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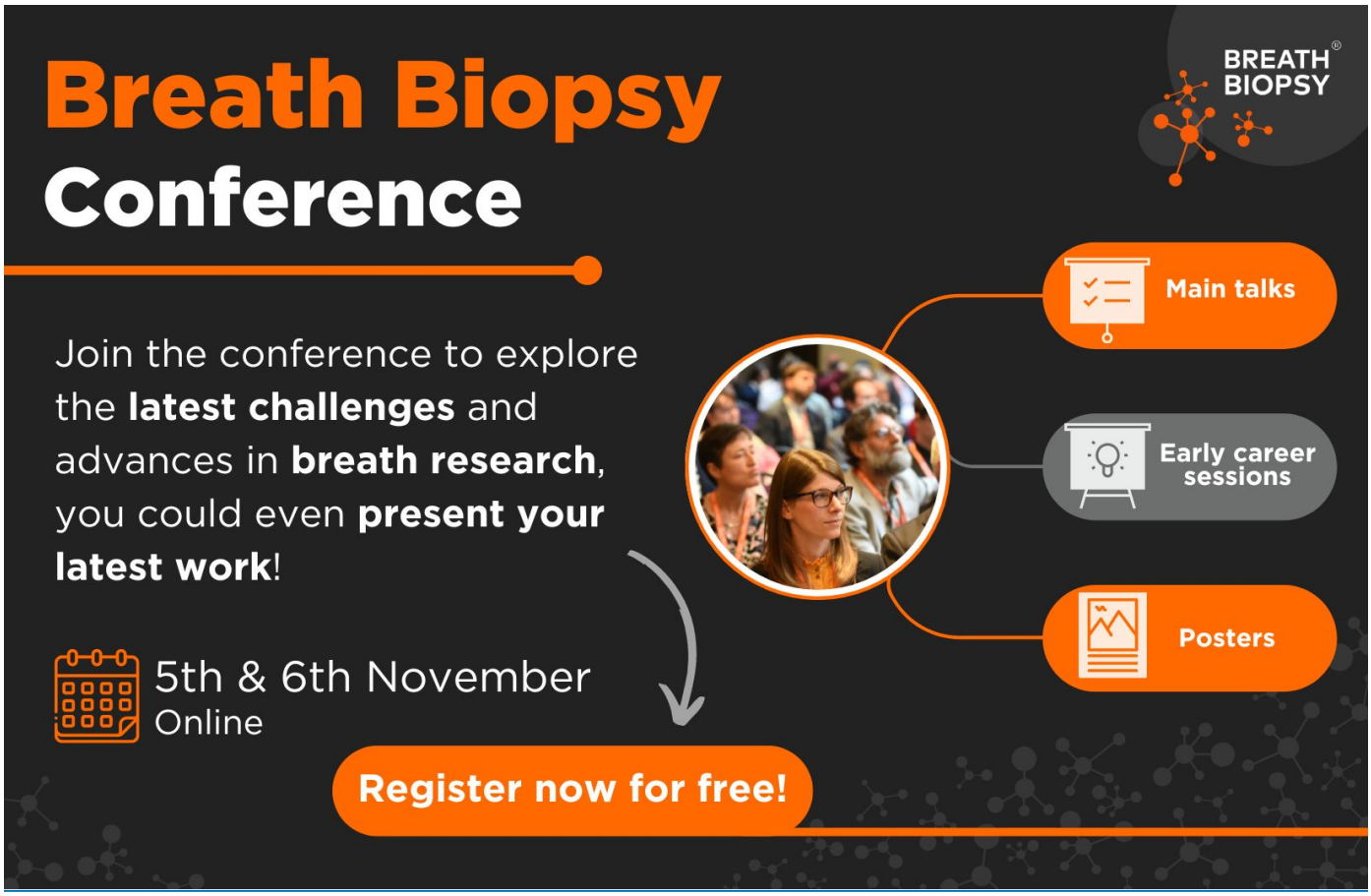

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PAPER

REPORT-SCS: minimum reporting standards for spinal cord stimulation studies in spinal cord injury

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Abstract

Objective. Electrical spinal cord stimulation (SCS) has emerged as a promising therapy for recovery of motor and autonomic dysfunctions following spinal cord injury (SCI). Despite the rise in studies using SCS for SCI complications, there are no standard guidelines for reporting SCS parameters in research publications, making it challenging to compare, interpret or reproduce reported effects across experimental studies. *Approach.* To develop guidelines for minimum reporting standards for SCS parameters in pre-clinical and clinical SCI research, we gathered an international panel of expert clinicians and scientists. Using a Delphi approach, we developed guideline items and surveyed the panel on their level of agreement for each item. *Main results.* There was strong agreement on 26 of the 29 items identified for establishing minimum reporting standards for SCS studies. The guidelines encompass three major SCS categories: hardware, configuration and current parameters, and the intervention. *Significance.* Standardized reporting of stimulation parameters will ensure that SCS studies can be easily analyzed, replicated, and interpreted by the scientific community, thereby expanding the SCS knowledge base and fostering transparency in reporting.

1. Introduction

Globally, an estimated 20.6 million people are currently living with spinal cord injury (SCI) [1], with approximately 769 000 individuals sustaining a traumatic SCI annually [2]. SCI can damage neural connections controlling motor (e.g. reaching, walking, core stability), sensory (e.g. touch, pain, proprioception), and autonomic (e.g. cardiovascular, bowel, bladder, sexual) functions [3, 4]. These interrelated dysfunctions have a profound impact on quality of life [5–7] increase overall disease burden and contribute to large healthcare-related expenditures [8, 9].

Electrical spinal cord stimulation (SCS) is a burgeoning approach for recovery of motor [10–17] and autonomic functions [18–30] in people with SCI. Implanted epidural spinal stimulation has long been used with approval from the United States Food and Drug Administration for treating neuropathic pain. In recent years, however, the number of published studies on the use of implanted epidural SCS and even non-invasive, transcutaneous SCS for improving motor and autonomic dysfunctions following SCI has increased considerably [31, 32]. From the late 1980s to mid-2010s, roughly 1–3 articles per year were published on the use of SCS for managing SCI-related dysfunctions other than pain. Currently, over 20 articles are being published per year, with this number expected to grow [31, 33, 34]. This is validated by the fact that as of September 2023, there are 125 actively recruiting SCS clinical trials for SCI on clinicaltrials.gov.

As evidence indicates that both epidural and transcutaneous SCS activate common neural structures [35, 36], this article will discuss both approaches together. Recent reviews on the use of epidural [37] and transcutaneous [38] SCS to improve motor function following SCI indicated that 18/18 and 21/25 articles, respectively, showed poor methodological quality. Small sample sizes, selection bias, inadequate reporting of adverse events and safety precautions taken to minimize risk, and limited validation of the outcome measures were common reasons for reduced quality across studies [31, 34, 37–39]. Unstandardized reporting of outcomes, SCS parameters, and terminology are common in both pre-clinical [40] and clinical studies [31, 34, 37, 38]. This limits the ability to interpret results, reproduce published findings, and contributes to the delay in translation of these experimental therapies to clinical practice and standard of care. While acknowledging that optimization of stimulation parameters may vary across targeted tissues and organ systems for a given study, a broader adoption of reporting standards would facilitate the appraisal, synthesis, and reproducibility of research within this field.

Minimum reporting requirements are essential for promoting transparent disclosure of methods used, study replication, standardization of SCS-related terminology, and the synthesis and interpretation of scientific findings [41]. Minimum reporting standards are common and have elevated the standards of biomedical research (e.g. MINimum Information for Medical AI Reporting) [42], randomized clinical trials (e.g. consolidated standards of reporting trials [43]), and pre-clinical research (e.g. ARRIVE [44, 45]). Reporting standards for participant demographics and pre-clinical experiments have already been introduced in SCI research. For example, the International Spinal Cord Injury Core Dataset has set standards for reporting participant characteristics (e.g. age at injury, sex, etiology of injury, etc) in clinical SCI research [46, 47] and the minimum information about a SCI guidelines are used to assess experimental procedures involving cell transplantation, histology, immunochemistry, etc in pre-clinical SCI models [48]. However, minimum reporting guidelines for studies involving the use of SCS for SCI research are currently lacking.

Herein, we introduce minimum information standards for reporting SCS parameters for researchers conducting pre-clinical and clinical SCI studies involving non-invasive and invasive electrical SCS. This is a first-generation minimum reporting guideline that is meant to encourage researchers to begin reporting SCS related information. Since such a system does not exists for SCS, this will aid in translating research practices into clinical use. The proposed guidelines focus on three areas identified as critical to the development and prescription of evidence-based electrical SCS for people living with SCI: (1) the SCS hardware used (2) the SCS configuration and current parameters; (3) the SCS intervention.

2. Methods for establishing reporting guidelines

2.1. Expert panel selection

Based on an appraisal of peer-reviewed publications related to development and application of SCS for individuals with SCI, 17 international expert clinicians, scientists, clinician-scientists, and engineers in the field of SCS for SCI recovery were identified and contacted. Of these, 14 participated in developing the minimum reporting guidelines. The authors included in this panel represents a wide range of expertise in pre-clinical and clinical research, including motor, sensory, and autonomic recovery following SCI. Panelists were considered experts according to the definition by Fink *et al* [49], which indicates that an expert qualifies for selection if they are 'representative of their profession, have power to

implement the findings, or because they are not likely to be challenged as experts in the field'.

2.2. Item selection and consensus

We used a Delphi approach to identify guideline items and obtain the expert panel's level of agreement on the items put forth [50, 51]. Guideline items were recommended by the expert panel, identified from previously published literature reviews that highlighted insufficiencies in the reporting of stimulation parameters for experiments utilizing electrical SCS following SCI [31, 32, 34, 37–39]. We also examined resources for developing minimal reporting guidelines [42–48, 52], such as the TIDieR checklist (i.e. reporting standards for interventions) [52], to identify items that are crucial for minimal reporting guidelines and intervention-based approaches. We then surveyed the expert panel on the guideline items proposed. Based on their feedback, we modified the items and split them into categories. A total of 29 items were identified and developed into a survey comprised of three SCS categories: (1) SCS hardware (3 items); (2) SCS configuration and current parameters (13 items); and (3) SCS intervention (13 items) (table 1).

To reach consensus on the items to be included in the minimum reporting guidelines for SCS parameters, each expert completed a survey on Qualtrics^{xm} (www.qualtrics.com) and rated their level of agreement for each item proposed on a 5-point Likert scale (scale anchors: 1 = strongly disagree; 5 = strongly agree) [53, 54]. Mean agreement scores (range from 1 to 5) were then calculated for all items. Based on this score, we categorized each item as strongly disagree (1-2), somewhat disagree (2.01-3), somewhat agree (3.01-4) and strongly agree (4.01-5). Only items above the strong agreement cut-off score (i.e. 4.01) were included in the minimum reporting guidelines.

3. Results

The expert panel had strong agreement on 89% (26/29) of the proposed guideline items (mean agreement = 4.71, range = 3.93–5.0). In the first category, reporting device characteristics (name, model number, manufacturer and software version), electrode characteristics (manufacturer, product number, and size), and the material and size of the electrodes when handmade all showed strong agreement (mean agreement $\geqslant$ 4.64) (figure 1).

In the second category, reporting items such as the frequency, intensity, waveform, width, temporal dynamics, use of a carrier waveform(s) if applicable, and location of the anode and cathode showed the strongest agreement (all $\geqslant$ 4.79) (figure 2). Characteristics such as charge-balance (4.57), and phase duration and inter-pulse interval (4.5) also received strong agreement. Two parameters (i.e. pulse period = 4.0, duty cycle = 4.0) were below the strong agreement cut-off and thus were not recommended for guideline inclusion.

In the third category, reporting items such as the method of delivery (e.g. epidural, transcutaneous), duration of SCS, number of sessions per week and the total number of sessions, and whether SCS was combined with another intervention (e.g. walking or balance program) showed the strongest agreement ($\geqslant$4.86) (figure 3). Items such as whether SCS was applied using an open or closed-loop (i.e. activity-dependent) system, reporting adverse events, defining the target function of the SCS program, reporting the position of the participant (e.g. standing, sitting, supine), indicating modifications to the initial SCS treatment plan, describing the environmental setting (e.g. home, research laboratory, clinic), and reporting program adherence also received strong agreement (between 4.57 and 4.79). The reporting of team qualifications (3.93) was below the strong agreement cut-off and thus not mandatory under the proposed guidelines.

Based on the survey results across all three categories, we included 26 items that met the strong agreement criteria into the expert recommended minimal reporting guidelines for SCS parameters, and excluded three items that did not meet the criteria. A 26-item checklist (figure 4), split into three categories, is provided as a guide for writing and peer-reviewing research related to electrical SCS following SCI.

4. Discussion

Reviews of clinical and pre-clinical work have consistently highlighted the challenges caused by inconsistent reporting of SCS parameters in SCI research, impeding the progression, synthesis, replication, and translation of data in this field [31, 34, 37, 38, 40]. To address this limitation, we assembled an expert panel comprising scientists and clinicians specialized in SCS for SCI research. The primary objective of this panel was to establish minimum reporting standards for SCS parameters. Strong agreement was achieved among the expert panelists for 26 out of 29 guideline items. The proposed minimum information checklist aims to promote transparent reporting standards for both pre-clinical and clinical studies investigating electrical SCS to accelerate the clinical translation of SCS.

The experts strongly agreed with most items for developing minimum reporting standards for SCS hardware, configuration and stimulation parameters, and the intervention program used. The expert panel indicated that a description of the hardware used for SCS is important and not well-reported in the existing literature. This formed the basis for our first category—system hardware. Identifying the name, manufacturer, model, and software of the device,

Table 1. Guideline items surveyed by the expert panel.

Items	Guideline
Category 1: SCS hardware	
Device name manufacturer, model, software	Reporting the device name, manufacturer, model number, and software version of the electrical stimulator used
Electrode manufacturer, product number, size	Reporting the manufacturer, product number, and size of the electrodes used
Materials and size of handmade electrodes	Reporting the material and size of the electrode(s) if handmade
Category 2: SCS configuration and current parameters	
Cathode(s) placement	Reporting the anatomical location(s) of the cathode(s) (i.e. negative electrode(s)) with respect to spinal roots and vertebral levels.
Anode(s) placement	Reporting the anatomical location(s) of the anode(s) (i.e. positive electrode(s)) with respect to spinal roots and vertebral levels.
Waveform	Report the waveform of the electrical pulse (e.g. Square, sine, sweep, monophasic, biphasic, polarity (i.e. cathodic-leading or anodic-leading), etc)
Pulse width	Report pulse width in units of time (i.e. the duration of the pulse in milliseconds)
Phase duration and IPI	For biphasic waveforms, reporting the anodic and cathodic phase durations and any interphase interval (IPI)
Intensity	Reporting the intensity of the stimulation as amplitude (constant-current) or voltage (constant-voltage)
Intensity threshold method	Reporting how the amplitude (i.e. intensity) of stimulation was determined (e.g. based on EMG, motor or sensory threshold)
Period	Reporting the period of the pulse in units of time (i.e. the time taken for the signal to complete one cycle)
Frequency	Reporting pulse frequency in Hertz (Hz) (i.e. the number of pulses per second)
Duty cycle	Reporting the duty cycle of the pulse (i.e. percentage of ON time)
Charge-balance	Reporting whether the electrical pulse was charge-balanced, and if so, symmetrically or asymmetrically
Temporal characteristics	Reporting the temporal characteristics of stimulation trains over time (e.g. burst, continuous, etc)
Carrier waveform	Reporting the presence and frequency of a carrier waveform (i.e. overlapping signal on top of the basic waveform) if applicable
Category 3: SCS intervention	
Target function	Reporting the primary target of the stimulation intervention (e.g. bladder function, upper extremity motor function, etc)
Delivery method	Reporting the method of stimulation (e.g. transcutaneous, epidural, intraspinal)
Session duration	Reporting the duration of each stimulation session in minutes
Sessions per week	Reporting the number of stimulation sessions per week
Total number of sessions	Reporting the total number of stimulation sessions conducted
Adjunct therapy	Reporting whether the stimulation treatment was combined with another modality (e.g., arm ergometry, robotic gait training, etc)
Open or closed loop	Reporting whether stimulation was under open-loop or closed-loop control, and the control signal (e.g. EEG, EMG, IMU) used for closed-loop
Environmental setting	Reporting the environmental setting during the treatment program (e.g. Laboratory under supervision, home but supervised (e.g. telehealth) or unsupervised home setting)
Participant position	Reporting the position of the participant during stimulation (e.g. supine, upright, side-lying)
Program adherence	Reporting program adherence (i.e. number of sessions completed or missed possibly with reasons)
Adverse events	Reporting the presence or absence of any adverse event(s) from the stimulation program
Team qualifications	Reporting the qualifications of the individual (or team) administering stimulation or of the individual that provided education training if self-administered
Modification to initial treatment program	Reporting whether the initial treatment program was modified, personalized, or titrated over the course of the intervention, and if so, how

Abbreviations: EMG, electromyography; EEG, electroencephalography; IMU, inertial measurement unit.

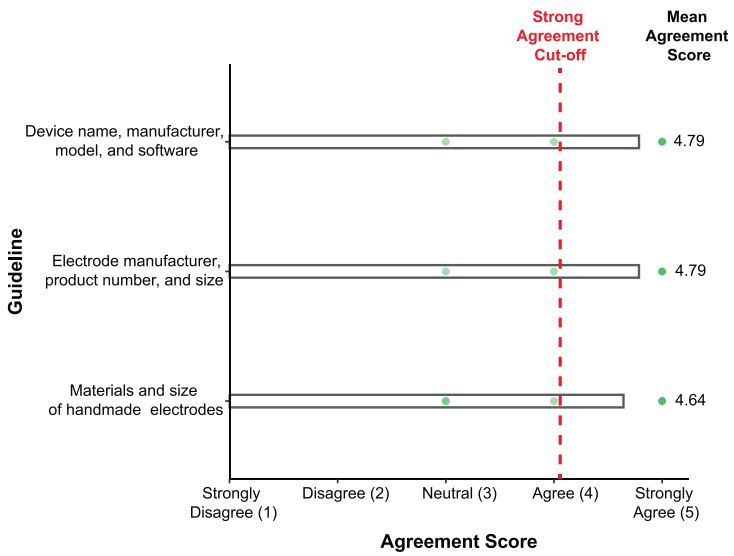

Figure 1. Panel agreement for Category 1: SCS hardware agreement ratings, ranging from 1 to 5, are shown for each expert (green dots) and for each item proposed in the guidelines for category 1. Horizontal bars depict the mean agreement score for each item and are organized from highest to lowest agreement. We only included items into the final guidelines that showed a mean agreement score that was greater than the cut-off score (i.e. 4.01; vertical red line). Refer to table 1 for full details regarding the minimum reporting standards of each item.

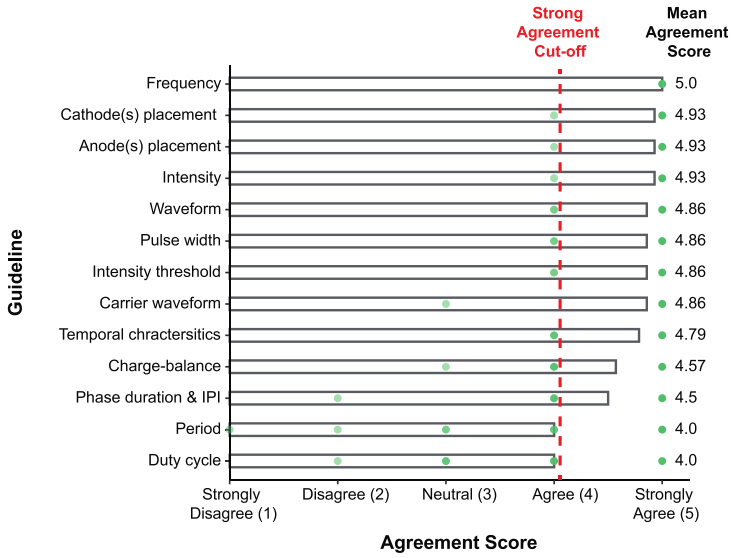

Figure 2. Panel agreement for Category 2: SCS configuration and current parameters agreement ratings, ranging from 1 to 5, are shown for each rater (green dots) and for each item proposed in the guidelines for category 2. Horizontal bars depict the mean agreement score for each item and are organized from highest to lowest agreement. We only included items in the final guidelines that obtained a mean agreement score that was greater than the strong agreement cut-off score (i.e. 4.01; vertical red line). Refer to table 1 for full details regarding the minimum reporting standards of each item. Abbreviations: IPI, inter-pulse interval.

as well as the manufacturer, product number and size of the electrodes will help ensure reproducibility between studies. It will also facilitate comparisons between devices approved by the United States Food and Drug Administration or CE marked devices (i.e. approved by the European General Medical Devices Directive), and experimental devices to establish appropriate spinal cord stimulators for research and home-use. Electrode specifications are of particular importance as these affect the area of stimulation and the charge density of SCS, which are important considerations for targeting specific spinal segments and avoiding adverse events [55–58].

The second category—SCS configuration and current parameters—included important items that can influence the effect of SCS on the nervous system. The location, frequency, intensity, waveform, width, durations, and charge of stimulation can influence the activation of various neural structures and downstream effects [40, 58–60]. For example, changing the frequency of stimulation can alter the firing rate of neurons and changing the pulse width

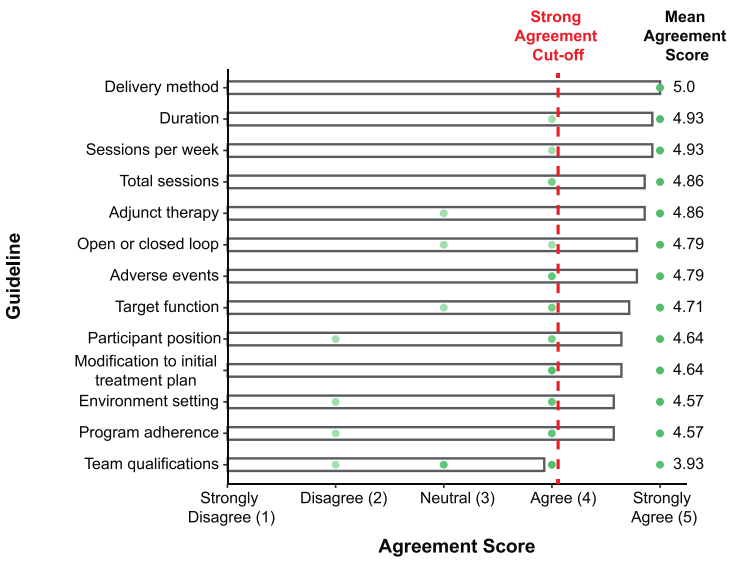

Figure 3. Panel agreement for Category 3: SCS intervention agreement ratings, ranging from 1 to 5, are shown for each expert (green dots) and for each item proposed in the guidelines for category 3. Horizontal bars depict the mean agreement score for each item and are organized from highest to lowest agreement. We only included items into the final guidelines that showed a mean agreement score that was greater than the cut-off score (i.e. 4.01; vertical red line). Refer to table 1 for full details regarding the minimum reporting standards of each item.

and intensity of SCS can alter the nerve fibers activated by stimulation [40, 58–61]. Furthermore, changing these parameters can also alter paresthesia associated with SCS [58, 62, 63]. It is also important to note that numerous groups have utilized motor threshold to standardize stimulation intensity [16, 60, 64–67]. However, researchers may determine intensity thresholds based on the specific objectives of their study and will report this in accordance with those aims. For instance, if the goal of the study is to enhance blood pressure regulation, the stimulation intensity may be based on the level required to elicit a meaningful change in blood pressure, and not necessarily on changes in motor responses.

Item selection for the third category—SCS intervention—was informed by established reporting standards for interventions (e.g. the TIDieR Checklist [52]). Reporting items such as the type of intervention, the target function (e.g. improve walking or reaching, blood pressure control), the dosage of SCS, the environmental setting, program adherence, adjunct therapy, and the number of adverse events, among other items, are necessary for replicating and understanding clinical research findings. When reporting closed-loop stimulation, the control signal (e.g. EMG, EEG, ECoG, IMU) should also be reported. It is expected that the control signal will also be well-described as part of a standard methods section. When stimulation parameters, such as SCS amplitude, are under the 'free' control of participants or researchers, it should be reported as open-loop stimulation, as stimulation is controlled manually and not triggered by a physiological signal. Authors should also report the ranges and specific parameters (i.e., amplitude, frequency, program cycling) that are open for free control. As with category 2 (SCS configuration and stimulation parameters), different SCS interventions likely have unique effects on neural plasticity [68, 69]; for instance, combining SCS with activity-based therapies should be reported, as neural plasticity is activity-dependent and can be modified with the addition of SCS [34, 70]. The inclusion of reporting adverse events in this category was guided by recent reviews indicating that scarce reporting of adverse events is a major limitation in the field [31, 37, 38, 40]. Although reporting of surgical complications associated with implanted electrodes has been reported [71, 72], adverse events associated with the delivery of SCS have not (e.g., burns, infections, pain, tissue damage). Notably, we excluded team qualifications, period, and duty cycle from the minimal reporting guidelines, as these characteristics did not meet the agreement cut-off. Period and duty cycle, however, can be derived from other included guideline items. It is important to note that these items only missed the strong-agreement cut-off by .01 units. An increase in 1 point from an expert would change the score by 0.07 units, thus a higher rating from a single expert could have raised these scores over the strong-agreement cut-off. Nonetheless, some of these items can be derived from others within the guidelines. Period can be determined by taking the inverse of frequency (i.e. # of pulses per second) of SCS; and duty cycle can be calculated by using pulse width and period (i.e. 1/frequency).

This first version of the minimum reporting standards presented herein is purposefully broad to capture pertinent information needed for pre-clinical and clinical SCS studies. Reporting only the most crucial information will decrease reporting burden and

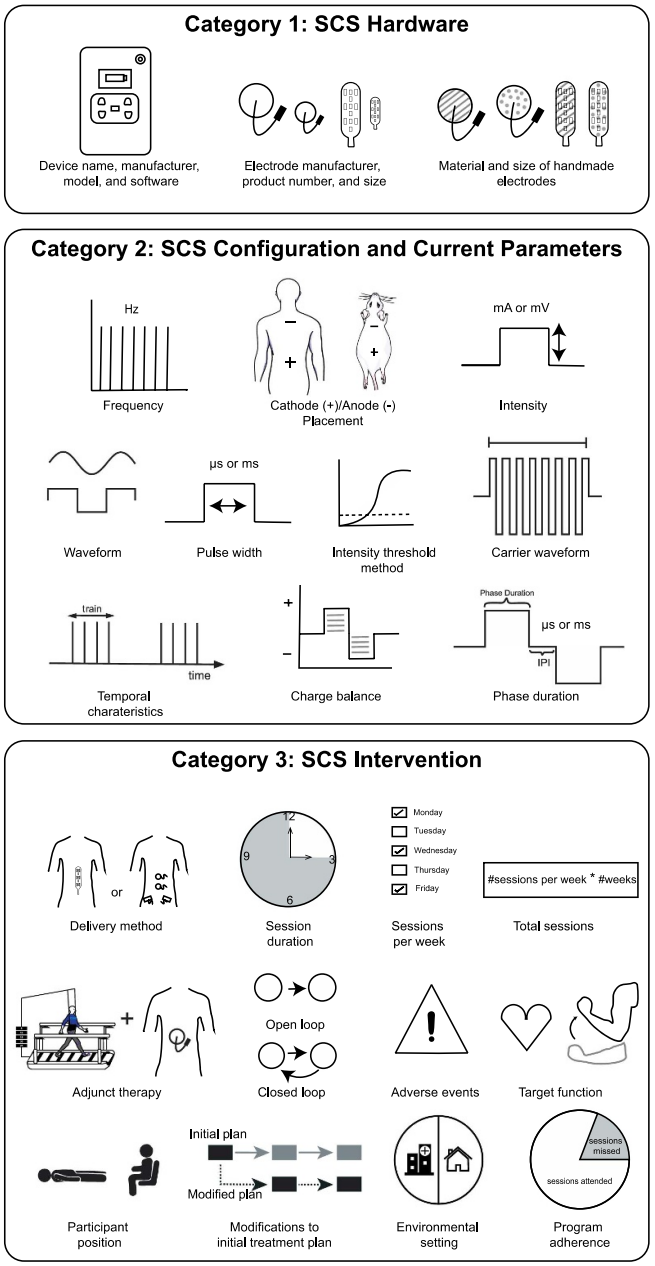

Figure 4. Expert recommended minimum reporting standards for SCS parameters A checklist for each category of the guidelines to ensure appropriate reporting of SCS parameters in SCI experiments. Abbreviations: mA, milliamps; mV, millivolts; IPI, inter-pulse interval.

increase adherence rates to our reporting guidelines [73]. The actual reporting of the guidelines should be customized based on the individual study parameters, thus avoiding any potential bias. Importantly, the guidelines do not emphasize what prospective SCS parameter should be used, but rather emphasize the importance of what should be reported retrospectively.

Future refinement of the expert recommended guidelines is expected with knowledge advancement, and with feedback from the scientific community. Although our expert panel is diverse, experts from different backgrounds may want more specific details regarding SCS parameters and protocols. For example, as technologies advance, the use of multi-channel spatiotemporally targeted stimulation may increase, hence the need to report the timing and pattern of stimulation delivered through them. Further, there could also be a need to report how electrode location was confirmed as researchers use different strategies for confirming electrode location, such as motor-recruitment or post-activation depression [11, 74–79]. Advancing minimum information standards is common practice in various disciplines [45, 47]. Accordingly, adoption of the proposed guidelines will provide a step-by-step guide in helping clinicians and scientists identify important parameters when designing, implementing, and reporting SCS studies in SCI research. This will enhance study quality and aid in the development

of evidence-based therapeutic approaches for those living with SCI.

5. Conclusions

We present recommendations for minimum reporting standards for studies using SCS (REPORT-SCS) in SCI research, based on expert panel consensus. The 26-item checklist promotes standardized reporting of SCS characteristics, the SCS intervention, and the SCS hardware used. Adherence to these reporting guidelines will generate data and publications fostering greater replication, synthesis, and comparison of SCS experiments, thereby aiding the scientific community in bringing this approach into clinical use.

Data availability statement

All data that support the findings of this study are included within the article (and any supplementary files).

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Author contributions

A V K, R S, R N M, and S S contributed to conceptualizing the content, scope and organizational structure of the manuscript. R N M was responsible for data acquisition and analysis. R N M, A V K, R S were primarily responsible for writing the manuscript. R N M created the figures and tables. All authors contributed to editing the entire document and approved the final document.

Conflict of interest

C M is a paid consultant for Onward Medical, Inc. D D hold equity in and serve as officers for Stim Sherpa, which has licensed optimization IP from the University of Minnesota. P G is shareholder in SpineX. A P holds shares of Agade srl and AllyArm srl. EE F serves as a consultant for Onward Medical, Inc. R S is a consultant with SpineX Inc., a company that manufactures SCS devices. A V K serves on the advisory board for Onward Medical Inc. All other authors have no potential conflicts of interest to disclose.

Ethics statement

Following the guidelines set by the Tri-Council Policy Statement (TCPS2) that oversee research ethics in Canada, this study did not receive full ethical review because it is not classified as research. In Canada, neither program assessments nor qualitative enhancement studies come under the jurisdiction of the TCPS or institutional Research Ethics Boards. We assure that we adhered to all relevant institutional and governmental guidelines regarding the ethical involvement of human participants throughout this project.

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