exercise program§	TENS**	Acupuncture**	MCBP§	BWSTT	RAT	FES and BWSTT
Comparison	Control*/sham**/waiting list§								Any other intervention		
Dyspnea FEV1	LOW										
VC MIP MEP	LOW										
QoL Respiratory complications	very low										
Pain (short-term)		LOW	very low	LOW	LOW	LOW	LOW	very low			
Pain (mid-term)		LOW			LOW	LOW	LOW				
Pain (long-term)		LOW	LOW								
Walking speed									MODE RATE	LOW	LOW
Walking capacity									LOW	LOW	LOW

NOTE. Map colors: white: favor intervention; black: favor comparison; light gray UPPERCASE: no effect; dark gray lowercase: not estimable.

Abbreviations: FEV₁, forced expiratory volume in 1 second; MCBP, multidisciplinary cognitive-behavioral program; MEP, maximum expiration pressure; MIP, maximum inspiration pressure; QoL, quality of life; RMT, respiratory muscle training; VC, vital capacity.

*Control.

†Sham.

‡Waiting list.

favor of the interventions (20%). One comparison provided low-quality evidence on no effect of tDCS on pain relief in the long term. Five comparisons provided low-quality evidence with no effect of cranial electrotherapy stimulation (CES), transcutaneous electrical nerve stimulation (TENS), acupuncture, BWSTT, robotic-assisted training (RAT), and functional electrical stimulation (FES) on pain at short and mid-term and on walking speed and capacity (50%). Two comparisons provided very low-quality evidence on the effect of repetitive transcranial magnetic stimulation (rTMS) and cognitive behavioral therapy on pain relief in the short term (20%), which was not estimable because of the heterogeneity of the primary studies included in CSR, not allowing us to perform the meta-analysis.

Findings in cervical spinal cord injury

There was low-quality evidence for the effect of respiratory muscle training on vital capacity, maximal inspiration, and expiration pressure in people with cervical SCI hospitalized and living in the community. There was no effect on dyspnea and forced expiratory volume in 1 second. One comparison provided very low-quality evidence on the effect of respiratory muscle training on QoL and respiratory complications in people with cervical SCI

hospitalized and living in the community. The effect was not estimable because of the heterogeneity of the primary studies included in the CSR, which did not allow performing the meta-analysis.

Discussion

We found that respiratory muscle training might improve vital capacity and maximal inspiratory and expiratory pressure in patients with cervical SCI, but it seems not to affect dyspnea and forced expiratory volume in 1 second. There is uncertainty on the effect of respiratory muscle training on QoL and respiratory complications. tDCS and exercise programs may improve pain relief in persons with SCI in the short and medium term. This improvement seems to remain in the long term for tDCS intervention. There is uncertainty on the effect of BWSTT, RAT, and FES on walking speed and capacity in persons with SCI. Even if these results could change in the future with higher-quality evidence, they already offer a clear picture of what can be done and what could or should be considered cautiously in this population with high needs. Moreover, there are clear indications for future research in the field.

The most interesting clinical results concern respiratory and pain rehabilitation interventions. Respiratory muscle training can effectively increase respiratory muscle strength and lung volumes for people with cervical SCI.²⁵ A study published in 2019 by Raab et al showed that the intensity of inspiratory muscle training was more relevant than the training volume for improving respiratory muscle strength in individuals with SCI. They recommend choosing training intensity as high as possible.²⁸ Concerning the non-pharmacologic treatment of chronic pain, tDCS reduced chronic pain in the short and mid-term. Moreover, exercise programs led to a reduction of chronic shoulder pain.²⁹ A systematic scoping review from 2021 suggested that leisure-time physical activity interventions can reduce chronic pain and improve subjective well-being for persons with SCI.³⁰ These results could drive future RCTs to integrate the current evidence.

We need to interpret the findings of this overview carefully because they are based on 3 CSRs only, which is a low number for a health condition considered by the WHO among the 20 most important for the development of its Package of Interventions for Rehabilitation. The current evidence was downgraded primarily because of the limited number of studies published and the small sample sizes. Further, there was a high risk of attrition bias because the reasons for missing outcome data were not reported. They could be related to true outcomes. This can induce a clinically relevant bias in the observed effect size. All of these aspects can easily be improved in future research, which is needed.

The methodological challenges within rehabilitation research for people with SCI have been widely discussed in the literature, particularly in clinical practice guidelines, which demonstrate significant gaps.³¹ The main reported issues are (1) few intervention studies to generate high-quality evidence for rehabilitation interventions for people with SCI and (2) outdated guidelines and none addressing recent innovations in management (devices and pharmacologic) likely to influence functional outcomes. These problems are frequent in many rehabilitation research fields as well as other methodological issues. Poor statistical analysis associated with a small sample size is one of the most critical issues. It leads to uncertain results and a lack of understanding of variations in participant response to treatment, not allowing generalizability of the results³² or their clinical applicability.³³ Another critical issue is the complexity of the health condition, with significant heterogeneity in terms of level and completeness of the SCI, comorbidities, and the person's functioning level.^{34,35} This issue makes it difficult to select the study population, potentially affecting the treatment outcomes.³⁶ Lastly, most studies in SCI address a particular impairment (hypotension, wound care, bladder management), essential for well-being, but do not always gather functioning data, which is the main aim of rehabilitation.¹³

The gaps highlighted by this overview of CSRs allow defining specific research priorities, like the production of reviews and intervention trials on the newer pharmacologic agents, robotics, and implantable devices, with functioning and participation as primary outcomes, taking into account the complexity of people with SCI. To improve the quality of evidence, we also need primary studies of higher quality using more sophisticated statistical analyses, such as subgroup analysis,³⁷ to manage the heterogeneity of persons with SCI.

Strengths and limitations

Our overview of CSRs focuses on the best current evidence. Still, other high-quality systematic reviews could not be considered in

the present article because they are not included in the Cochrane Library. Nevertheless, the uniformity of the Cochrane methodology gives coherence to the overview and is currently suggested by Cochrane.¹⁵ Having GRADE for all included CSRs is another strength of the article, even if the post hoc methodology followed for the older CSRs when Cochrane did not yet require GRADE could introduce some bias too.

The limitations include not providing a full evidence map that should start from an a priori grid developed according to a specific methodology, including all of the possible outcomes and interventions. According to the reported intervention and outcomes, we provided only the GRADEd evidence of the current CSRs. This did not allow us to fully identify the evidence gaps (areas with no recent evidence available) because of any other outcome or intervention. Nevertheless, this was beyond our aims and what the WHO required: to effectively summarize the integration between outcomes and rehabilitation interventions, giving immediate information about the quality of evidence. An evidence map synthesis offers an easy understanding of the current literature and facilitates its dissemination. Another limit arises from using the free term "spinal cord injury," such as selecting CSRs in which the population was only people with SCI. Therefore, we may have missed some CSRs of possible interest for SCI rehabilitation such as Harvey et al³⁸ and Derry et al.³⁹ Indeed, they discussed the effects of stretch on contractures in people with, or at risk of developing, contractures in neurologic diseases including SCI and the analgesic efficacy and adverse effects of pregabalin for chronic neuropathic pain in adults, respectively. These findings could be useful for the management of SCI rehabilitation.

Conclusions

Respiratory muscle training and tDCS and exercise programs may improve respiratory outcomes and pain relief in people with SCI, respectively. There is uncertainty whether BWSTT, RAT, and FES affect walking speed and capacity. These results need to be confirmed by better-quality evidence. Therefore, future research priorities are the improvement of methodological quality of the studies in people with SCI, particularly considering the complexity of this health condition. Further, there is a need for more CSRs in the field.

Suppliers

- Knack platform, Copyright © 2022, Evenly Odd, Inc. (d/b/a Knack)
- GRADEpro, Copyright © 2021, McMaster University and Evidence Prime Inc.

Keywords

Evidence-based practice; Pain; Rehabilitation; Respiration; Spinal cord injuries; Systematic reviews as topic; Walking

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References

- Gimigliano F, Negrini S. The World Health Organization "Rehabilitation 2030: a call for action. *Eur J Phys Rehabil Med* 2017;53:155–68.
- Negrini S, Arienti C, Patrini M, Kiekens C, Rauch A, Cieza A. Cochrane collaborates with the World Health Organization to establish a package of rehabilitation interventions based on the best available evidence. *Eur J Phys Rehabil Med* 2021;57:478–80.
- Rauch A, Negrini S, Cieza A. Toward strengthening rehabilitation in health systems: methods used to develop a WHO package of rehabilitation interventions. *Arch Phys Med Rehabil* 2019;100:2205–11.
- Cieza A, Causey K, Kamenov K, Hanson SW, Chatterji S, Vos T. Global estimates of the need for rehabilitation based on the Global Burden of Disease study 2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2021;396:2006–17.
- Rupp R. Spinal cord lesions. *Handb Clin Neurol* 2020;168:51–65.
- Wilson JR, Cronin S, Fehlings MG, et al. Epidemiology and impact of spinal cord injury in the elderly: results of a fifteen-year population-based cohort study. *J Neurotrauma* 2020;37:1740–51.
- Algahtany M, McFaul S, Chen L, et al. The changing etiology and epidemiology of traumatic spinal injury: a population-based study. *World Neurosurg* 2021;149:e116–27.
- Mitchell J, Nunnerley J, Frampton C, Croot T, Patel A, Schouten R. Epidemiology of traumatic spinal cord injury in New Zealand (2007–2016). *N Z Med J* 2020;133:47–57.
- Beck B, Cameron PA, Braaf S, Nunn A, Fitzgerald MC, Judson RT. Traumatic spinal cord injury in Victoria, 2007–2016. *Med J Aust* 2019;210:360–6.
- Barbara-Bataller E, Mendez-Suarez JL, Aleman-Sanchez C, Sanchez-Enriquez J, Sosa-Henriquez M. Change in the profile of traumatic spinal cord injury over 15 years in Spain. *Scand J Trauma Resusc Emerg Med* 2018;26:27.
- Devivo MJ. Epidemiology of traumatic spinal cord injury: trends and future implications. *Spinal Cord* 2012;50:365–72.
- Smith E, Fitzpatrick P, Lyons F, Morris S, Synnott K. Epidemiology of non-traumatic spinal cord injury in Ireland—a prospective population-based study. *J Spinal Cord Med* 2022;45:76–81.
- Gerber LH, Bush H, Cai C, Garfinkel S, Chan L, Cotner B, et al. Scoping review of clinical rehabilitation research pertaining to traumatic brain injury: 1990–2016. *NeuroRehabilitation* 2019;44:207–15.
- Cumpston M, Li T, Page MJ, et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. *Cochrane Database Syst Rev* 2019;10:ED000142.
- Higgins J, Thomas J, Chandler J, et al. *Cochrane Handbook for systematic reviews of interventions*. 2nd ed. Chichester, UK: John Wiley & Sons; 2019.
- Hetrick SE, Parker AG, Callahan P, Purcell R. Evidence mapping: illustrating an emerging methodology to improve evidence-based practice in youth mental health. *J Eval Clin Pract* 2010;16:1025–30.
- Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *J Clin Epidemiol* 2021;134:178–89.
- GBD 2016 Neurology Collaborators. Global, regional, and national burden of neurological disorders, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2019;18:459–80.
- Levack WMM, Rathore FA, Pollet J, Negrini S. One in 11 Cochrane reviews are on rehabilitation interventions, according to pragmatic inclusion criteria developed by Cochrane Rehabilitation. *Arch Phys Med Rehabil* 2019;100:1492–8.
- Gates M, Gates A, Guitard S, Pollock M, Hartling L. Guidance for overviews of reviews continues to accumulate, but important challenges remain: a scoping review. *Syst Rev* 2020;9:254.
- Cochrane Rehabilitation. <https://rehabilitation.cochrane.org/evidence>. Accessed July 20, 2022.
- Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ* 2017;358:j4008.
- Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924–6.
- Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64:383–94.
- Berlowitz DJ, Tamplin J. Respiratory muscle training for cervical spinal cord injury. *Cochrane Database Syst Rev* 2013(7):CD008507.
- Boldt I, Eriks-Hoogland I, Brinkhof MW, de Bie R, Joggi D, von Elm E. Non-pharmacological interventions for chronic pain in people with spinal cord injury. *Cochrane Database Syst Rev* 2014(11):CD009177.
- Mehrholz J, Kugler J, Pohl M. Locomotor training for walking after spinal cord injury. *Cochrane Database Syst Rev* 2012;11:CD006676.
- Raab AM, Krebs J, Pfister M, Perret C, Hopman M, Mueller G. Respiratory muscle training in individuals with spinal cord injury: effect of training intensity and volume on improvements in respiratory muscle strength. *Spinal Cord* 2019;57:482–9.
- Cardenas DD, Felix ER, Cowan R, Orell MF, Irwin R. Effects of home exercises on shoulder pain and pathology in chronic spinal cord injury: a randomized controlled trial. *Am J Phys Med Rehabil* 2020;99:504–13.
- Todd KR, Lawrason SVC, Shaw RB, Wirtz D, Martin Ginis KA. Physical activity interventions, chronic pain, and subjective well-being among persons with spinal cord injury: a systematic scoping review. *Spinal Cord* 2021;59:93–104.
- Gerber LH, Deshpande R, Prabhakar S, et al. Narrative review of clinical practice guidelines for rehabilitation of people with spinal cord injury: 2010–2020. *Am J Phys Med Rehabil* 2021;100:501–12.
- Arienti C, Armijo-Olivo S, Minozzi S, et al. Methodological issues in rehabilitation research: a scoping review. *Arch Phys Med Rehabil* 2021;102. 1614–22.e14.
- Negrini S, Arienti C, Pollet J, et al. Clinical replicability of rehabilitation interventions in randomized controlled trials reported in main journals is inadequate. *J Clin Epidemiol* 2019;114:108–17.
- Martin Ginis KA, van der Scheer JW, Latimer-Cheung AE, et al. Evidence-based scientific exercise guidelines for adults with spinal cord injury: an update and a new guideline. *Spinal Cord* 2018;56:308–21.
- Rapidi CA, Tederko P, Moslavac S, et al. Evidence-based position paper on physical and rehabilitation medicine (PRM) professional practice for persons with spinal cord injury. The European PRM position (UEMS PRM Section). *Eur J Phys Rehabil Med* 2018;54:797–807.
- Tomaschek R, Gemperli A, Rupp R, Geng V, Scheel-Sailer A. A systematic review of outcome measures in initial rehabilitation of individuals with newly acquired spinal cord injury: providing evidence for clinical practice guidelines. *Eur J Phys Rehabil Med* 2019;55:605–17.
- Varadhan R, Wang SJ. Standardization for subgroup analysis in randomized controlled trials. *J Biopharm Stat* 2014;24:154–67.
- Harvey LA, Katalinic OM, Herbert RD, Moseley AM, Lannin NA, Schurr K. Stretch for the treatment and prevention of contractures. *Cochrane Database Syst Rev* 2017;1:CD007455.
- Derry S, Bell RF, Straube S, Wiffen PJ, Aldington D, Moore RA. Pregabalin for neuropathic pain in adults. *Cochrane Database Syst Rev* 2019;1:CD007076.