Plan Overview

A Data Management Plan created using DMPonline

Title: Exoskeleton Training for Spinal Cord Injury Neuropathic Pain (ExSCIP): A Phase 2 Feasibility Randomised Trial

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Project abstract:

Background: Following Spinal Cord Injury (SCI), 53% of people develop neuropathic pain (NP). NP can be more debilitating than other consequences of SCI, and a persistent health issue. Pharmacotherapies are commonly recommended for NP management in SCI, although severe pain often remains refractory to these treatments in many sufferers. Furthermore, poor medication adherence exists, stemming from unacceptable side-effects and fear of dependency.
Sensorimotor stimulation using active walking with robotic assistance has not been well studied in NP after SCI, despite convincing locomotor-based pre-clinical studies, identifying prevention and reversal of NP.
Our primary aim is to assess the impact of exoskeleton-based walking on NP intensity and interference after SCI and examine feasibility outcomes for progression to a definitive trial.

Methods and Analysis: This is a phase 2 single-blinded, randomised feasibility study. It will test the feasibility and acceptability of exoskeleton-based walking 3 times per week for 12 weeks (intervention), as a mechanistic-based intervention for NP after SCI. The comparator will be an equally dosed, blended relaxation programme devoid of motor imagery prompts. 40 participants with moderate-to-severe NP post SCI will be recruited and randomised to intervention and comparator groups.
The primary outcomes are feasibility outcomes for progression to definitive trial which include recruitment and retention rates, adverse events and acceptability of the intervention. Secondary outcomes explore changes in NP intensity and interference as measured by the International Spinal Cord Injury Pain Basic Data Set 3.0 (ISCIPBDS) at baseline, post-intervention (week 13) and at 6-month follow-up.

Discussion: There is a need to explore non-pharmacological management of NP after SCI.

The findings of this feasibility trial will inform the development of a future multicentre, international RCT.

Trial Registration: This trial protocol is registered prospectively on ClinicalTrials.gov (NCT06463418).

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Exoskeleton Training for Spinal Cord Injury Neuropathic Pain (ExSCIP): A Phase 2 Feasibility Randomised Trial

Data description and collection or re-use of existing data

How will new data be collected or produced and/or how will existing data be re-used?

The ExSCIP feasibility trial generates new, primary data. The following data will be collected throughout the trial:
● Screening questionnaire (confirmation of diagnosis, Spinal Cord Injury Pain Instrument (SCIPI), confirmation of exoskeleton naivity, confirmation of stable medication regimen, confirmation of no unstable medical/psychiatric condition)
● Demographic data (age, sex, neurological level of injury, ASIA impairment score, etc).
● The full International Spinal Cord Injury Pain Basic Data Set Version 3.0 (ISCIPBDS 3.0) with items addressing pain classification, intensity, interference, mood and sleep.
● Feasibility outcome metrics; recruitment rates, programme adherence, attrition rates and reasons for dropout.
● Neuropathic Pain Symptom Inventory.
● EEG data
● Health related quality of life (EQ-5D-5L) questionnaires.
● Discrete choice questionnaire
● Bespoke ExSCIP health economic questionnaire items relating to; health resource and pharmacotherapy, work presenteeism and absenteeism
● Qualitative data based on focus group discussions and debriefing interviews.

This data will be collected in-person by an independent assessor blinded to participants allocation via written questionnaires.
Data will be entered into an electronic REDCAP database (password protected) by the researchers, supported by CSTAR at UCD.
Security measures include password protected computers, firewall protection, file encryption and access rules, power failure/surge and malware protection. All data collected against each participant will be pseudomymised at point of entry into databases.
All quantitative data will be inputted and cleaned in SPSS (version 29) from electronic or paper forms and analysed using this software. Qualitative data garnered from focus group exit interviews will be uploaded, stored and analysed in NVivo software.

What data (for example the kind, formats, and volumes), will be collected or produced?

It is estimated that the project will generate the following types of data:

Type of data	Collection procedure	Purpose of data collection	Data format	Volume of data
Quantitative (pain intensity and pain interference scores)	Case report form, standardised questionnaires (Neuropathic Pain Symptom Inventory, ISCIPBDS 3.0, Numerial Rating Scale)	To determine and compare the effects of an exoskeleton walking intervention and equally dosed relaxation program on neuropathic pain after spinal cord injury.	.xlsx (Excel); .sav (SPSS 29)	It is anticipated this data will be collected for 40 participants at 3 time points (baseline, post intervention and 6 month follow up).
Quantitative (EEG biomarker)	EEG recordings will be measured using the NeuroCONCISE 8 electrode device. Participants will be seated in a dimly lit room shielded from sound and stray electrical fields. Resting EEGs will be recorded with eyes open for 3 minutes followed by eyes closed for 3 minutes.	There is evidence to suggest that EEG can serve as a useful biomarker for the presence of chronic neuropathic pain. Continuous NP is associated with an EEG power signal with an increase in theta band and high beta band along with a decrease in the high alpha, low beta band.		It is anticipated this data will be collected for 40 participants at 3 time points (baseline, post intervention and 6 month follow up).

Quantitative (Feasibility outcomes)	Data will be collected on the following feasibility outcomes: • Total number of eligible participants with moderate to severe neuropathic pain after SCI recruited. • Recruitment rates disaggregated by SII and NRH channels (recruitment capacity at named sites). • Trial uptake rates. • Retention and follow-up/attrition rates i.e. those that provide data at 13 weeks and 6 months. • Adherence with the programme over time (attendance and total number of steps taken). • Any safety/adverse events. • Feasibility of stratified randomisation. • Feasibility of assessment procedures. • Availability of baseline data required. • Time needed to collect and analyse data.	This data will be collected to determine whether progressing this feasibility trial to definitive trial across multiple centres is warranted and feasible. Threshold criteria for onward progression to a definitive trial is determined as the following: • Successful intervention uptake, with recruitment rates of ≥35% of eligible rates. • Loss to follow up/attrition rates ≤20%. • Process evaluation and qualitative data that indicates that EXSCIP is an acceptable intervention to individuals with NP following SCI and to physiotherapists delivering the intervention, where no insurmountable barriers were identified. • Safe and successful implementation of the EXSCIP intervention: no serious adverse events and average programme adherence of ≥ 80% of all sessions. • A non-inferior effect is observed in comparison with the control arm and the Minimal Clinically Important Difference (MCID) for the NP pain intensity in an SCI population (1.74 points decrease on NRS) is observed within the 95% confidence interval for mean change for the intervention arm.	.xlsx (Excel)	Pain related measures will be collected for 40 participants at 3 time points as outlined above. The remaining data related to feasibility will be collected after delivery of the intervention.
Quantitative (Health Economic Evaluation)	Bespoke data collection tools will be prepared. These will include resource use and include work (paid and unpaid) absenteeism and presenteeism. participants. The intervention will be costed with consideration of time and resource use related to planning, training, implementation and running costs. Direct cost of the ExSCIP programme and average for each participant will be estimated. Downstream resource use and costs will be obtained from participants by means of a retrospective questionnaire. We will measure quality of life using the EQ-5D-5L questionnaire including quality-adjusted life years (QALYs), and assess the subsequent down-stream use and cost of health and social care resources.	The available data will be presented in a cost-effectiveness framework to enable assessment of the ExSCIP programme's value for money. The analysis will explore Value-of Information to describe the potential benefit from future research and in particular allow opportunity to explore how we might devise a discrete choice experiment in a future clinical trial.	.xlsx (Excel); .sav (SPSS 29)	It is anticipated this data will be collected for 40 participants at 3 time points (baseline, post intervention and 6 month follow up).

Qualitative (Participants)	Qualitative focus group discussions with participants will be conducted and recorded following the intervention to ascertain their experiences of the EXSCIP programme The qualitative semi-structured question schedule will be developed in collaboration with our PPI panel. A person unknown to the participants will complete the exit discussions.	As perceived pain is multidimensional and often dependent on factors such as attitudes, self-efficacy and thoughts, inclusion of a qualitative study is important to inform additional development and improvement to the intervention. Key areas to be discussed will be; • satisfaction with and acceptability of the EXSCIP programme, • perceptions of exoskeleton use, • barriers and facilitators to attendance and implementation • and sustainability of a walking programme following intervention	Transcripts (.docx); Audio recordings (.MP4, .AVI)	This data will be collected in 3-4 focus groups consisting of 5-6 people (15-20 people total) after the delivery of the intervention. There will be 3-4 transcripts and audio recordings associated with this portion of the data collection.
Qualitative (Staff)	Qualitative focus group discussions will be conducted and recorded following the intervention with staff who delivered the EXSCIP intervention to evaluate physiotherapists' perspectives of delivering an exoskeleton walking programme for pain.	The following questions will be addressed in relation to the perspectives of staff who delivered the ExSCIP intervention: • Beliefs • Views on implementation • Therapist burden • Skill level required to deliver an intervention of this nature	Transcripts (.docx); Audio recordings (.MP4, .AVI)	This data will be collected in 1-2 focus groups consisting of 2-4 people total after the delivery of the intervention. There will be 1-2 transcripts and audio recordings associated with this portion of the data collection.

Documentation and data quality

What metadata and documentation (for example the methodology of data collection and way of organising data) will accompany data?

An appropriate metadata standard will be used to describe the data. Zenodo will be used to preserve and share the research data after the project. On Zenodo, each record contains a minimum of mandatory terms, with optionally additional DataCite recommended terms and Zenodos enrichments to enable discovery and re-use. Metadata will be openly licensed with a CC0 license.

The data collected from this study will be stored on UCD's secure institutional infrastructure for a total of 10 years as required by UCD's research data management policy. Personal data will be pseudonomised and the pseudonomised key will be stored for a total of four years, within a separate folder. The key will be deleted after four years and data will be stored as anonymised. The non-specific personal data and data concerning health will be stored on a separate encrypted Google Drive folder. All data will be deleted after 10 years.

The documentation for this study that will be stored are as follows:

● Consent form
● Participant Information Leaflet
● Screening Questionnaire
● Ethical Approval

This will be accompanied by a README text file (.txt) which will aid in explaining the datasets and linking the documentation. It will outline the following:

● Name of dataset
● Name of researchers involved in data acquisition
● Brief description of the dataset
● Contact information of the PI for queries related to data acquistion or the protocol.
● References of published works.
● Conflicts of interest.

Other text files (.txt) will include:

● CLINICAL_INFO.txt which will be defined age, neurological level of injury, ASIA impairment scale and number of each participant. No identifiable personal data will be provided.
● RECORDS.txt file where is defined the names of all data files and documents that create the dataset with a brief description of what contains each file/document.
● EMG_FILE_INFO.txt file describing the software, devices used to collect the electromyography data, characteristics of the signal (frequency, sample size), and the structure of the file.
● USAGE.txt file text where is described what the data has been used for and possible ways and disciplines where it is useful to use this data. Suggestions of tools to change file formats and recommended software to use will also be mentioned.

What data quality control measures will be used?

Data collection will use standardized tools where possible and research staff will be trained in their use. This will help to ensure uniformity in data collection, minimize data omissions and streamline collection and storage process.
Examples include:
● Pain intensity and interference will be measured using the ISCIPBDS 3.0
● Health related quality of life (HRQOL) will be measured using the EQ-5D-5L
● Neuropathic pain symptom severity will be measured using the NPSI
● Screening questionnaire will be completed over the phone to confirm study eligibility criteria.
● Anthropometric measurements (height, weight, hip width, leg length) will be assessed in person to confirm compatibility with the exoskeleton.

Data collection and data management training for research staff by CSTAR is included, standardising both the collection and the filing/storing of all data and meta-data. Published data collection tools with validity and reliability will be utilised specific to SCI NP, where available. Published standards for the design, conduct and reporting of trials (e.g. CONSORT, SPIRIT, etc) will be used, optimising validity.

Researchers will be certified for Research Integrity Training; Good Clinical Practice, Data Management Training and GDPR Fundamentals. Research data will be handled in line with data protection statutory requirements. Existing institutional infrastructure will be used for the storage of electronic research data, using both encryption and password protection for security purposes with regular back-ups.

Approximately 10% of paper-based proforma will be independently cross-checked against electronic files foraccuracy. Data discrepancies will be discussed with the researchers and amended accordingly. Assoc. Professor Ricardo Segurado will provide training on data management to the researchers.

Storage and backup during the research process

How will data and metadata be stored and backed up during the research process?

All members of the research team will install operating system and application updates when they are available, install Sophos endpoint protection software provided by UCD and use a secure network connection when connected to the Internet. While on campus either the cabled network or the Eduroam Wi-Fi network will be used and when off-site the Staff Virtual Private Network (VPN) will be used to secure the network connection .

Data will be entered into an electronic database (password protected) by the researcher, supported by CSTAR at UCD. Security measures include password protected computers, firewall protection, file encryption and access rules, power failure/surge and malware protection.

Existing institutional infrastructure (Google Drive and Novell Drive (Net Storage)) will be used for the storage of electronic research data, using both encryption, password protection and Multi-Factor Authentication for security purposes with weekly back-ups to both google drive and external hard drives.

How will data security and protection of sensitive data be taken care of during the research?

Ethical approval is in place from UCD HREC and NRH HREC. All research will be guided and conducted in line with the UCD Policy on Research Ethics, UCD Code of Good Practice in Research with Humans and Animals and UCD Research Integrity Policy.

Written informed consent will be obtained from every participant for data collection and any future use of data prior to collection of any data.

When transferring data between users, HEAnet FileSender will be used as a secure application which provides for end-to-end encryption.

Data will be entered into an electronic database (password protected) by the researcher, supported by CSTAR at UCD. Security measures include password protected computers, firewall protection, file encryption and access rules, power failure/surge and malware protection.

1 year after the conclusion of the project, the master sheet will be destroyed and anonymised files will be deposited in a trusted data repository (e.g. Zenodo) with a permanent identifier (DOI) and available to the wider research community with an open license (CC0). Participants will have an opportunity to consent or not to anonymised data archiving. In line with HRB Open Research Policy, repositories hosting the data will be cited in research papers.

All obtaining, use and storage of data will be in line with GDPR legislation and UCD data protection policy. All researchers will be certified for Research Integrity Training, Data management training and GDPR fundamentals.

Legal and ethical requirements, codes of conduct

If personal data are processed, how will compliance with legislation on personal data and on security be ensured?

All collection and future use of data will be fully in line with the terms of written informed consent obtained from participants.
All collection and future use of data will be guided by and in line with GDPR regulations and UCD's data protection policy.
All personal data will be pseudonymised/anonymised when transferred from case report forms to electronic softwares (REDCAP, Google Drive, Novell Drive, SPSS, NVIVO, etc.)
Data collection from participants will be completed by an independent assessor not involved in the delivery of the interventions.
Associate Professor Ricardo Segurado from UCD Centre for Support and Training in Analysis and Research (CSTAR) will be overseeing that data collection, data use and data analysis is conducted in line with all aforementioned relevant legislation and policies including providing training on data management to all researchers who will be involved in this activity.

How will other legal issues, such as intellectual property rights and ownership, be managed? What legislation is applicable?

Participants in this study who provide their personal data will be owners of their data. When providing written informed consent, they provide permission to the research team for compliant collection, use and sharing of their data in line with what was agreed within the consent process.

Publication of research articles/thesis, presentation of posters and any other dissemination of information associated with this research to third parties external from UCD will be compliant with terms and conditions of research funding provided by the HRBI, the UCD authorship policy and the UCD IP policy.

What ethical issues and codes of conduct are there, and how will they be taken into account?

Full ethical approval is in situ from UCD HREC and NRH HREC prior to the commencement of human research.

Participants will be free to withdraw from the study at any stage and without penalty and with no impact on their usual care and support structures. Data collected to the point of withdrawal will be used in the analysis unless that participant requests it is redacted.

Adverse events and near misses will be logged throughout the study period and reported to the Data Management Committee, including date it occurred, the circumstances, assistance provided or onward medical referral (i.e. medical attention required) and what was implemented to prevent this occurring again.

The Project Manager and PI will be advised of each event immediately and will determine what strategies need to occur based on the severity of the event. Serious adverse events (SAEs) will be reported to the SAE oversight committee and the trial will be paused pending investigation.

SAEs will be reported to the Ethics Committee within 15 days of occurrence. In relation to COVID-19 and other community transmissible diseases, we will follow public health advice and HSE policies in relation to infection control measures when the study starts.

The following codes of conduct and guidelines will be followed in all aspects of conducting this research:

- UCD HREC guideline on informed consent
- UCD HREC guideline on vulnerable groups in research
- UCD HREC guideline on risk and harm in research
- UCD Code of Good Practice in Research with Humans and Animals, 2019
- UCD Research Integrity Policy

Data sharing and long-term preservation

How and when will data be shared? Are there possible restrictions to data sharing or embargo reasons?

An inter institutional data sharing agreement will be developed and approved by UCD legal to allow data to be shared with RCSI for the health economic evaluation work package of this project. This will be a controller-processor agreement. A data sharing agreement (controller-controller) will also be developed with the National Rehabilitation Hospital (NRH) to enable sharing of health demographic data pertaining to participant's injury if the participant does not know this information themselves (time since injury, neurological level of injury and ASIA impairment score). All data sharing will be conducted using secure, encryption protected HEAnet software. Data and the encryption key will be stored on separate drives (i.e. one on Novell Drive, one on Google Drive) and the encryption key will be sent via separate means to the data to minimise any risk of data breaches.

Data sharing agreements are with organisations within Ireland and the EU so no restrictions or embargos apply. However, data sharing will be implemented in line with GDPR legislation namely the data minimisation principle. This data will be retained for a

minimum of 10 years in line with UCD's RDM policy.

A Data Availability Statement relating to underlying data needed to validate the results presented in scientific publications will be included with publication outputs at the time of publication or as soon as possible.

At the end of the project, data selected for preservation will be archived in Zenodo repository. As outlined above, metadata and documentation describing the data and research process will also be made available, in compliance with the FAIR data principles.

How will data for preservation be selected, and where data will be preserved long-term (for example a data repository or archive)?

1 year after the conclusion of the project, the master sheet containing patient data will be destroyed and anonymised files will be deposited in a trusted data repository (Zenodo) with a permanent identifier (DOI) and available to the wider research community under a CC0 license. Participants will have an opportunity to consent or not to anonymised data archiving. In line with HRB Open Research Policy, repositories hosting the data will be cited in research papers. This data will be retained for a minimum of 10 years in line with UCD's RDM policy.

What methods or software tools are needed to access and use data?

It is not envisaged that any special software will be required to access the datasets on Zenodo.

How will the application of a unique and persistent identifier (such as a Digital Object Identifier (DOI)) to each data set be ensured?

Anonymised files will be deposited in a trusted data repository (Zenodo) which automatically assigns a permanent identifier (DOI)

Data management responsibilities and resources

Who (for example role, position, and institution) will be responsible for data management (i.e. the data steward)?

UCD and the PI Assoc Professor Olive Lennon will be the data controllers with responsibility for the data collection, storage, use as per consent, and compliance with FAIR data principles supported by UCD data protection champions. CSTAR will be responsible for data and metadata management.

DMP's and data sharing agreements will be curated for UCD, NRH and RCSI who will be involved in data management. This will be done in collaboration with the Data Protection Officer (DPO) of each institution. The PI will be responsible for implementing and updating the DMP as necessary.

What resources (for example financial and time) will be dedicated to data management and ensuring that data will be FAIR (Findable, Accessible, Interoperable, Re-usable)?

Within the scope of the grant provided by the HRB, funding has been allocated to acquiring the necessary hardware and software for the creation & reuse of data and deposition & preservation and to prepare the data for sharing/preservation (data curation). Funding has also been allocated to the costing of a repository for future use of data. Breakdowns are as follows:

Data science costs (use of CSTAR resources): €1800

Data collection and management training provided by CSTAR: €2250

Data and metadata management (CSTAR): €3750

Ethics application and approval (UCD Clinical Research Centre): €1888

GDPR compliance/DPIA approval (UCD CRC): €2350