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TITLE PAGE

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ABSTRACT

Introduction A spinal cord injury (SCI) and its consequences predispose to s physical inactivity and weight gain and thus death due to cardiovascular diseases is even more frequent among people with SCI compared to the general population. In the literature, consensus is established about an interdisciplinary multimodal approach for prevention and treatment of cardiovascular risk factors including overweight and obesity in people with SCI, focusing on diet, physical activity (PA) and behavioral interventions. This study, focus on how to implement and use multimodal approaches as elements in patient education in a clinical setting, i.e. describing not only the effect of the multimodal intervention but also the effectiveness.

Methods and analysis All patients who are 18 years or older, with an SCI within the last 12 months and admitted to highly specialized rehabilitation, are included regardless of etiology to the SCI or neurological level. The project consists of a primary study designed as a controlled pre-post multi modal pragmatic clinical intervention study, designed with 6-months of follow up. A national cohort study on Body Mass Index (BMI) is conducted and serves as historic control. A central part of the intervention in the primary study is to create a new uniform and systematic approach to patient education about cardiovascular risk factors, PA and a healthy diet, in complement to standard rehabilitation. The strategic approaches to cardiovascular risk factors, beginning at the onset of the primary SCI rehabilitation and integrated into the existing setting at predetermined time points throughout the rehabilitation continuum, constitutes the aims for cardiovascular prevention. Outcome measures are collected at admission, discharge and follow-up 6 months after discharge and includes measures of VO2peak (primary outcome), BMI, body composition, metabolic profile, neurologic status, level of functioning, depression, quality of life, objective PA (accelerometry), self-reported PA, self-assessed ability to be physically active, shared decision making, and measurement of dietary habits. In relation to VO2peak, the test- retest reliability of four different test protocols will be investigated in a clinical context. Likewise the test-retest reliability of a multisensor accelerometer in a clinical rehabilitation setting will be investigated.

Ethics and dissemination

Informed consent is retrieved from all participants by the principal investigator. The interventions in the project are closely related to the content of the present rehabilitation, and the risk of pain and discomfort is considered modest. Any unintended events related to the elements of the intervention are reported according to existing regional procedures. Data is stored in a web-based database (Redcap) with limited access and ID-code. The prospective cohort study and the primary study in the project are registered at Clinicaltrials.gov. Attempts to publish positive and negative results in relevant scientific journals concerning SCI will be made. Important protocol modifications are reported to the Committees on Health Research Ethics in the Capital Region of Denmark.

Registration details

The project is approved by the Committees on Health Research Ethics in the Capital Region of Denmark on 10.07.2018 (Journal-nr.: H-18018325) and the Danish Data Protection Agency (j.nr. VD-2018-380, I-Suite nr.: 6631) and (RH-2017-345, I-Suite nr.: 06052). The project is registered at Clinicaltrials.gov (NCT03689023) and (NCT03369080). See the World Health Organization Trial Registration Data Set in table 1.

Article summary

Strengths and limitations of this study

It is a strength that the cohort study on BMI is representative and includes both SCI-centers in Denmark and the intervention study includes all newly injured people with SCI admitted to rehabilitation at the East Denmark SCI-center.

It is a strength that several predefined protocols for assessing VO2peak in a clinical setting are used due to the heterogeneity of the functional level in the SCI population.

It is a strength that the controlled intervention study is based on a pragmatic real-life approach by including existing settings and work flows to a large extent.

It is a limitation however, that the controlled intervention study is based on a pragmatic real-life approach whereby the implementation of multimodal interventions may be challenged due to changes in the clinical setting.

It is a limitation that the intervention study is not randomized .

INTRODUCTION

The incidence of traumatic spinal cord injury (SCI) in Denmark is 10-15/mill. annually [1], while non-traumatic SCI in recent years has constituted approximately 60% of all newly injured admitted to the two SCI-centers in Denmark. It is a life changing event that may affect all bodily functions below the level of lesion with significant costs for the individual and society and requires highly specialized interdisciplinary rehabilitation aiming at the highest possible level of independent functioning. The rehabilitation at Clinic for Spinal Cord Injuries in Eastern Denmark (CSCI) generally includes functional training, strength training, cardiovascular exercise and fine motor training of the upper extremities. Moreover, continuously assessment and action is taken in relation to circulation, respiration, thermoregulation, bowel, bladder, skin, pain and spasticity, as well as aids compensating the level of functioning, including communication aids and splinting. Likewise counseling related to social and economic issues, sexual function and psychological issues is provided.

On the long-term, SCI and its impairments predispose to increased cardiovascular risk and premature cardiovascular death, and recently a clinical practice guideline addressing cardiometabolic disease after SCI has been published [2]. However, targeted strategic patient education based on principles that includes an individualized face to face interaction between patients and health care professionals, including individualized counselling on long term cardiovascular risk is not systematically integrated at early stages of specialized SCI rehabilitation at CSCI, although there may be an opportunity at this stage of the

rehabilitation to target the link between the injury-related immediate impact on functionality and long-term health consequences. Likewise, systematic health promotion related to Body Mass Index (BMI), diet, smoking, alcohol intake and physical activity (PA) is not provided systematically, and assessment of metabolic profile and body composition is not a part of standard care. A systematic approach related to health care promotion may ensure that all patients at CSCI receive information and knowledge related to health promotion and the risk of cardiovascular disease which may support patient adaptation and adherence to recommended PA and healthy diet.

Therefore, the cardiovascular risk factors, including weight gain and consequences of an inactive lifestyle during and after the primary rehabilitation, defines the primary systematic approach in the current controlled study and sub-investigations.

The course of overweight

The prevalence of overweight in people with SCI is conservatively estimated to 66% and has been found to be one of the most common cardiometabolic risk factors in people with SCI, and contributes to, and increases, the cardiovascular risk profile in wheelchair dependent people with paraplegia [3], [4] [5, 6]. Energy expenditure decreases significantly after sustaining a SCI and remains low. Body fat and body weight, although decreasing in the acute phase, increases in the subacute phase, and a loss of lean body mass in the lower extremities and trunk respectively has been observed during the first year after injury [7]. BMI increases gradually during the first years after discharge from the primary rehabilitation [8]. Obese people with SCI achieve a lower level of functioning during primary rehabilitation than people with normal weight [9]. Overweight in people with SCI is associated with increased risk of depression, while PA may contribute to a decreased prevalence of depression and increased quality of life [10, 11].

Surveys concerning the course of BMI and body composition during, and after discharge from the primary rehabilitation, do not exist for people with SCI in Denmark.

Impact of physical activity on health and fitness

In the general population PA is associated with beneficial effects on diseases contributing to the metabolic syndrome, and combined with diet therapy the effect increases [12]. Similar effects of PA among people with SCI is described previously and greater aerobic capacity is associated with greater cardiovascular health [13].Evidence based exercise guidelines for cardiometabolic health in people with SCI recommends a minimum of 30 minutes of moderate to vigorous aerobic exercise three times weekly to reduce cardiovascular risk factors [14]. However, participation in leisure time PA and joining sports activities after discharge from the primary rehabilitation is low in people with SCI [10, 15]. Intra- and extra personal factors are influencing participation in PA, including self-efficacy related to being physically active [16]. Therefore a new paradigm is focusing on avoiding inactivity [15]. Descriptions of the amount and intensity of objectively measured PA in people with SCI is relatively rare and is not known in a Danish setting. Likewise the course of VO2peak during and after discharge from primary rehabilitation is less described.

There is a gap in the literature describing the effect of interventions targeting cardiovascular risk reduction. Thus there seems to be a need for studies describing the effect of interventions in a real clinical setting through a pragmatic study design, as supplement to studies investigating the effect of interventions in a homogeneous and standardized setting [17]. Likewise, the course of BMI, body composition, VO2peak and

amount of PA during and after primary rehabilitation, as well as the associations and interactions between the risk of depression, quality of life, overweight and PA in a Danish context has not been described previously.

Objectives

This study will investigate the effect of a uniform and systematic institutional strategy in a clinical setting, incorporating targeted strategic patient education about cardiovascular risk factors, PA and a healthy diet lifestyle initiated early in the primary rehabilitation process, compared to a historic control.

STUDY DESIGN

The study consists of a primary study designed as a controlled pre-post multi modal pragmatic clinical intervention study, with 6-months of follow up and a historic control conducted as a prospective cohort study (fig 1).

Sub-investigations:

BMI is considered a high risk determinant due to the impact of overweight on the cardiovascular risk profile and level of functioning in wheelchair dependent people with SCI [3], [4] [5, 6]. Therefore, a prospective representative longitudinal national survey of BMI is conducted in collaboration with SCI Center of Western Denmark, before the onset of the controlled intervention, and serves as historic control (sub-study 1). Additional objective outcomes measures will be collected at CSCI during the historic survey period including measures of PA, physical capacity and body composition. Accordingly, two sub-studies regarding test – retest reliability of a VO2 peak test (sub study 2) and a multi sensor accelerometer (sub study 3) respectively will be performed for two reasons. First, VO2 peak and accelerometry are considered valid methods to measure the effect, amount and intensity of PA at discharge from the primary SCI rehabilitation. Secondly, these measures will be collected repeatedly during the prospective controlled intervention study and serve as individual motivational components in the patient-clinician educative PA communication, besides being outcome measures. For this reason, assessing the test retest reliability of the two procedures is essential.

METHODS AND ANALYSIS

The SPIRIT reporting guidelines are used in the reporting of the clinical trial [18].

Patient involvement

A user panel consisting of both newly injured as well as experienced people with SCI was established and involved in the early phase of the protocol development. All the participants were hospitalized at CSCI when they were interviewed about their perception of the present health promoting practice at the clinic. The user panel called for more information in the early phase of rehabilitation about cardiovascular risk, PA and diet as well as more support and guidance about appropriate diet and being physical active, which is the main aim of the project. The results of the project will be disseminated to project participants.

Participants and eligibility criteria

Inpatients who are 18 years or older and injured with SCI within the last 12 months and admitted at CSCI, are included regardless of etiology, being traumatic or non-traumatic, neurological level or completeness[1] of the lesion if informed consent is retrieved. In sub study 1 all newly injured people with SCI admitted at the SCI Centre of Western Denmark are also included. Sub study 1 serves as historic control group and the intervention in the primary study is a part of new standard care. Therefore, randomization or blinding is not appropriate.

Exclusion criteria for the VO2peak test includes motor complete SCI (AIS A and B) at C4 level or above, and a need for ventilator. Other exclusion criteria are the presence of decubitus, severe spasticity or musculoskeletal problems considered at risk of aggravation during testing or preventing completion of the test.

Sub study 3 includes a convenience sample of 20 patients aiming at ensuring a broad variation of age, gender, neurological level and completeness of SCI.

Primary study: A systematic interdisciplinary multimodal intervention which, as a part of usual care, facilitates physical activity, healthy diet and maintenance after discharge through strategic patient education, with the aim of decreasing cardiovascular risk

This pre-post study includes all patients, 18 years or older, with a new SCI who are admitted at CSCI during a period of 12- 18 months. The study includes a follow up 6 months after discharge from primary rehabilitation.

Approximately 70 patients with a new SCI are admitted to CSCI annually and with a great variation in length of rehabilitation. Therefore, complete data sets from admission to follow up are expected for approximately 50-60 patients during this period.

Intervention

The multimodal intervention will be an integrated part of usual care during the project period, and all newly injured patients will receive all the multimodal components, or parts of them, dependent on e.g. the level of injury. Rehabilitation of the physical level of functioning and physical capacity (e.g. physiotherapy) will take place unchanged as usual and is a mandatory core component of highly specialized SCI rehabili-

[1] The completeness of the injury is graded according to the ASIA Impairment Scale (AIS). AIS is used to determine the degree of motor and sensory function below the level of the SCI. A complete or incomplete injury is defined as absence or presence of sensory and motor function in the most caudal sacral segments. A = sensory and motor complete; B = sensory incomplete without motor function > 3 levels below the motor level of injury on both sides of the body; C = motor incomplete, with preserved motor function below the level of injury and where > 50% of the key muscles below the injury level have a degree < 3 by manual muscle test (MMT); D = motor incomplete with preserved motor function below the level of injury and where > 50% of key muscles below the injury level have a degree > 3 by MMT; E = normal sensory and motor function in all segments.

tation, although decisions made by the patient during the rehabilitation about PA may be integrated into the rehabilitation program in order to achieve the patients goals for PA during and after the rehabilitation period.

A central part of the intervention is to create a uniform and systematic approach to targeted strategic patient education of the patients about cardiovascular risk factors, PA and a healthy diet through a systematization of the existing clinical setting and treatment interventions.

In the process of preparing and reorganizing the institutional approach towards addressing cardiovascular risks, *pre-education* of the interdisciplinary health care personnel and peers with SCI, clarifying the roles of each profession in relation to the targeted patient education, are mandatory. Moreover, pocket cards with evidence- based recommendations related to PA, diet and BMI in people with SCI are provided to all health care professionals and peers with SCI. Also, a timeline for systematic targeted approaches during the primary rehabilitation will be illustrated on the pocket card (Fig. 2)

The patients receive information and instructions about PA and healthy diet through targeted strategic patient education based on principles that includes an individualized face to face interaction between patients and health care professionals, while working towards, and improving a specific health related outcome through adherence to the working processes as e.g. lifestyle [19]. The strategic approaches, beginning at the onset of the primary SCI rehabilitation and integrated into the existing setting at predetermined time points throughout the rehabilitation continuum, constitutes the aims for secondary and tertiary cardiovascular prevention.

Targeted strategic patient education of the patients and their relatives is generally carried out by all the health care professions in different educational settings of [20, 21], with a focus on clarifying the importance of PA and a healthy diet. This involves training sessions [22], and feedback on physiological outcome measures and tests, that also serves as motivational tools. Additionally, goal setting meetings, tools for shared decision making [23] [24] [25], and use of mentors with SCI are also integrated as components supporting decision making about PA and healthy diet. BMI and diet is evaluated 3 months after discharge in an outpatient setting (see appendix for a more detailed description of the strategic interventions).

All components of the strategic intervention are offered the patients as a mandatory part of the systematic intervention, ensuring that information and education of the patients is provided and decisions about PA and healthy diet are made. However, the extent to which the patients engage in e.g. decision making and goalsetting about PA and healthy diet is an individual decision. Deciding not to set goals or make decisions about PA and healthy diet, is respected by the interdisciplinary health care professionals in respect of the autonomy of the patient.

Several outcome measures used to evaluate the intervention at admission, discharge and at follow up 6 months after discharge, are also part of the intervention as motivational components and comprises of the following: BMI, body composition measured by Dual- energy X-ray Absorptiometry (DXA), physical capacity (VO2peak), PA (Actiheart multisensor accelerometer) and blood samples describing metabolic profile.

Sub study 1. Prospective representative national survey of Body Mass Index.

This study includes all patients with a new SCI hospitalized at CSCI or SCI Center of Western Denmark during a period of 10 months whereby 100 patients are expected to participate. Data concerning BMI, level of functioning (SCIM III) and neurological status (ISNCSCI) are collected at both centers. Patients with a new SCI (within the last 12 months) who are admitted for rehabilitation several months after the time of injury, are also included in the prospective survey, and therefore BMI at the time of injury is collected for all patients at admission to primary rehabilitation from both the patient's medical record and by asking the patient about weight and height at the time of injury. At CSCI, BMI every 6 weeks, quality of life (QoL SCI)), depression (PHQ-2)), amount of PA (Leisure Time Physical Activity Questionnaire for people With Spinal Cord Injury (LTPAQ-SCI)) and self- assessed ability to be physically active (ESES) will be collected additionally during this period, at admission, discharge and at follow up 6 months after discharge. A measure for physical capacity (VO2peak), and body composition (DEXA) is performed as well at discharge. Data from this sub study serves as a historic control for the Intervention study.

Sub study 2. Test-retest reliability of a VO2 peak test

This study includes all patients participating in sub study 1 who are able to perform the test at discharge from primary rehabilitation. The patients are allocated by randomization to a test session of either intra- or interrater reliability. Four different pre -defined exercise protocols are used, due to the complexity of a SCI, in order to reach pre-defined criteria for VO2peak. For people with an incomplete SCI, a seated cross-trainer is used (NuStep T5XR®) with an incorporated standard, as well as modified, test protocol in the equipment software. Equipment and modified protocol is reliable in people with traumatic brain injury and has been validated in healthy persons [26, 27]. In people with an incomplete SCI the equipment is safe and involves a large amount of muscle mass ensuring completion of the test [28]. In case the equipment and protocols are too difficult for people with a complete tetraplegia, paraplegia or very deconditioned patients, which may hinder reaching VO2peak, an arm cranking ergometer will be used (SCI FIT Pro1®). The test protocols used on the SCI FIT arm ergometer is established from the most common protocols for people with tetra- and paraplegia during rehabilitation, reported in a recent systematic review [29]. If predefined criteria for VO2peak are not reached at test 1, a more suitable protocol is chosen for test 2 in order to reach VO2peak and retested at test 3. The test-retest study takes place at discharge, separated by 48 hours or within maximum 5 days between tests at the same time of the day. The participants refrain from caffeine, alcohol and intensive physical exercise on the day of testing as well as tobacco smoking two hours before the test. Bladder emptying is to be performed before the test.

Sub study 3. Test-retest reliability of a multi censor accelerometer.

This study includes a convenience sample of 20 patients ensuring a representative sample of individuals with para- and tetraplegia, complete and incomplete injuries, age and gender. The equipment used for monitoring amount and intensity of PA consists of sensors registering acceleration and heart rate and is placed on the thorax of the participant with two surface electrodes. The equipment has previously been used in wheelchair dependent people with SCI, although the reliability of the equipment in an inpatient setting has not previously been assessed [30]. The precision of the equipment is higher when calibrated

individually to the participant using measures of energy expenditure during rest and during an exercise testing whereby heart rate is retrieved as well. [31]. In this study the individual calibration will be made in relation to the VO2peak test, and continuous measurements of amount and intensity of PA will be made during a period of 48 hours. The test-retest is performed over a period of two weeks on identical days of the week in order to ensure comparability.

Outcome measures

Outcome measures evaluating the intervention comprises of the following.

Primary outcome

Oxygen uptake: Is measured as VO2peak during a maximal exercise test and is gold standard for measuring aerobic capacity. For people with a SCI several test protocols have been used [36].

Secondary outcomes

Objective PA: Is measured in a sub-sample in the historic control cohort and the participants in the intervention study with a multisensor device (Actiheart®) recording accelerations and heart rate. It is previously used for wheelchair users with SCI and individual calibration is important to get the most accurate data [31]. Individuals with SCI should participate in at least 150 minutes of physical exercise per week, according to their ability, beginning as soon as possible following acute spinal cord injury. When individuals with SCI are not able to meet these guidelines, they should avoid inactivity [2].

Bodyweight: Is measured as BMI which is the most widely used outcome measure for measuring bodyweight in people with SCI. BMI is not sensitive enough to distinguish between fat mass and lean body mass nor overweight in people with SCI. The cut-off for overweight in adult people with SCI is >22kg/m^2 [32] [2]. BMI is already collected as part of the existing routines and data for BMI every 6 weeks until discharge will be included in the project.

Body composition: Is determined by Dual energy x-ray absorptiometry (DXA) which is gold standard for assessing obesity and body composition. In people with SCI, adult men with >22% bodyfat and adult women with >35% bodyfat should be classified as obese [2].

Metabolic profile: Consists of CRP as a marker for inflammation, lipid profile describing Total cholesterol, Triglycerides, HDL cholesterol and LDL cholesterol which are all included in the International SCI Endocrine and Metabolic Function Basic Data Set. Triglycerides should not exceed ≥ 150 mg/dL (1.7 mmol/L). HDL cholesterol should not be less than 40 mg/dL (1.03 mmol/L) in men and less than 50 mg/dL (1.29 mmol/L) in women [2]. LDL cholesterol should not exceed 3,0 mmol/l [33]. Hemoglobin A1c serves as a marker for carbohydrate metabolism and is included in the International SCI Endocrine and Metabolic Extended Data Set [34, 35]. Criteria for the diagnosis of pre-diabetes include A1C 5.7 to 6.4% (39 to 47 mmol/mol) and for diabetes the criteria include A1C >6.5% (48 mmol/mol) [2]. According to the approval by the Committees on Health Research Ethics in the Capital Region of Denmark, blood samples will not be stored after analysis.

Blood pressure (BP): Hypertension in people with SCI varies depending on the injury level, severity and etiology. BP should not exceed ≥ 130/85 mm Hg.

Level of functioning: Is determined by the Spinal Cord Injury Independence Measure III (SCIM III) which is a valid and reliable outcome measure designed to assess level of functioning in people with SCI in a clinical setting and in research [36] [37, 38] [39].

Neurologic status: Is determined by the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) and is the most widely used classification in people with SCI [40, 41].

Depression: Is measured by the Patient Health Questionnaire- 2 (PHQ-2) which is a generic outcome measure for measuring depression. In people with SCI a cut-off score of 3 is associated with a sensitivity of 83,3% and specificity of 95,7% [42].

Quality of Life: Is measured by the International SCI Quality of Life Basic Data Set (QoL SCI) which consists of three questions regarding satisfaction with life in general as well as physical and mental health. It is a valid outcome measure with good internal consistency [43] [44].

Self - reported PA: Is measured by the Leisure Time Physical Activity Questionnaire for people with SCI (LTPAQ-SCI) which is a self- administered questionnaire concerning leisure time PA, including amount and intensity the past 7 days. Reliability and validity of the self- reported activity level is satisfactory in the moderate and high intensity area [13]. An additional question concerning PA beyond leisure time PA (i.e. PA as part of the rehabilitation) is added in sub-study 1. The question is designed as the original questions and the same intensity scale is used. During the intervention study a version of LTPAQ-SCI adjusted to a Danish context will be used. This version is approved by the developers of the original LTPAQ-SCI and includes active transportation and active physiotherapy.

Self-assessed ability to be physically active: Is measured by the Exercise Self Efficacy Scale for people with SCI (ESES). It is an outcome measure developed for assessing self-efficacy related to PA in people with SCI and consists of 10 questions which are answered on a 0-4 scale. ESES is reliable with a high internal consistency (Cronbach`s alpha 0.94). Also content validity in the form of face and construct validity are satisfactory [45].

Measure of shared decision making related to patient decision aids for PA and healthy diet:

Is measured by the 9-item Shared Decision Making Questionnaire (SDM-Q-9) and describes the process of Shared Decision Making between health care professionals and the patient from the patient's perspective. SDM-Q-9 consists of nine statements, which can be rated on a six-point scale from ''completely disagree'' (0) being the worse score to ''completely agree'' (5) being the best score. Summing up all items leads to a raw total score between 0 and 45. SDM Q-9 is only used at discharge.

Measure for a varied and healthy diet in an appropriate amount: Is measured by the Nordic monitoring of diet, PA and overweight (NORMON) developed in a Nordic collaboration and used for common monitoring [46]. The questionnaire explores how often 16 food indicators are consumed the last 12 months, of which several are recommended in the Nordic national nutritional recommendations. Also questions related to alcohol intake, smoking and PA are included The questionnaire was validated in 2009 against existing

questionnaires about diet [47]. In this study the questionnaire will be modified, so that the patients will be asked to recall their diet habits the last month.

Statistics

Numeric continuous data collected at admission, discharge and follow up is reported descriptively as mean and standard deviation together with 95% confidence intervals, or as median, upper and lower quartile as well as interquartile range. Changes over time are reported on the basis of paired t-test. In sub study 3 and 4 the reliability of the outcome measures is analyzed by paired t-test, Pearson´s product-moment correlation and coefficient of variation or intraclass correlation coefficient between the test- retest sessions. Dropout analysis is made for the primary outcomes. All available data are analyzed as intention to treat with no imputation made.

Ethics and dissemination

During the intervention period, all newly injured patients who are admitted for rehabilitation at CSCI are offered the treatment and tests included in the intervention to the extent they are able to participate depending on e.g. the level of lesion and completeness of the injury, as a mandatory part of usual care. Informed consent is retrieved in order to get permission to analyze the data generated during the project. The intervention in the project is closely related with the content of the present rehabilitation, and the risk of pain and discomfort is considered modest. During the VO2peak test, there will be special attention on symptoms of autonomic dysreflexia (AD) in people with SCI above Th5-6. In case of AD, the exercise test is disrupted and relevant actions are initiated. It is assumed that any risks are by far surpassed by the therapeutic gains, such as an expected risk reduction of cardiovascular disease and consequently mortality. Any unintended events related to the elements of the intervention are reported according to existing regional procedures, and compensation is covered by the normal procedures for unintended harm during hospitalization. The study is reported to the Committees on Health Research Ethics in the Capital Region of Denmark, the Danish Data Protection Agency and is registered at Clinicaltrials.gov.

Data statement section

Data from the patient's electronic medical record and the outcome measures used, is stored in a web-based database (Redcap) with limited access and ID-code to which data is transferred directly, or by an encrypted USB-stick. Only the unique identification number of the patient will be exported from Redcap during data analysis. Data is stored until December 31, 2027 after which paper material is shredded and data files are deleted. The Redcap database will no longer be accessible after this date. The principal investigator has access to all trial data. Data can be accessed by request to the corresponding author after publications related to the Ph.D project are made. A data monitoring committee is not established.

DISCUSSION

This study will investigate the effectiveness of a uniform and systematic institutional strategy incorporating targeted strategic patient education about cardiovascular risk factors, PA and a healthy diet lifestyle with an early off-set in the SCI diagnosis during primary rehabilitation, compared to a historic control. Our findings will be discussed against recent studies suggesting that an interdisciplinary and multimodal approach in prevention of cardiovascular risks among people with SCI with a focus on diet, PA and

behavioral interventions, is favorable [15] [48] [49] [16, 50] [51]. Crucial components in the present intervention, of which several also acts as outcome measures, are autonomy in relation to decision making as well as support and follow up from health care professionals and mentors with SCI. Of considerable interest a qualitative meta-synthesis concluded, that timely information about PA and its benefits in relation to the diagnosis and behavioral interventions using goalsetting and motivational feedback trough physical tests might be an important patient activating tools [52], and is line with a recent systematic review by Greaves et al [24]. As incorporated in the present intervention, the review by Greaves et al. also strongly recommend, that interventions in the clinical setting should contain both group sessions and individual sessions as well as interdisciplinary interventions that focus on maintaining PA and healthy diet [24].

Several of the outcome measures used to evaluate the intervention, are a part of the intervention as recommended in the clinical guidelines for identification and management of cardiometabolic risk after spinal cord injury [2]. The outcome measures also serve as individual motivational tools. The primary outcome measure chosen, is VO2peak while a significant and positive relationship exists betweenVO2peak and some cardio metabolic markers such as lipid profiles and fasting insulin in people with SCI [13].Therefore, physical activity and exercise increasing physical capacity may also reduce the risk of cardio-vascular disease [53]. Furthermore physical capacity measured as VO2peak is positively associated with functional independence [54], less physical strain during activities of daily living[55] and life satisfaction [56] in people with SCI, although other measures of physical capacity have an important, and in some cases stronger impact on functional independence [54].

For people with SCI, several test protocols have been used for assessing VO2peak [36]. In this study four different pre -defined exercise protocols are used, to make VO2peak testing feasible for clinical physiotherapist who, although trained in using the test equipment, are inexperienced in determining the appropriate workload during VO2peak testing, which is difficult due to the complexity of a SCI. In this way- if predefined criteria for VO2peak are not reached, a more suitable protocol is chosen to reach VO2peak. The protocol and equipment used at admission in the intervention study must be identical at discharge. If a patients neurological and functional level has improved to an extent where using a different protocol and equipment will help improving the actual VO2peak, an additional test at discharge will be performed on a separate day. Data from both tests will be evaluated and published and the new protocol will be repeated at follow up 6 months after discharge. This approach to testing VO2peak in a clinical setting has, to the best of our knowledge, not been described previously

Among the secondary outcome measures used to evaluate the intervention are measures of PA. Objective PA will be measured by the Actiheart accelerometer, which has previously been used for wheelchair users with SCI in a laboratory or outpatient setting [31]. In this study it will be used in an inpatient setting and in people with SCI and ambulatory function, which has not been described previously. As a measure of self-reported PA, a validated Danish version of the Leisure Time Physical Activity Questionnaire for people with Spinal Cord Injury will be used. This version has been adapted to a Danish context in close collaboration with the developers of the original questionnaire, whereby PA in relation to active transportation, i.e. hand biking or wheeling as transportation to work or school, as well as active physiotherapy exercises are included, as this is common PA for people with SCI in Denmark.

The primary study is possible due to the length of stay during initial rehabilitation at CSCI, which is in average 85 and 86 days respectively for people with incomplete tetra- and paraplegia while average length of stay is 110- and 123 days respectively for people with complete tetra- and paraplegia (originates from internal inventory, 2014). The study is highly dependent of the interdisciplinary health care professionals and the patients' adherence to the new intervention. The interdisciplinary health care professionals adherence to the intervention is described and secured by a process inspired by a previously used prospective effect and process evaluation for complex trials, where at least 75% of the health care professionals must agree that a specific element of strategic patient education has become a part of clinical practice routines before it is considered implemented [57]. This evaluation is repeated every 6-8 weeks throughout the intervention period by the project manager. Likewise, perceived barriers for the implementation process is evaluated throughout the intervention period every 6-8 weeks by the project manager, in order to facilitate the implementation. Interdisciplinary coordination meetings three times weekly is used by the moderators to facilitate the implementation of the different elements of the intervention.

Patient adherence may be challenged as described previously where patients missed out in average 2.5 hours weekly of their rehabilitation [58]. Patient adherence to the intervention is described at discharge by the patient, who will document participation in the different targeted education elements by a checklist. On the other hand, a study from 2016 found that the most important factors facilitating participation in clinical studies, were the possibility of learning more about SCI and health which is made possible in the intervention study [59]. A review by Van Wyk et al. emphasizes that patient education is an important part of the interdisciplinary rehabilitation of people with SCI and recommend an individualized approach and the use of different settings in which the patient can receive the education [29].

Author Contributions

Nicolaj Jersild Holm has been primarily responsible for writing the protocol. Tom Møller (head supervisor),Fin Biering-Sørensen and Lone Schou (co- supervisors) have all contributed to the development of the protocol and study design, as well as feedback, supervision and contributions to the text writing. Lis Adamsen has read and commented on several of the protocol drafts and have contributed to ideas of how to ensure the adherence of the participants during the intervention. Line Dalsgaard has, in particular, contributed with sparring about the clinical setting and workflows integrated in the project and the initial development and writing of the protocol. All authors have approved the final version of the manuscript.

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Competing interest's statement

The authors have no interests of conflict related to the project in general or any of the subprojects.

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Table 1. World Health Orgainzation Trial Registration Data Set (Version 1.3.1)

Data category	Information
Primary registry and trial identifying number	ClinicalTrials.gov (NCT03369080) and (NCT03689023).
Date of registration in primary registry	12.11.2017 and 26.09.2018
Secondary identifying numbers	The Committees on Health Research Ethics in the Capital Region of Denmark on 10.07.2018 (Journal-nr.: H-18018325) and the Danish Data Protection Agency (j.nr. VD-2018-380, I-Suite nr.: 6631) and (RH-2017-345, I-Suite nr.: 06052)
Source(s) of monetary or material support	This work was supported by a mutual cooperation about the research program "Centre for Integrated Rehabilitation of Cancer Patients (CIRE) - Neuro/Psychology", between the University Hospitals Centre for Health Research, UCSF Copenhagen University Hospital Rigshospitalet Department 9701 Denmark, University College Copenhagen, Department of Nursing and Nutrition, and the NeuroScience Centre, Rigshospitalet.
Primary sponsor	This work was supported by a mutual cooperation about the research program " Centre for Integrated Rehabilitation of Cancer Patients (CIRE) - Neuro/Psychology", between the University Hospitals Centre for Health Research, UCSF Copenhagen University Hospital Rigshospitalet Department 9701 Denmark, University College Copenhagen, Department of Nursing and Nutrition, and the NeuroScience Centre, Rigshospitalet.
Secondary sponsor(s)	

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Public title	Health promotion and cardiovascular risk reduction in people with spinal cord injury - physical activity, healthy diet and maintenance after discharge: study protocol for a national cohort study followed by a clinical intervention study.
Scientific title	Health promotion and cardiovascular risk reduction in people with spinal cord injury - physical activity, healthy diet and maintenance after discharge: study protocol for a prospective national cohort study followed by a pre-post intervention study.
Countries of recruitment	Denmark
Health condition(s) or problem(s) studied	Spinal Cord Injury and the cardiovascular risk factor, including weight gain and consequences of an inactive lifestyle during and after the primary rehabilitation.
Intervention(s)	A controlled pre-post multi modal pragmatic clinical intervention study, with 6-months of follow up containing “new usual care” consisting of a uniform and systematic institutional strategy incorporating targeted strategic patient education about cardiovascular risk factors, physical activity and a healthy diet lifestyle starting early in the primary rehabilitation process.

	Comparator: A historic control conducted as a national prospective cohort study before “new usual care”
Key inclusion and exclusion criteria	Inclusion criteria: All patients who are 18 years or older, and with a Spinal Cord Injury (SCI) within the last 12 months and admitted at Clinic for Spinal Cord Injuries, are included regardless of etiology to the SCI, neurological level or completeness of the lesion if informed consent is retrieved.
	Exclusion criteria: Exclusion criteria for VO2peak test in the study includes motor complete SCI at C4 level or above, and assisted ventilatory function. Other exclusion criteria are the presence of decubitus, severe spasticity or musculoskeletal problems considered at risk of aggravation during testing or preventing completion of the VO2peak test.
Study type	Interventional. The study consists of a primary study designed as a controlled pre-post clinical intervention study and a historic control conducted as a prospective cohort study.
	Allocation: The intervention in the primary study is a part of new standard care. Therefore randomization or blinding is not appropriate.
	Primary purpose: prevention
Date of first enrolment	November 2017
Target sample size	160 in total based on both studies
Recruitment status	Recruiting
Primary outcome(s)	Oxygen uptake measured as VO2peak.
Key secondary outcomes	Body Mass Index, Body composition (determined by Dual energy x-ray absorptiometry), metabolic profile consisting of CRP as a marker for inflammation, lipid profile describing Total cholesterol, Triglycerides, HDL cholesterol, and LDL

	cholesterol and Hemoglobin A1c as a marker for carbohydrate metabolism, and blood pressure (BP).
Ethics Review	The project is approved by the Committees on Health Research Ethics in the Capital Region of Denmark on 10.07.2018 (Journal-nr.: H-18018325)
Completion data	June 2020
IPD sharing statement	Data can be accessed by request to the corresponding author after publications related to the Ph.D project are made.

Figure 1.

Timeline for all sub studies and used outcome measures. Figure A and B illustrates the prospective historic control study and the intervention study respectively

Fig. A

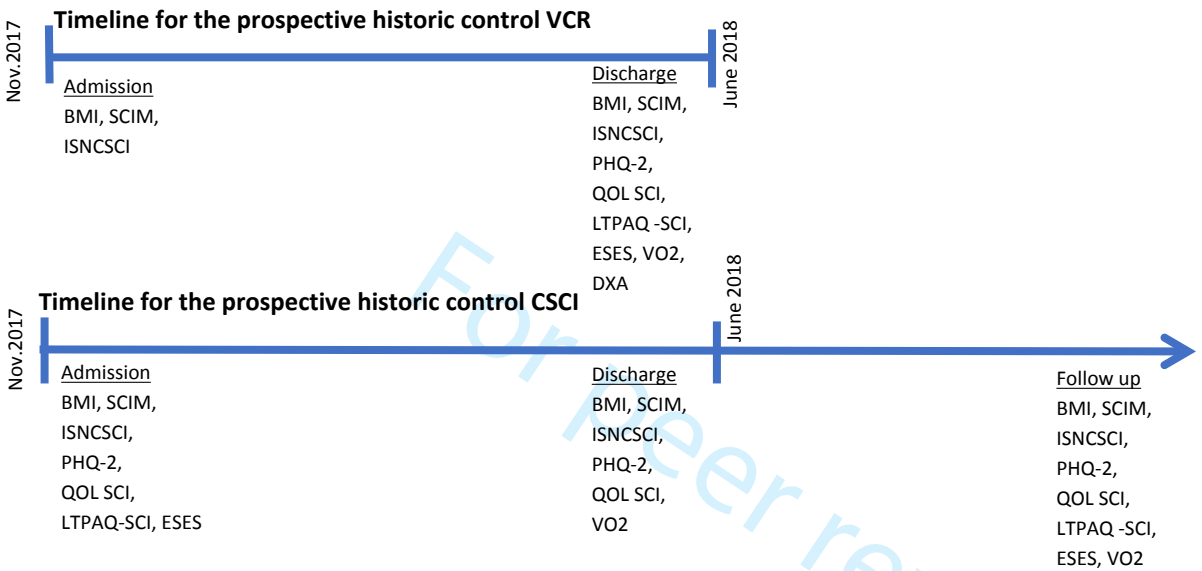
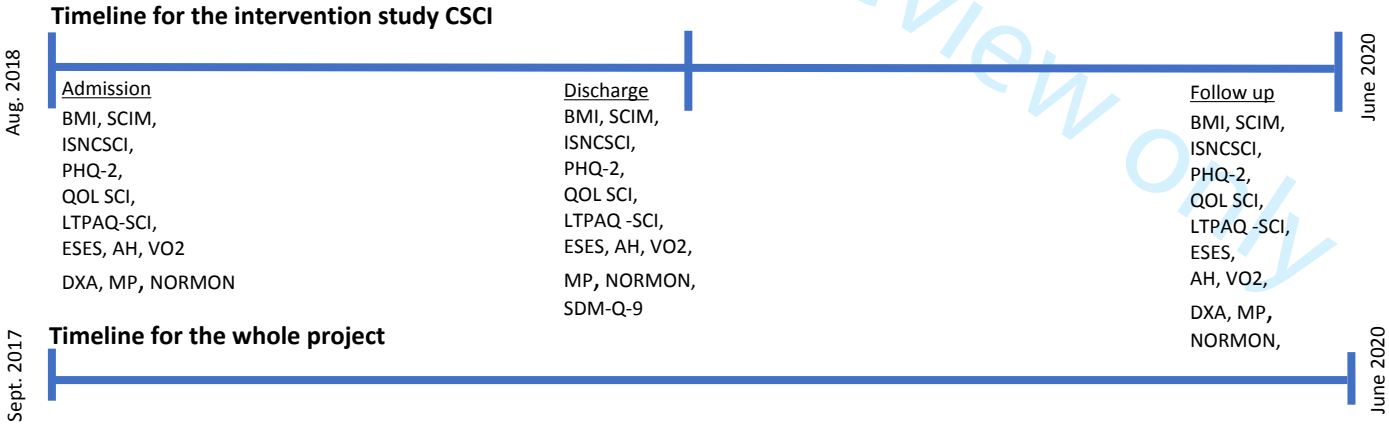


Fig. B



VCR: Center for Spinal Cord Injury, Western Denmark **; CSCI:** Clinic for Spinal Cord Injuries, Eastern Denmark; **BMI:** Body Mass Index**; SCIM**: Spinal Cord Injury Independence Measure; **ISNCSCI**: International Standards for Neurological Classification of Spinal Cord Injury; **PHQ-2**: Patient Health Questionnaire- 2; **QOL SCI**: International SCI Quality of Life Basic Data Set; **LTPAQ-SCI**: Leisure Time Physical Activity Questionnaire for people With Spinal Cord Injury; **ESES**: Exercise Self Efficacy Scale **;AH:** Actiheart (accelerometer)**; VO2peak**:peak oxygen uptake **;DXA:** Dual- energy X-ray Absorptiometry; **MP**: Metabolic profile; **NORMON:** Nordic monitoring of diet, physical activity and overweight**; SDM-Q-9:** 9-item Shared Decision Making Questionnaire

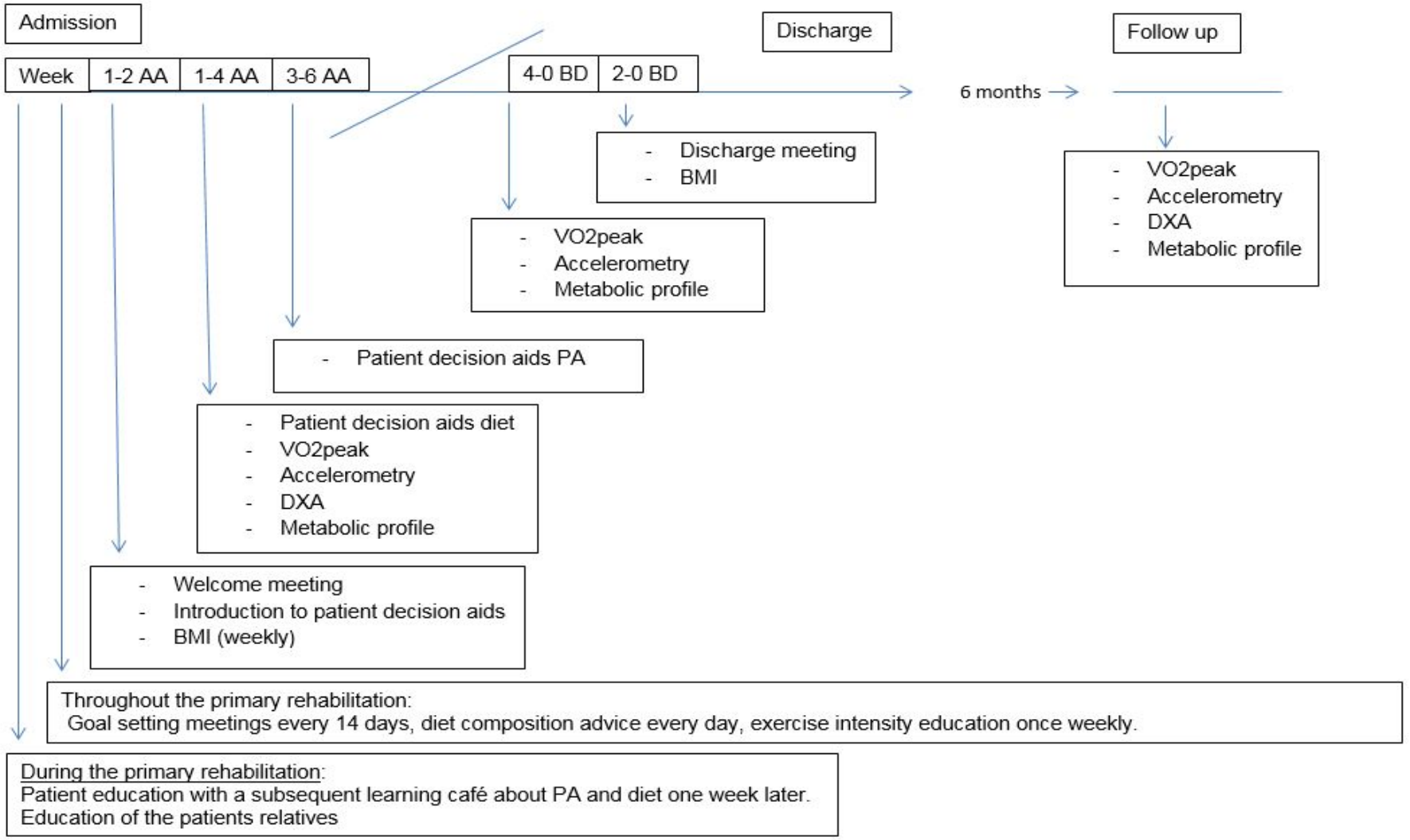


Figure 2. Timeline illustrated on the pocket card for systematic targeted approaches during primary rehabilitation within 2, 4 and 6 weeks after admission (AA) and during the last 4 and 2 weeks before discharge (BD) and at follow up 6 months after discharge. **PA:** Physical activity; **VO2peak**: peak oxygen uptake; **BMI:** Body Mass Index; **DXA:** Dual- energy X-ray Absorptiometry.

Appendix: Strategic interventions

	Strategic interventions	Scope/ Content	Procedure	Health care staff	Process
Information and education in group sessions	Pre- education of all health care professionals and peers with SCI	To prepare a uniform and systematic approach and clarifying the roles of each profession in relation to the targeted patient education, an evidence-based pre-education of the inter-disciplinary health care personnel and peers with SCI is performed about cardiovascular risk, PA and healthy diet.	Pre-education is performed by stakeholders, as one session just before the intervention start-up. Pocket cards with evidence based basic recommendations related to PA and healthy diet in people with SCI are provided to all professions and peers with SCI.	All health care professionals at the clinic, and all peers from the peer corps.	The pre-education is performed multiple times until all health care professionals have attended the pre-education.
	Patient education + session about diet and PA	To Inform the patients about SCI in general, including specific evidence based information about cardiovascular risk and overweight as a mandatory part, facilitating patients discussing healthy diet and PA	Patient education is performed face- to-face as a group session. Afterwards the patients discuss PA and healthy diet. Interdisciplinary health care professionals facilitates the session from evidence based information in the patient decision aids material.	Patient education: Medical doctors. Session about diet and PA: Interdisciplinary health care professionals.	Once
	Education of relatives	To inform the relatives about SCI in general, including specific evidence based information about cardiovascular risk and overweight and the benefits of healthy diet and PA as a mandatory element.	The session last a full day with face-to-face information and discussion about several aspects related to SCI and the role as a relative.	Interdisciplinary+ invited relatives to former patients sharing their experiences about being a relative to a person with SCI	Once
	Admission meeting	A group setting where patients and relatives are informed about the scope of the rehabilitation and consequences of a SCI.	Information face- to-face about cardiovascular risk and overweight and the benefits of healthy diet and PA is provided	Interdisciplinary team	Once

	Discharge meeting	A group setting where the patient and relatives are informed about the discharge in general, and how to manage consequences of the SCI in a new context after discharge	Information face- to-face about how to transfer the achieved knowledge and behaviors related to PA and healthy diet to a new context and information about the risk of low PA and gaining weight after discharge is provided.	Interdisciplinary team	Once
	Diet composition advice	Recommendations about the diet composition at lunch servings is presented, based on the national nutrition guidelines.	Servings take place in a dining room. Visual material with diet composition recommendations is available and a plate model for inspiration is presented, with 200-300 gram of vegetables.	Kitchen staff	Every day
	Exercise intensity education	Education about evidence based exercise amount and intensity for reducing cardiovascular risk and how to monitor intensity by using ratings of perceived exertion	The education is delivered by trained physiotherapists during group sessions of wheelchair skills training and cardiovascular exercise sessions.	Physiotherapist	Once weekly
Motivational physiologic outcome measures and face-to-face feedback	BMI	BMI is assessed as part of existing routines and the patient is informed about the course of BMI. Serves as motivational tool.	Information is delivered to the patient face to face, in a private setting, with no other agendas. Evidence based actions related to BMI are discussed if relevant. Physiotherapists makes sure that the patient is up to date with total weight of the wheelchair and cushion before assessment	Nurses + Physiotherapists.	BMI and feedback is performed every week throughout the rehabilitation
	VO2peak	VO2peak serves as a marker of physical capacity and the patient is informed about the test result and the course of physical capacity. Serves as motivational tool.	Information is delivered to the patient face to face, in a private setting, with no other agendas. Evidence based actions related to physical capacity are discussed if relevant.	Physiotherapists	Measurement and subsequently feedback at: Admission Discharge Follow up

	Accelerometry	Accelerometry serves as a marker of amount and intensity of PA and the patient is informed about the result and the course of PA. Serves as motivational tool.	Information is delivered to the patient face to face, in a private setting, with no other agendas. Evidence based actions related to are discussed if relevant	Physiotherapists	Measurement and subsequently feedback at: Admission Discharge Follow up
	DXA	DXA serves as a marker of body composition (percentage lean mass and fat mass) and the patient is informed about the result and the course of body composition. Serves as motivational tool.	Information is delivered to the patient face to face, in a private setting, with no other agendas. Evidence based actions to change body composition are discussed if relevant	Medical doctors	Measurement and subsequently feedback at: Admission Follow up
	Metabolic profile	Metabolic profile serves as a biomarker for diabetes and atherosclerotic disease and the patient is informed about the result and the course of measurements. Serves as motivational tool.	Information is delivered to the patient face to face, in a private setting, with no other agendas. Evidence based actions related to metabolic disease are discussed if relevant	Medical doctors	Measurement and subsequently feedback at: Admission Discharge Follow up
Goalsetting and action planning (lifestyle changes)	Introduction to patient decision aids for diet and PA and a brochure about food, weight and health for people with SCI	A setting in the early rehabilitation phase, where the decision aids and brochure are provided to the patient. The structure and goal of the two decision aids is introduced. The brochure supports the aim and rationale of the two decision aids.	A private setting between the patient and nurse face-to-face with no other agendas. From the time of introduction until the first goal setting meetings about diet and PA, the patient may read the information coupled to the recommendations for diet and PA.	Nurses + Physiotherapists	Once
	Goal setting using patient decision aids for diet and PA	Consists of two different patient decision aids. They are evidence-based tools describing several options, recommendations and consequences of choices, and creates the basis for the decision process. The aim is	The tool consists of written information material. The decision process together with the health care professionals, takes place face to face, in a private setting, with no other agendas. If requested by the	Interdisciplinary team	A continuous process until a decision is made by the patient. The tools for diet and PA are introduced at the

	to help the patient consider each option in relation to his/her overall life situation and make a choice that fits the patient well.	patient, peers with SCI are accessible, ready to share their own experiences related to PA and diet.		***goalsetting meetings*** approx. 4 and 5 weeks after admission respectively.
Goal setting meetings	A setting with the patient where goals for the rehabilitation are defined including goals related to PA and healthy diet.	Previous goals are evaluated and new goals are defined for the next 14 days. Asking the patient about goals for PA and healthy diet is mandatory.	Interdisciplinary team	Every 14 days
Follow up 3 months after discharge.	Follow up in an outpatient setting on the course of BMI and healthy diet.	The follow-up is a face-to-face interaction based on the patient decision aids for diet	Nurses	Once

Interdisciplinary team: Medical doctor, nurse, physiotherapist, occupational therapist, social worker, psychologist.

SCI: Spinal Cord Injury; PA: Physical Activity; BMI: Body Mass Index; DXA: Dual-energy X-ray Absorptiometry

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

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		Reporting Item	Page Number
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	3
Protocol version	#3	Date and version identifier	2
Funding	#4	Sources and types of financial, material, and other support	13
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	13

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	13
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	13
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	3-4
Objectives	#7	Specific objectives or hypotheses	5
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5

Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-9
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	N/A Decisions related to the intervention are made by the clinical staff
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	12-13
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	7
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical	7

		assumptions supporting any sample size calculations	
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	6
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	N/A due to consecutive enrollment
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	N/A due to consecutive enrollment
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N/A due to consecutive enrollment
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A due to consecutive enrollment
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A due to consecutive enrollment
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	9

Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	13
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	11
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	11
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	-
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	11
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A The trial evaluates elements in standard care which are not terminated.

Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	11
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	3
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	3
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	3
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	11
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	13
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	11
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	11

Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	3
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	13
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	11
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	3
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	9

BMJ Open

Health promotion and cardiovascular risk reduction in people with spinal cord injury - physical activity, healthy diet and maintenance after discharge: study protocol for a prospective national cohort study and pre-post intervention study

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Keywords:	Spinal Cord Injuries, Metabolic Syndrome, Health Promotion, Exercise, Diet Therapy

TITLE PAGE

Health promotion and cardiovascular risk reduction in people with spinal cord injury - physical activity, healthy diet and maintenance after discharge: study protocol for a prospective national cohort study and pre-post intervention study

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ABSTRACT

Introduction Spinal cord injury (SCI) predisposes those who suffer from it to physical inactivity and weight gain; consequently, death due to cardiovascular diseases is more frequent among people with SCI than in the general population. The literature documents a consensus about an interdisciplinary multimodal approach for the prevention and treatment of cardiovascular risk factors including overweight and obesity in people with SCI, focusing on diet, physical activity (PA) and behavioral interventions. This study will investigate implementation of recommendations from a recent clinical practice guideline for identification and management of cardiometabolic risk after SCI through multimodal patient education in a subacute clinical setting.

Methods and analysis All patients who are aged 18 years or older with an SCI within the previous 12 months and admitted to highly specialized rehabilitation are included, regardless of SCI etiology or neurological level. A primary study designed as a controlled pre-post pragmatic intervention study with 6-month follow up evaluates the effect of the clinical intervention; a prospective national cohort study on body mass index (BMI) serves as a historical control. The intervention consists of a standardized approach to patient education about cardiovascular risk factors, PA and a healthy diet that begins at the outset of primary SCI rehabilitation and is integrated into existing settings and workflows. Outcome measures are collected at admission, discharge and 6 months after discharge and include VO2peak (primary outcome), BMI, body composition, metabolic profile, neurologic status, level of functioning, depression, quality of life, objective PA (accelerometry), self-reported PA, self-assessed physical activity ability, shared decision making, and dietary habits. Test-retest reliability of four VO2peak test protocols are investigated, as is test-retest reliability of a multisensor accelerometer in a rehabilitation setting.

Ethics and dissemination

The principal investigator obtains Informed consent from all participants. The interventions in the project are closely related to existing rehabilitation care, and the risk of pain and discomfort is considered modest. Any unintended events related to the elements of the intervention are reported, according to existing regional procedures. Data are stored in a secure web-based database (Redcap). The primary study and prospective cohort study are registered at Clinicaltrials.gov. Positive and negative results will be submitted to relevant scientific journals related to SCI for publication. Important protocol modifications are reported to the Committees on Health Research Ethics in the Capital Region of Denmark.

Article summary

Strengths and limitations of this study

The prospective cohort study includes both SCI centers in Denmark and the intervention study includes all newly injured people with SCI admitted to rehabilitation at the East Denmark SCI-center.

Four predefined protocols for assessing VO2peak are used due to the heterogeneity of functional level in the SCI population.

The pre-post intervention study is based on a pragmatic real-life approach by including existing settings and work flows, which is a strength, but consistent implementation of multimodal interventions may be challenging due to changes in the clinical setting.

Lack of randomization is a study limitation.

Registration details

The project is approved by the Committees on Health Research Ethics in the Capital Region of Denmark on 10.07.2018 (Journal-nr.: H-18018325) and the Danish Data Protection Agency (j.nr. VD-2018-380, I-Suite nr.: 6631) and (RH-2017-345, I-Suite nr.: 06052). The project is registered at Clinicaltrials.gov (NCT03689023) and (NCT03369080). See the World Health Organization Trial Registration Data Set in table 1.

Table 1. World Health Orgainzation Trial Registration Data Set (Version 1.3.1)

Data category	**Information**[32]
Primary registry and trial identifying number	ClinicalTrials.gov (NCT03369080) and (NCT03689023).
Date of registration in primary registry	12.11.2017 and 26.09.2018
Secondary identifying numbers	The Committees on Health Research Ethics in the Capital Region of Denmark on 10.07.2018 (Journal-nr.: H-18018325) and the Danish Data Protection Agency (j.nr. VD-2018-380, I-Suite nr.: 6631) and (RH-2017-345, I-Suite nr.: 06052)
Source(s) of monetary or material support	This work was supported by a mutual cooperation about the research program " Centre for Integrated Rehabilitation of Cancer Patients (CIRE) - Neuro/Psychology", between the University Hospitals Centre for Health Care Research, University hospital Copenhagen, Rigshospitalet, University College Copenhagen, Department of Nursing and Nutrition, and the NeuroScience Centre, Rigshospitalet.
Primary sponsor	This work was supported by a mutual cooperation about the research program " Centre for Integrated Rehabilitation of Cancer Patients (CIRE) - Neuro/Psychology", between the University Hospitals Centre for Health Care Research, University hospital Copenhagen, Rigshospitalet, University College Copenhagen, Department of Nursing and Nutrition, and the NeuroScience Centre, Rigshospitalet.

Secondary sponsor(s)	
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Public title	Health promotion and cardiovascular risk reduction in people with spinal cord injury - physical activity, healthy diet and maintenance after discharge: study protocol for a national cohort study followed by a clinical intervention study.
Scientific title	Health promotion and cardiovascular risk reduction in people with spinal cord injury - physical activity, healthy diet and maintenance after discharge: study protocol for a prospective national cohort study followed by a pre-post intervention study.
Countries of recruitment	Denmark
Health condition(s) or problem(s) studied	Spinal Cord Injury and the cardiovascular risk factor, including weight gain and consequences of an inactive lifestyle during and after the primary rehabilitation.
Intervention(s)	A controlled pre-post multi modal pragmatic clinical intervention study, with 6-months of follow up containing “new usual care” consisting of a uniform and systematic institutional strategy incorporating targeted strategic patient education about cardiovascular risk factors, physical activity and a healthy diet lifestyle starting early in the primary rehabilitation process.
	Comparator: A historic control conducted as a national prospective cohort study before “new usual care”
Key inclusion and exclusion criteria	Inclusion criteria: All patients who are 18 years or older, and with a Spinal Cord Injury (SCI) within the last 12 months and admitted at Clinic for Spinal Cord

	Injuries, are included regardless of etiology to the SCI, neurological level or completeness of the lesion if informed consent is retrieved.
	Exclusion criteria: Exclusion criteria for VO2peak test in the study includes motor complete SCI at C4 level or above, and assisted ventilatory function. Other exclusion criteria are the presence of decubitus, severe spasticity or musculoskeletal problems considered at risk of aggravation during testing or preventing completion of the VO2peak test.
Study type	Interventional. The study consists of a primary study designed as a controlled pre-post clinical intervention study and a historic control conducted as a prospective cohort study.
	Allocation: The intervention in the primary study is a part of new standard care. Therefore randomization or blinding is not appropriate.
	Primary purpose: prevention
Date of first enrolment	November 2017
Target sample size	160
Recruitment status	Recruiting
Primary outcome(s)	Oxygen uptake measured as VO2peak.
Key secondary outcomes	Body Mass Index, Body composition (determined by Dual energy x-ray absorptiometry), metabolic profile consisting of CRP as a marker for inflammation, lipid profile describing Total cholesterol, Triglycerides, HDL cholesterol, and LDL cholesterol and Hemoglobin A1c as a marker for carbohydrate metabolism, and blood pressure (BP).
Ethics Review	The project is approved by the Committees on Health Research Ethics in the Capital Region of Denmark on 10.07.2018 (Journal-nr.: H-18018325)
Completion data	June 2020
IPD sharing statement	Data can be accessed by request to the corresponding author after publications related to the Ph.D project are made.

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INTRODUCTION

The annual incidence of traumatic spinal cord injury (SCI) in Denmark is 10-15 per million [1], while nontraumatic SCI has accounted for approximately 60% of all newly injured patients admitted to the two SCI centers in Denmark in recent years. SCI is a life-changing event that may affect all bodily functions below the level of the lesion, requiring highly specialized interdisciplinary rehabilitation aiming at the highest possible level of independent functioning and resulting in significant costs to affected individuals and society. Rehabilitation at the Clinic for Spinal Cord Injuries in Eastern Denmark (CSCI) generally includes functional training, strength training, cardiovascular exercise and fine motor training of the upper extremities. In addition, circulation, respiration, thermoregulation, bowel and bladder function, skin integrity, pain and spasticity are continually assessed and addressed, and aids are provided to compensate for functional losses, including communication aids and splinting. Counseling to address social and economic issues, sexual function and psychological issues is provided.

Over the long term, SCI and resulting impairments predispose affected individuals to increased cardiovascular risk and premature cardiovascular death; a clinical practice guideline addressing cardiometabolic disease after SCI was recently published [2]. However, targeted patient education addressing long-term cardiovascular risk, based on individualized face-to-face interaction between patients and health care professionals and aiming at a core clinical outcome, is not systematically integrated into early stages of specialized SCI rehabilitation at CSCI, even though an opportunity may exist to target the link between injury-related immediate impacts on functionality and long-term health consequences [3 4]. Similarly, health promotion education and activities related to body mass index (BMI), diet, smoking, alcohol intake and physical activity (PA) are not systematically provided, and assessment of physical capacity, metabolic profile and body composition is not a part of standard care. A systematic approach may ensure that all patients at CSCI receive information and knowledge related to health promotion and the risk of cardiovascular disease, which may support patient adaptation and adherence to recommended PA and healthy diet.

As a result, cardiovascular risk factors, including weight gain and the consequences of an inactive lifestyle during and after primary rehabilitation, are the focus of the current study.

The course of overweight

The prevalence of overweight in people with SCI is conservatively estimated at 66%. Overweight has been found to be one of the most common cardiometabolic risk factors among people with SCI, increasing the cardiovascular risk profile of wheelchair-dependent people with paraplegia [5], [6] [7 8]. Energy expenditure decreases significantly after sustaining a SCI and remains low. Although body fat and body weight decrease in the acute injury phase, they increase in the subacute phase, and a loss of lean body mass in the lower extremities and trunk has been observed during the first year after injury [9]. BMI increases gradually during the first years after discharge from primary rehabilitation [10]. Obese people with SCI achieve a lower level of functioning during primary rehabilitation than do those of normal weight [11]. Overweight in people with SCI is associated with increased risk of depression [12]. Nutritional education delivered by a dietician or lifestyle coach has been found promising [13-15], although it is often not offered in a clinical setting [16]. Increased knowledge about weight management among clinicians is

recommended, but weight management is often not prioritized in rehabilitation settings. Clinicians have called for evidence-based knowledge and clinical guidelines [16 17].

Impact of physical activity on health and fitness

In the general population, PA is associated with beneficial effects on diseases contributing to the metabolic syndrome, and its beneficial effect increases when it is combined with diet therapy [18]. Similar effects of PA among people with SCI have been described; numerous studies have reported the positive effects of PA intervention programs in people with both acute and chronic SCI on physical capacity, strength and functional performance, including the effect of exercise interventions on cardiometabolic health [19 20]. Evidence-based exercise guidelines for cardiometabolic health in people with SCI recommend a minimum of 30 minutes of moderate to vigorous aerobic exercise three times weekly to reduce cardiovascular risk factors [21]. The long-term effect increases when PA is combined with behavioral interventions [22]. However, not all people with SCI are able to participate in PA intervention programs or maintain PA. Rates of participation in leisure time PA and in sports activities after discharge from primary rehabilitation are low among people with SCI [23 24]. Intra- and extrapersonal factors influence participation in PA, including self-efficacy related to being physically active [25]. PA alone is insufficient to induce weight loss in people with SCI [2]. Therefore, a broader approach to cardiovascular risk reduction may be appropriate, and a combination of several interventions is required to promote a physically active lifestyle and weight loss [26]. Examples of key intervention components are autonomy in relation to decision-making and behavioral interventions comprising goal setting and feedback via physical assessments [26 27].

Although the separate or combined effects of PA, diet and behavioral interventions have been investigated previously in people with SCI with generally positive results, this study will investigate the effect of educational and behavioral interventions related to PA and diet in a subacute clinical rehabilitation setting. The study will investigate implementation of recommendations from the recent clinical practice guideline for identification and management of cardiometabolic risk after SCI, including assessments of physical capacity, body composition, bodyweight, dyslipidemia and impaired fasting glucose, as well as PA and diet [2]. Feedback on these assessments and goal setting will be part of the patient education delivered by clinical staff across settings during primary rehabilitation.

To the best of our knowledge, only a single study has investigated outcomes related to cardiovascular risk factors following PA and behavioral interventions during subacute inpatient rehabilitation using outcomes related to cardiovascular risk factors, but this study only included wheelchair users [28 29]. The current study will contribute to existing knowledge by consecutively enrolling all patients, aged 18 years or older, with a new SCI who are admitted to CSCI, regardless of mobility status, and by evaluating the implementation of evidence-based guidelines for identification and management of cardiometabolic risk after SCI in a clinical setting.

Objectives

This study will investigate the effect of a systematic approach to incorporating targeted patient education about cardiovascular risk factors, PA and a healthy diet early in the primary rehabilitation process, compared to a historical control group.

STUDY DESIGN

The primary study comprises a primary study designed as a controlled pre-post pragmatic intervention study with 6 months of follow up. A prospective national cohort study provides a historical control (Fig 1).

Substudies

BMI is considered a high-risk determinant due to the impact of overweight on the cardiovascular risk profile and level of functioning among wheelchair-dependent people with SCI [5], [6] [7 8]. A prospective representative longitudinal survey of BMI conducted before the controlled intervention in collaboration with SCI Center of Western Denmark serves as a historical control (substudy 1). Additional outcome measures will be collected at CSCI during the survey period, including measures of PA, physical capacity and body composition. Two substudies of test-retest reliability of a VO2peak test (substudy 2) and a multisensor accelerometer (substudy 3) will be performed. VO2peak and accelerometry are considered valid methods to measure the effect, amount and intensity of PA at discharge from primary SCI rehabilitation. Both will be collected repeatedly during the primary study and serve as individual motivational components in education and communication, as well as outcome measures. Assessing test-retest reliability of the two procedures is essential.

METHODS AND ANALYSIS

The SPIRIT reporting guidelines are used in the reporting of the clinical trial [30].

Patient involvement

A user panel consisting of six patients (three women and three men aged 23 to 78 years), including both recently injured people and those who had been living with SCI for some time, was established and involved in the early phase of study protocol development. All participants were hospitalized at CSCI when they participated in semi-structured focus group interviews about their perceptions of health promotion practices in the clinical setting [31]. The interview focused on both the existing level of information about increased risk of overweight and cardiovascular disease after SCI and education about diet and PA as a way of reducing those risks. Data were analyzed using constant comparative analysis [32]. The user panel recommended more information in the early phase of rehabilitation about cardiovascular risk, PA and diet and more support and guidance about appropriate diet and being physically active, which is the primary aim of the project. The study results will be disseminated to project participants.

Participants and eligibility criteria

Inpatients who are aged 18 years or older, injured with SCI within the last 12 months and admitted at CSCI are recruited and consecutively included after providing informed consent, regardless of SCI etiology (i.e., traumatic or non-traumatic), neurological level or completeness[1] of the lesion. In substudy 1, all newly

[1] The completeness of the injury is graded according to the ASIA Impairment Scale (AIS). AIS is used to determine the degree of motor and sensory function below the level of the SCI. A complete or incomplete injury is defined as absence or presence of sensory and motor function in the most caudal sacral segments. A = sensory and motor complete; B = sensory incomplete without motor function > 3 levels below the motor level of injury on both sides of the body; C = motor incomplete, with preserved motor function below the level of injury and where > 50% of the key muscles below the injury level have a degree < 3 by

injured people with SCI admitted at the SCI Centre of Western Denmark are also included. Substudy 1 serves as a historical control group, and the intervention in the primary study is part of a new standard of care. Therefore, randomization, blinding and sample size calculation are not appropriate.

Exclusion criteria for the VO2peak test include motor complete SCI (AIS A and B) at cervical (C)4 level or above and a need for artificial ventilation. Other exclusion criteria are the presence of decubiti, severe spasticity or musculoskeletal problems at risk of exacerbation or aggravation during testing or preventing completion of the test.

Substudy 3 includes a convenience sample of 20 patients with the goal of ensuring variation in age, gender, neurological level and completeness of SCI.

Primary study: A systematic interdisciplinary multimodal intervention that facilitates physical activity, healthy diet and maintenance after discharge through strategic patient education as part of usual care, with the aim of decreasing cardiovascular risk

This pre-post study includes all patients aged 18 years or older with a new SCI who are admitted at CSCI during a period of 12 to 18 months. The study includes follow up 6 months after discharge from primary rehabilitation.

Approximately 70 patients with a new SCI are admitted to CSCI annually; but due to expected missing data , complete data sets from admission through follow up may be fewer.

Intervention

The intervention is based on recommendations in a recently released clinical practice guideline for the identification and management of cardiometabolic risk after SCI and conclusions from a meta- synthesis by Williams et al. and a systematic review by Greaves et al. [2 26 27]. A combination of several interventions is most effective at promoting a physically active lifestyle and weight loss after SCI. Crucial intervention components are autonomy in relation to decision-making about PA, support and follow up from health care professionals and mentors with SCI, information about adapted PA and behavioral interventions comprising goal setting and feedback from, for example, physical tests. Greaves et al. recommend group sessions, individual sessions and interdisciplinary interventions in the clinical setting that focus on maintaining PA and healthy diet [26].

The intervention will be integrated into usual care during the project period, and all newly injured patients will receive all multimodal components as appropriate to individual circumstances, such as level of injury. At discharge, the patient will describe adherence to the intervention and document participation in targeted education elements on a checklist. Similarly, health care professionals will use a checklist to document adherence to interventions at the start, midpoint and end of the study period. Medical records and schedules for goal-setting meetings will also be reviewed to monitor health care professionals'

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manual muscle test (MMT); D = motor incomplete with preserved motor function below the level of injury and where > 50% of key muscles below the injury level have a degree > 3 by MMT; E = normal sensory and motor function in all segments.

adherence to the interventions. Rehabilitation of the physical level of functioning and physical capacity (e.g., physiotherapy) will occur as part of usual care and is a mandatory core component of highly specialized SCI rehabilitation. However, decisions about PA made by the patient during rehabilitation may be integrated into the rehabilitation program to achieve his or her goals for PA during and after the rehabilitation period.

A central part of the intervention is to create a standardized approach to targeted strategic patient education of patients about cardiovascular risk factors, PA and a healthy diet by systematizing the existing clinical setting and treatment interventions.

In the process of reorganizing the institutional approach to addressing cardiovascular risks, *pre-education* of interdisciplinary health care personnel and peers with SCI is mandatory to clarify their roles in relation to targeted patient education. Pocket cards with evidence-based recommendations related to PA, diet and BMI in people with SCI are provided to all health care professionals and peers with SCI and will also illustrate the timeline for systematic targeted approaches during primary rehabilitation (Fig. 2)

Patients receive information and instructions about PA and healthy diet through patient education based on principles that include individualized face-to-face interaction between patients and health care professionals while working towards a specific health-related outcome [33]. The interventions begin at the outset of primary SCI rehabilitation and are integrated into usual care at predetermined time points (e.g., dual- energy X-ray absorptiometry (DXA) scan, VO2peak, metabolic profile with feedback early after admission to rehabilitation and goal setting meetings about PA and diet within 6 weeks after admission) throughout the entire rehabilitation continuum, with the goal of secondary and tertiary cardiovascular prevention.

Representatives of all the health care professions generally carry out education of patients and their relatives in a variety of educational settings [34 35], with a focus on clarifying the importance of PA and a healthy diet. Patient education involves training sessions [36] and feedback on physiological outcome measures and tests that also serve as motivational tools. Additionally, goal-setting meetings, tools for shared decision making [37] [26] [38] and use of mentors with SCI are also integrated as components supporting decision making about PA and healthy diet. BMI and diet are evaluated 3 months after discharge in an outpatient setting (see appendix for a more detailed description of the strategic interventions).

All components are offered to patients as a mandatory part of the intervention, ensuring that information and patient education are provided and decisions about PA and healthy diet are made. However, patients individually determine the extent to which they engage in making decisions and setting goals about PA and healthy diet. Interdisciplinary health care professionals respect the decisions and autonomy of patients who choose not to set goals or make decisions about PA and healthy diet.

Several outcome measures used to evaluate the intervention at admission, discharge and at follow up 6 months after discharge are also motivational components of the intervention: BMI, body composition measured by DXA, physical capacity (VO2peak), PA (Actiheart multisensor accelerometer) and blood samples describing metabolic profile.

Substudy 1. Prospective national survey of body mass index among people with SCI

This study includes all patients with a new SCI hospitalized at CSCI or SCI Center of Western Denmark during a period of 10 months; 100 patients are expected to participate. Data on BMI, level of functioning (Spinal Cord Injury Independence Measure III [SCIM III]) and neurological status (International Standards for Neurological Classification of SCI [ISNCSCI] are collected at both centers. Patients with an SCI within the last 12 months who are admitted for rehabilitation several months after injury are also included in the prospective survey. Data on BMI at the time of injury are collected for all patients at admission to primary rehabilitation from the patient's medical record. At CSCI, BMI every 6 weeks, quality of life (QoL SCI), depression (PHQ-2), amount of PA (Leisure Time Physical Activity Questionnaire for people with Spinal Cord Injury [LTPAQ-SCI]) and self- assessed ability to be physically active (Exercise Self Efficacy Scale [ESES]) will be collected at admission, discharge and follow up 6 months after discharge. Measures of physical capacity (VO2peak) and body composition (DXA) are also obtained at discharge. Data from this substudy serve as a historical control for the Intervention study.

Substudy 2. Test-retest reliability of VO2peak testing

This study includes all patients participating in substudy 1 who are able to perform the VO2peak test at discharge from primary rehabilitation. Patients are randomized to a test session of either intra- or interrater reliability. Due to the complexity of SCI, four pre-defined exercise protocols are used to reach criteria for VO2peak, defined as a respiratory exchange ratio (RER) > 1.0 [39]. As a starting point, people with an incomplete SCI, as defined by ISNCSCI, will use a seated cross-trainer (NuStep T5XR®), which has software incorporating both a standard and a modified test protocol. The standard protocol starts at 50 watts (W) with 25W incremental increases every 2 minutes in the first three stages, 30 W increments thereafter and 115 steps per minute (SPM). The modified protocol starts at 25W with 15W increments every 2 minutes and 80 SPM. The equipment and modified protocol are reliable in people with traumatic brain injury and has been validated in healthy persons [40 41]. In people with an incomplete SCI, the equipment is safe and involves a large amount of muscle mass [42]. People with an ISNCSCI-defined complete SCI, very de-conditioned patients or those with an incomplete SCI but a poor ISNCSCI lower extremity motor score that may hinder reaching VO2peak on the seated cross trainer will use an arm-cranking ergometer (SCI FIT Pro1®). Test protocols used on the SCI FIT ergometer are established from the most common protocols for people with tetra- and paraplegia during rehabilitation reported in a recent systematic review [39]. The study protocols are designed as stage protocols starting at 5 W with an increase every minute of 5W for people with tetraplegia and 10W for people with paraplegia and 60 revolutions per minute.

If predefined criteria for VO2peak are not reached during test 1, a more suitable protocol to reach VO2peak is chosen for test 2 and will be retested at test 3. However, this is not possible if the protocol designed for people with tetraplegia is used. The test-retest study takes place at discharge, with 48 hours to 5 days between tests occurring at the same time of the day. Participants refrain from caffeine, alcohol and intensive physical exercise on the day of testing, as well as tobacco smoking two hours before testing. Bladder emptying occurs immediately before testing.

In the intervention study, the four exercise protocols are used to ensure that a true VO2peak is reached during the rehabilitation process. VO2peak is highly dependent on the level and completeness of the SCI and the testing equipment; for instance, a patient may be initially tested on the protocol designed for

people with a complete tetraplegia and later tested on the non-modified standard protocol in the seated cross trainer due to neurological recovery and improvement in functional level.

Substudy 3. Test-retest reliability of a multisensor accelerometer

This study includes a convenience sample of 20 patients ensuring a representative sample of individuals with para- and tetraplegia, complete and incomplete SCI, age and gender. The equipment used for monitoring the amount and intensity of PA consists of sensors registering acceleration and heart rate and is placed on the thorax of the participant with two surface electrodes. Data are expressed as daily PA energy expenditure (kcal/min) and the time spent in different activity intensities on the basis of metabolic equivalents. The equipment has been previously used among wheelchair-dependent people with SCI, although its reliability in an inpatient setting has not been assessed [43]. Precision is higher when the equipment is calibrated to individual participants using measures of energy expenditure and corresponding heart rate during rest and during exercise testing, covering a range of submaximal and maximal intensities. The equipment software uses these data to estimate energy expenditure using branched model equations [44]. This method will also take into account compromised cardiac sympathetic innervation in individuals with an injury above T6. In this study, individual calibration is based on activity performed during the VO2peak test (substudy 2), with resting metabolic rate measured before testing for 10 minutes following a rest period of 20 minutes [45 46]. Continuous measurements of the amount and intensity of PA will occur over 48 hours with sampling epochs every 15 seconds and a minimum wear-time of 80% [47]. To ensure comparability, test-retest procedures are performed over a period of two weeks on identical days of the week .

Outcome measures

Outcome measures evaluating the intervention comprise the following.

Primary outcome

Oxygen uptake Is measured as VO2peak during a maximal exercise test and is the gold standard for measuring aerobic capacity. For people with SCI, several test protocols have been used [36].

Secondary outcomes

Objective PA is measured in a subsample of the historical control cohort and participants in the intervention study with a multisensor device (Actiheart®) recording accelerations and heart rate. It has been previously used for wheelchair users with SCI, and individual calibration is important to get the most accurate data [47]. Evidence-based exercise guidelines for cardiometabolic health in people with SCI recommend a minimum of 30 minutes of moderate to vigorous aerobic exercise three times weekly [21].

Bodyweight is measured as BMI, which is the most widely used outcome measure for body weight in people with SCI. BMI is not sensitive enough to distinguish between fat mass and lean body mass or overweight in people with SCI. Overweight among adults with SCI is defined as ≥ 22kg/m^2 [48] [2]. BMI is

already collected as part of usual care, and data for BMI every 6 weeks until discharge will be included in the project.

Body composition is determined by DXA, which is the gold standard for assessing obesity and body composition. Among adults with SCI, men with >22% body fat and women with >35% body fat should be classified as obese [2].

Metabolic profile consists of C-reactive protein (CRP) as a marker for inflammation and lipid profile including total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C), which are included in the international SCI Endocrine and Metabolic Function Basic Data Set. Triglycerides should not be ≥ 150 mg/dL (1.7 mmol/L). HDL-C should not be < 40 mg/dL (1.03 mmol/L) in men or < 50 mg/dL (1.29 mmol/L) in women [2]. LDL-C should not be > 3.0 mmol/l [49]. Hemoglobin A1c (HbA1c) serves as a marker for carbohydrate metabolism and is included in the International SCI Endocrine and Metabolic Extended Data Set [50 51]. Criteria for a diagnosis of prediabetes include HbA1c 5.7-6.4% (39-47 mmol/mol) and criteria for a diagnosis of diabetes include HbA1c > 6.5% (> 48 mmol/mol) [2]. As approved by the Committees on Health Research Ethics in the Capital Region of Denmark, blood samples will not be stored after analysis.

Blood pressure (BP) is measured by sphygmomanometry. Criteria for a diagnosis of hypertension in people with SCI vary with injury level, severity and etiology. BP should not exceed 130/85 mm Hg.

Level of functioning is determined by the SCIM III, which is a valid and reliable outcome measure designed to assess level of functioning in people with SCI in clinical care and research [52] [53 54] [55].

Neurologic status is determined by the ISNCSCI and is the most widely used classification in people with SCI [56 57].

Depression is measured by the Patient Health Questionnaire-2 (PHQ-2), which is a generic measure of depression. Among people with SCI, a cut-off score of 3 is associated with sensitivity of 83.3% and specificity of 95.7% [58].

Quality of life is measured by the International SCI Quality of Life Basic Data Set (QoL SCI), which consists of three questions about satisfaction with life in general and physical and mental health. It is a valid outcome measure with good internal consistency [59] [60].

Self-reported PA is measured by the LTPAQ-SCI, which is a self-administered questionnaire about leisure time PA, including amount and intensity during the past 7 days. Reliability and validity of self-reported activity are satisfactory in moderate and high intensity levels [61]. An additional question concerning PA outside of leisure time PA (i.e., PA as part of rehabilitation) is included in substudy 1. The question is designed to be similar to the original questions and is scored using the same intensity scale. During the intervention study, a version of LTPAQ-SCI adjusted to a Danish context will be used. This version is approved by the developers of the original LTPAQ-SCI and includes active transportation and active physiotherapy.

Self-assessed ability to be physically active is measured by ESES. It is an outcome measure developed for assessing self-efficacy related to PA in people with SCI and consists of 10 questions on a 0-4 response scale.

ESES is reliable with high internal consistency (Cronbach`s alpha 0.94) and satisfactory content validity in the form of face and construct validity [62].

Shared decision making related to patient decision aids for PA and healthy diet is measured by the 9-item Shared Decision Making Questionnaire (SDM-Q-9), which assesses the process of shared decision making between health care professionals and the patient from the patient's perspective. SDM-Q-9 consists of nine statements, which can be rated on a six-point scale from 0 to 5, with higher scores indicating greater shared decision making. All items are summed to yield a raw total score of 0 to 45. SDM Q-9 is only used at discharge.

Varied and healthy diet in an appropriate amount is measured by the Nordic monitoring of diet, PA and overweight (NORMON) developed in a Nordic collaboration and commonly used for monitoring [63]. The questionnaire explores how frequently 16 food indicators, several of which are recommended in the Nordic national nutritional recommendations, have been consumed over the previous 12 months. NORMON also includes questions related to alcohol intake, smoking and PA. The questionnaire was validated in 2009 against existing questionnaires about diet [64]. In this study, a modified version of the questionnaire will ask patients to recall their dietary habits over the previous month.

Statistics

All continuous data collected at admission, discharge and follow up are reported descriptively. In the intervention study, differences in the primary and secondary outcomes between baseline and follow up will be analyzed using analysis of covariance. The same approach will be used between baseline and follow up in the historic control study. Likewise differences between the intervention study and the historic control is analyzed using analysis of covariance. Due to the small sample size, participants in the intervention study and historic control will not be matched but participants will be compared to each other controlling for ISNCSCI classification, gender and functional level. Linear regression is used to measure the strength and association between BMI and DXA results and the association between the psychometric variables e.g. QoL and depression compared to VO2peak and BMI. Ordinal regression analysis is made for ordinal data e.g. ESES. Missing data on primary and secondary data are analyzed as intention to treat without imputation, but dropout analysis is made with baseline characteristics for participants completing and not completing the study. In sub-studies 3 and 4, the reliability of the outcome measures are analyzed by paired t-test, Pearson´s product-moment correlation and coefficient of variation or intraclass correlation coefficient between the test-retest sessions.

Ethics and dissemination

During the intervention period, all newly injured patients who are admitted for rehabilitation at CSCI are offered treatment and tests included in the intervention as a mandatory part of usual care to the extent they are able to participate, which may vary with the level of lesion and completeness of SCI. Because the intervention is part of usual care and comprises a standardized approach to patient education, no data monitoring or interim analysis is planned.Informed consent is obtained to analyze the data generated during the project. The intervention in the project is closely related with the content of the present rehabilitation, and the risk of pain and discomfort is considered modest. During the VO2peak test, special attention is paid to potential symptoms of autonomic dysreflexia (AD) in people with SCI above T5-6. In

case of AD, the exercise test is stopped and relevant actions are initiated. It is assumed that any risks are surpassed by therapeutic gains, i.e, expected reductions in the risk of cardiovascular disease and mortality. Any unintended events related to the intervention are reported according to existing regional procedures, and compensation is covered by the normal procedures for unintended harm during hospitalization. The study is reported to the Committees on Health Research Ethics in the Capital Region of Denmark and the Danish Data Protection Agency and is registered at Clinicaltrials.gov.

Data statement section

All patient data are stored in a secure web-based database (Redcap) with limited access and ID code to identify patients, to which data are transferred directly or by an encrypted USB stick. Patients are assigned unique identification numbers, which is the only identifier exported from Redcap during data analysis. Data are stored until December 31, 2027, after which paper material is shredded, data files are deleted and the Redcap database is no longer accessible. The principal investigator has access to all trial data. Data can be accessed upon request to the corresponding author after reports related to the Ph.D. project are published. No data monitoring committee is established.

DISCUSSION

This study will investigate the effectiveness of a systematic institutional strategy incorporating individualized patient education and testing about cardiovascular risk factors, PA and a healthy diet lifestyle early after SCI diagnosis during primary rehabilitation, compared to a historical control group. Our findings will be discussed in light of recent studies suggesting that an interdisciplinary multimodal approach in prevention of cardiovascular risks among people with SCI with a focus on diet, PA and behavioral interventions is beneficial [23] [65] [66] [13 25] [14]. Crucial components of the intervention are autonomy in relation to decision-making and support and follow up from health care professionals and mentors with SCI. A qualitative meta-synthesis concluded that timely information about PA and its benefits in relation to SCI and behavioral interventions using goal setting and motivational feedback through physical tests might be important patient-activating tools [27]. This is consistent with a recent systematic review by Greaves et al. [26], who also strongly recommended that interventions in the clinical setting contain both group sessions and individual sessions as well as interdisciplinary interventions that focus on maintaining PA and healthy diet [26]. These elements are incorporated into the intervention investigated in this study.

Several of the outcome measures used to evaluate the intervention are components of the intervention, as recommended in the clinical guideline for identification and management of cardiometabolic risk after SCI [2]. Outcome measures also serve as individual motivational tools. The primary outcome measure is VO2peak, for which a significant positive relationship exists with some cardiometabolic markers in people with SCI, such as lipid profiles and fasting insulin levels [61]. Consequently, PA that increases physical capacity may also reduce the risk of cardiovascular disease [67]. Physical capacity measured as VO2peak is positively associated with functional independence [68], less physical strain during activities of daily living [69] and life satisfaction [70] among people with SCI, although other measures of physical capacity have an important and, in some cases, stronger impact on functional independence [68].

Among people with SCI, several test protocols have been used for assessing VO2peak [36]. In this study, four exercise protocols make VO2peak testing feasible for clinical physiotherapists who, although trained in

using the testing equipment, are inexperienced in determining the appropriate workload during VO2peak testing, which is difficult due to the complexity of a SCI. If predefined criteria for VO2peak are not reached, a more suitable protocol is selected. The protocol and equipment used in the study are identical at admission and discharge. If a patient's neurological and functional level has improved to the point where a different protocol and equipment will more accurately measure VO2peak, an additional test at discharge will be performed on a separate day. Data from both tests will be evaluated and the new protocol will be repeated at follow up 6 months after discharge. This approach to testing VO2peak in a clinical setting has, to the best of our knowledge, not been described previously

Secondary outcome measures include PA. Objective PA will be measured by the Actiheart accelerometer, which has previously been used for wheelchair users with SCI in laboratory and outpatient settings [47]. In this study, it will be used in an inpatient setting and among people with SCI and some ambulatory function, which has not been previously described. As a measure of self-reported PA, a validated Danish version of the LTPAQ-SCI will be used. This version has been adapted to a Danish context in close collaboration with the developers of the original questionnaire; PA-related active transportation, such as hand biking or wheeling to work or school, as well as active physiotherapy exercises are included, as both are common PA for people with SCI in Denmark.

The primary study is possible due to the average length of stay during initial rehabilitation at CSCI, which is 85 and 86 days, respectively, for people with incomplete tetra- and paraplegia and 110 and 123 days, respectively, for people with complete tetra- and paraplegia (unpublished data, 2014). The study is highly dependent on adherence by interdisciplinary health care professionals and patients to the new intervention. Health care professionals' adherence to the intervention is both supported and measured by a process inspired by a prospective effect and process evaluation for complex trials, in which at least 75% must agree that a specific element of strategic patient education has become a part of routine clinical practice before it is considered implemented [71]. This evaluation is repeated every 6-8 weeks throughout the intervention period. Similarly, perceived barriers to implementation are also evaluated every 6-8 weeks throughout the intervention period. Interdisciplinary coordination meetings occurring three times weekly facilitate the implementation of all interventions.

Patient adherence may be challenging; in one report, patients missed an average of 2.5 hours weekly of rehabilitation [72]. Patient adherence to the intervention is described at discharge by the patient, who will document participation in targeted education elements using a checklist. However, a 2016 study found that the most important factor facilitating participation in clinical studies was the possibility of learning more about SCI and health, which is a clear potential in the intervention study [73]. A review by Van Wyk et al. emphasizes that patient education is an important part of the interdisciplinary rehabilitation of people with SCI and recommend an individualized approach and the use of different settings in which the patient can receive the education [29].

Author Contributions

Nicolaj Jersild Holm has been primarily responsible for writing the protocol. Tom Møller (head supervisor), Fin Biering-Sørensen and Lone Schou (co-supervisors) have all contributed to the development of the protocol and study design, as well as feedback, supervision and contributions to the text writing. Lis Adamsen has read and commented on several of the protocol drafts and contributed ideas for ensuring

adherence of participants during the intervention. Line Dalsgaard has, in particular, contributed critical insights into the clinical setting and workflows involved in the project and the initial development and writing of the protocol. All authors approved the final version of the manuscript.

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Competing interest statement

The authors have no conflicts of interest.

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Figure 1. Timeline for all sub studies and used outcome measures. Figure A and B illustrates the prospective historic control study and the intervention study respectively.

Figure 2. Timeline illustrated on the pocket card for systematic targeted approaches during primary rehabilitation within 2, 4 and 6 weeks after admission (AA) and during the last 4 and 2 weeks before discharge (BD) and at follow up 6 months after discharge. **PA:** Physical activity; **VO2peak**: peak oxygen uptake; **BMI:** Body Mass Index; **DXA:** Dual- energy X-ray Absorptiometry.

Fig. A

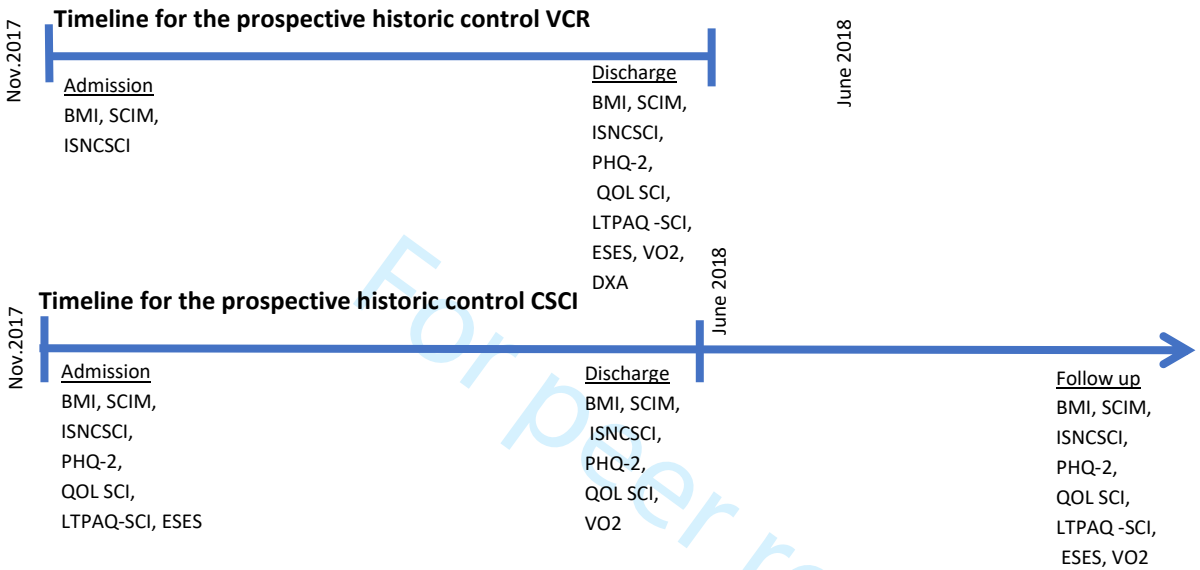
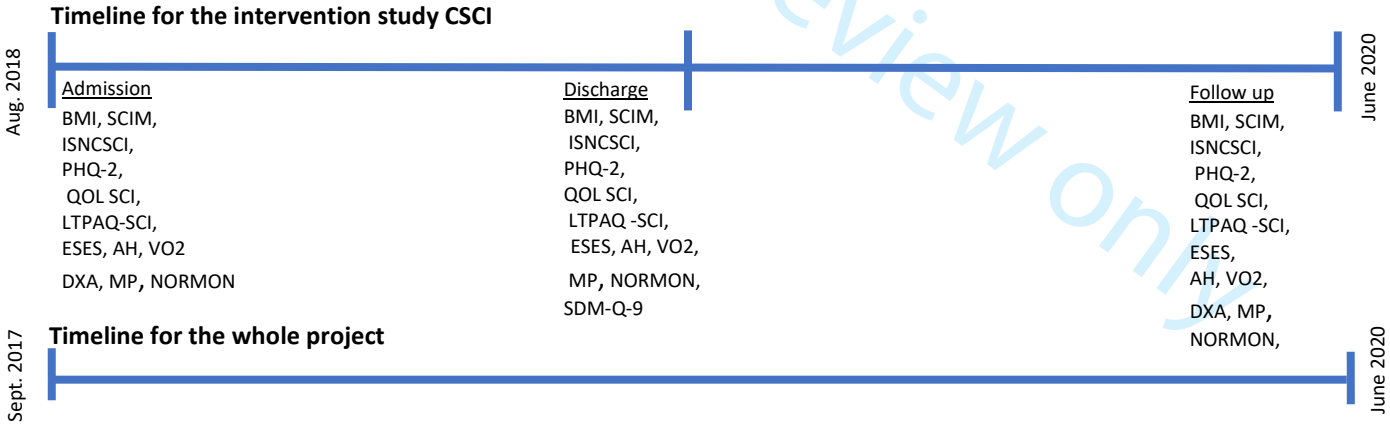
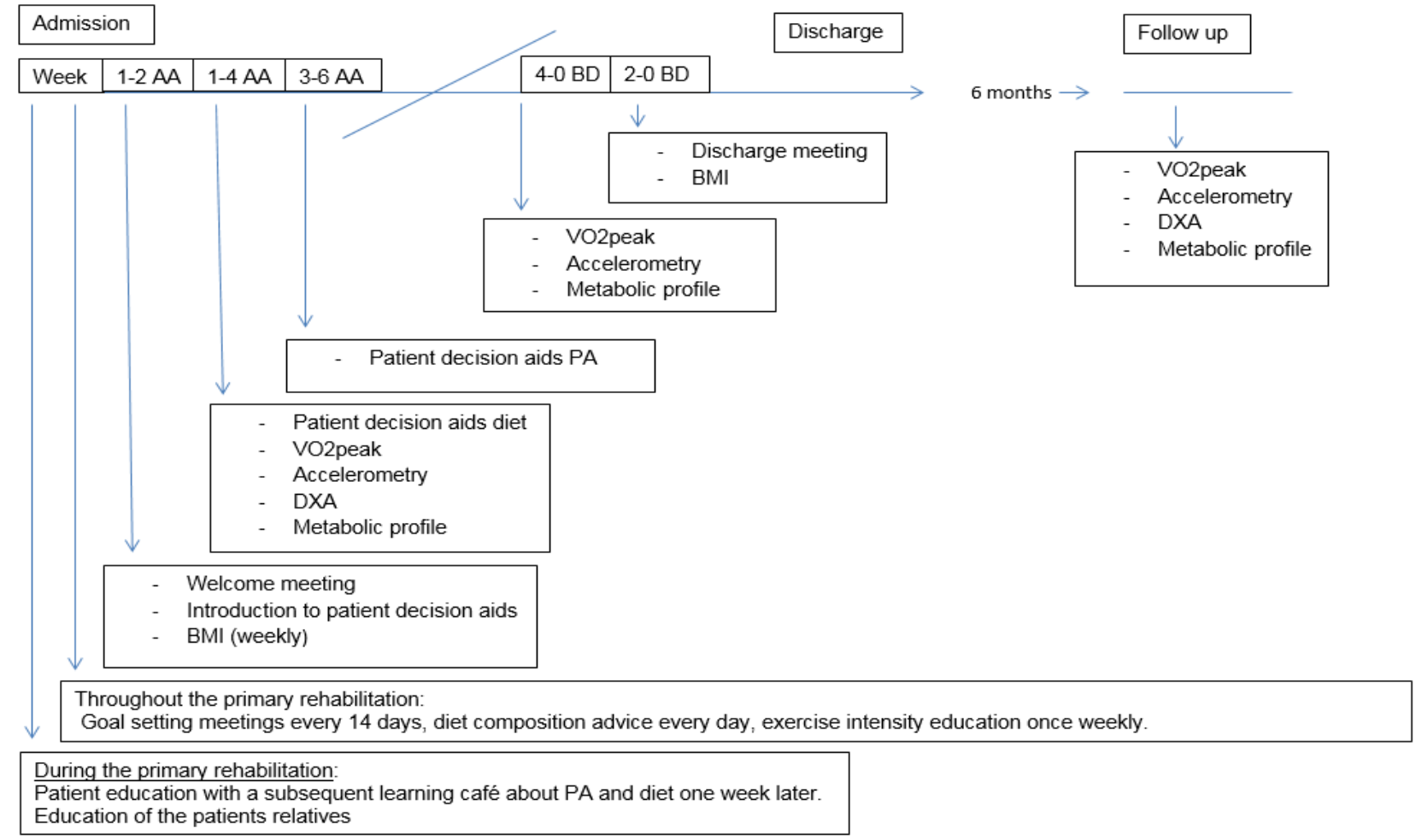


Fig. B



VCR: Center for Spinal Cord Injury, Western Denmark **; CSCI:** Clinic for Spinal Cord Injuries, Eastern Denmark; **BMI:** Body Mass Index**; SCIM**: Spinal Cord Injury Independence Measure; **ISNCSCI**: International Standards for Neurological Classification of Spinal Cord Injury; **PHQ-2**: Patient Health Questionnaire- 2; **QOL SCI**: International SCI Quality of Life Basic Data Set; **LTPAQ-SCI**: Leisure Time Physical Activity Questionnaire for people With Spinal Cord Injury; **ESES**: Exercise Self Efficacy Scale **;AH Actiheart (accelerometer); VO2peak**:peak oxygen uptake **;DXA**; Dual- energy X-ray Absorptiometry **MP**: Metabolic profile;**; NORMON: Nordic monitoring of diet, physical activity and overweight; SDM-Q-9: 9-item Shared Decision Making Questionnaire**


Admission
Week
1-2 AA
1-4 AA
3-6 AA
Discharge
4-0 BD
2-0 BD
6 months
Follow up
- Discharge meeting
- BMI
- VO2peak
- Accelerometry
- Metabolic profile
- VO2peak
- Accelerometry
- DXA
- Metabolic profile
- Patient decision aids PA
- Patient decision aids diet
- VO2peak
- Accelerometry
- DXA
- Metabolic profile
- Welcome meeting
- Introduction to patient decision aids
- BMI (weekly)
Throughout the primary rehabilitation:
Goal setting meetings every 14 days, diet composition advice every day, exercise intensity education once weekly.
During the primary rehabilitation:
Patient education with a subsequent learning café about PA and diet one week later.
Education of the patients relatives

Appendix: Strategic interventions

	Strategic interventions	Scope/ Content	Procedure	Health care staff	Process
Information and education in group sessions	Pre- education of all health care professionals and peers with SCI	To prepare a uniform and systematic approach and clarifying the roles of each profession in relation to the targeted patient education, an evidence-based pre-education of the inter-disciplinary health care personnel and peers with SCI is performed about cardiovascular risk, PA and healthy diet.	Pre-education is performed by stakeholders, as one session just before the intervention start-up. Pocket cards with evidence based basic recommendations related to PA and healthy diet in people with SCI are provided to all professions and peers with SCI.	All health care professionals at the clinic, and all peers from the peer corps.	The pre-education is performed multiple times until all health care professionals have attended the pre-education.
	Patient education + session about diet and PA	To Inform the patients about SCI in general, including specific evidence based information about cardiovascular risk and overweight as a mandatory part, facilitating patients discussing healthy diet and PA	Patient education is performed face- to-face as a group session. Afterwards the patients discuss PA and healthy diet. Interdisciplinary health care professionals facilitates the session from evidence based information in the patient decision aids material.	Patient education: Medical doctors. Session about diet and PA: Interdisciplinary health care professionals.	Once
	Education of relatives	To inform the relatives about SCI in general, including specific evidence based information about cardiovascular risk and overweight and the benefits of healthy diet and PA as a mandatory element.	The session last a full day with face-to-face information and discussion about several aspects related to SCI and the role as a relative.	Interdisciplinary+ invited relatives to former patients sharing their experiences about being a relative to a person with SCI	Once
	Admission meeting	A group setting where patients and relatives are informed about the scope of the rehabilitation and consequences of a SCI.	Information face- to-face about cardiovascular risk and overweight and the benefits of healthy diet and PA is provided	Interdisciplinary team	Once

	Discharge meeting	A group setting where the patient and relatives are informed about the discharge in general, and how to manage consequences of the SCI in a new context after discharge	Information face- to-face about how to transfer the achieved knowledge and behaviors related to PA and healthy diet to a new context and information about the risk of low PA and gaining weight after discharge is provided.	Interdisciplinary team	Once
	Diet composition advice	Recommendations about the diet composition at lunch servings is presented, based on the national nutrition guidelines.	Servings take place in a dining room. Visual material with diet composition recommendations is available and a plate model for inspiration is presented, with 200-300 gram of vegetables.	Kitchen staff	Every day
	Exercise intensity education	Education about evidence based exercise amount and intensity for reducing cardiovascular risk and how to monitor intensity by using ratings of perceived exertion	The education is delivered by trained physiotherapists during group sessions of wheelchair skills training and cardiovascular exercise sessions.	Physiotherapist	Once weekly
Motivational physiologic outcome measures and face-to-face feedback	BMI	BMI is assessed as part of existing routines and the patient is informed about the course of BMI. Serves as motivational tool.	Information is delivered to the patient face to face, in a private setting, with no other agendas. Evidence based actions related to BMI are discussed if relevant. Physiotherapists makes sure that the patient is up to date with total weight of the wheelchair and cushion before assessment	Nurses + Physiotherapists.	BMI and feedback is performed every week throughout the rehabilitation
	VO2peak	VO2peak serves as a marker of physical capacity and the patient is informed about the test result and the course of physical capacity. Serves as motivational tool.	Information is delivered to the patient face to face, in a private setting, with no other agendas. Evidence based actions related to physical capacity are discussed if relevant.	Physiotherapists	Measurement and subsequently feedback at: Admission Discharge Follow up

	Accelerometry	Accelerometry serves as a marker of amount and intensity of PA and the patient is informed about the result and the course of PA. Serves as motivational tool.	Information is delivered to the patient face to face, in a private setting, with no other agendas. Evidence based actions related to are discussed if relevant	Physiotherapists	Measurement and subsequently feedback at: Admission Discharge Follow up
	DXA	DXA serves as a marker of body composition (percentage lean mass and fat mass) and the patient is informed about the result and the course of body composition. Serves as motivational tool.	Information is delivered to the patient face to face, in a private setting, with no other agendas. Evidence based actions to change body composition are discussed if relevant	Medical doctors	Measurement and subsequently feedback at: Admission Follow up
	Metabolic profile	Metabolic profile serves as a biomarker for diabetes and atherosclerotic disease and the patient is informed about the result and the course of measurements. Serves as motivational tool.	Information is delivered to the patient face to face, in a private setting, with no other agendas. Evidence based actions related to metabolic disease are discussed if relevant	Medical doctors	Measurement and subsequently feedback at: Admission Discharge Follow up
Goalsetting and action planning (lifestyle changes)	Introduction to patient decision aids for diet and PA and a brochure about food, weight and health for people with SCI	A setting in the early rehabilitation phase, where the decision aids and brochure are provided to the patient. The structure and goal of the two decision aids is introduced. The brochure supports the aim and rationale of the two decision aids.	A private setting between the patient and nurse face-to-face with no other agendas. From the time of introduction until the first goal setting meetings about diet and PA, the patient may read the information coupled to the recommendations for diet and PA.	Nurses + Physiotherapists	Once
	Goal setting using patient decision aids for diet and PA	Consists of two different patient decision aids. They are evidence-based tools describing several options, recommendations and consequences of choices, and creates the basis for the decision process. The aim is	The tool consists of written information material. The decision process together with the health care professionals, takes place face to face, in a private setting, with no other agendas. If requested by the	Interdisciplinary team	A continuous process until a decision is made by the patient. The tools for diet and PA are introduced at the

	to help the patient consider each option in relation to his/her overall life situation and make a choice that fits the patient well.	patient, peers with SCI are accessible, ready to share their own experiences related to PA and diet.		***goalsetting meetings*** approx. 4 and 5 weeks after admission respectively.
Goal setting meetings	A setting with the patient where goals for the rehabilitation are defined including goals related to PA and healthy diet.	Previous goals are evaluated and new goals are defined for the next 14 days. Asking the patient about goals for PA and healthy diet is mandatory.	Interdisciplinary team	Every 14 days
Follow up 3 months after discharge.	Follow up in an outpatient setting on the course of BMI and healthy diet.	The follow-up is a face-to-face interaction based on the patient decision aids for diet	Nurses	Once

Interdisciplinary team: Medical doctor, nurse, physiotherapist, occupational therapist, social worker, psychologist.

SCI: Spinal Cord Injury; PA: Physical Activity; BMI: Body Mass Index; DXA: Dual-energy X-ray Absorptiometry

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

		Reporting Item	Page Number
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	3
Protocol version	#3	Date and version identifier	2
Funding	#4	Sources and types of financial, material, and other support	13
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	13

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	13
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	13
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	3-4
Objectives	#7	Specific objectives or hypotheses	5
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5

Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-9
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	N/A Decisions related to the intervention are made by the clinical staff
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	12-13
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	7
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical	7

		assumptions supporting any sample size calculations	
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	6
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	N/A due to consecutive enrollment
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	N/A due to consecutive enrollment
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N/A due to consecutive enrollment
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A due to consecutive enrollment
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A due to consecutive enrollment
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	9

Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	13
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	11
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	11
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	-
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	11
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A The trial evaluates elements in standard care which are not terminated.

Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	11
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	3
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	3
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	3
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	11
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	13
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	11
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	11

Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	3
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	13
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	11
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	3
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	9

BMJ Open

Health promotion and cardiovascular risk reduction in people with spinal cord injury - physical activity, healthy diet and maintenance after discharge: study protocol for a prospective national cohort study and pre-post intervention study

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Primary Subject Heading:	Rehabilitation medicine
Secondary Subject Heading:	Neurology
Keywords:	Spinal Cord Injuries, Metabolic Syndrome, Health Promotion, Exercise, Diet Therapy

TITLE PAGE

Health promotion and cardiovascular risk reduction in people with spinal cord injury - physical activity, healthy diet and maintenance after discharge: study protocol for a prospective national cohort study and pre-post intervention study

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Word count: 5.757

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ABSTRACT

Introduction Spinal cord injury (SCI) predisposes those who suffer from it to physical inactivity and weight gain; consequently, death due to cardiovascular diseases is more frequent among people with SCI than in the general population. The literature documents a consensus about an interdisciplinary multimodal approach for the prevention and treatment of cardiovascular risk factors including overweight and obesity in people with SCI, focusing on diet, physical activity (PA) and behavioral interventions. This study will investigate implementation of recommendations from a recent clinical practice guideline for identification and management of cardiometabolic risk after SCI through multimodal patient education in a subacute clinical setting.

Methods and analysis All patients who are aged 18 years or older with an SCI within the previous 12 months and admitted to highly specialized rehabilitation are included, regardless of SCI etiology or neurological level. A primary study designed as a controlled pre-post pragmatic intervention study with 6-month follow up evaluates the effect of the clinical intervention; a prospective national cohort study on body mass index (BMI) serves as a historical control. The intervention consists of a standardized approach to patient education about cardiovascular risk factors, PA and a healthy diet that begins at the outset of primary SCI rehabilitation and is integrated into existing settings and workflows. Outcome measures are collected at admission, discharge and 6 months after discharge and include VO2peak (primary outcome), BMI, body composition, metabolic profile, neurologic status, level of functioning, depression, quality of life, objective PA (accelerometry), self-reported PA, self-assessed physical activity ability, shared decision making, and dietary habits. Test-retest reliability of four VO2peak test protocols are investigated, as is test-retest reliability of a multisensor accelerometer in a rehabilitation setting.

Ethics and dissemination

The project is approved by the Committees on Health Research Ethics in the Capital Region of Denmark on 10.07.2018 (Journal-nr.: H-18018325). The principal investigator obtains Informed consent from all participants. The interventions in the project are closely related to existing rehabilitation care, and the risk of pain and discomfort is considered modest. Any unintended events related to the elements of the intervention are reported, according to existing regional procedures. Data are stored in a secure web-based database (Redcap). The primary study and prospective cohort study are registered at Clinicaltrials.gov. Positive and negative results will be submitted to relevant scientific journals related to SCI for publication. Important protocol modifications are reported to the Committees on Health Research Ethics in the Capital Region of Denmark.

Registration details

The project is approved by the Danish Data Protection Agency (j.nr. VD-2018-380, I-Suite nr.: 6631) and (RH-2017-345, I-Suite nr.: 06052). The project is registered at Clinicaltrials.gov (NCT03689023) and (NCT03369080).

Article summary

Strengths and limitations of this study

The prospective cohort study includes both SCI centers in Denmark and the intervention study includes all newly injured people with SCI admitted to rehabilitation at the East Denmark SCI-center.

Four predefined protocols for assessing VO2peak are used due to the heterogeneity of functional level in the SCI population.

The pre-post intervention study is based on a pragmatic real-life approach by including existing settings and work flows, which is a strength, but consistent implementation of multimodal interventions may be challenging due to changes in the clinical setting.

Lack of randomization is a study limitation.

INTRODUCTION

Table 1. World Health Orgainzation Trial Registration Data Set (Version 1.3.1)

Data category	**Information**[32]
Primary registry and trial identifying number	ClinicalTrials.gov (NCT03369080) and (NCT03689023).
Date of registration in primary registry	12.11.2017 and 26.09.2018
Secondary identifying numbers	The Committees on Health Research Ethics in the Capital Region of Denmark on 10.07.2018 (Journal-nr.: H-18018325) and the Danish Data Protection Agency (j.nr. VD-2018-380, I-Suite nr.: 6631) and (RH-2017-345, I-Suite nr.: 06052)
Source(s) of monetary or material support	This work was supported by a mutual cooperation about the research program " Centre for Integrated Rehabilitation of Cancer Patients (CIRE) - Neuro/Psychology", between the University Hospitals Centre for Health Care Research, University hospital Copenhagen, Rigshospitalet, University College Copenhagen, Department of Nursing and Nutrition, and the NeuroScience Centre, Rigshospitalet.
Primary sponsor	This work was supported by a mutual cooperation about the research program " Centre for Integrated Rehabilitation of Cancer Patients (CIRE) - Neuro/Psychology", between the University Hospitals Centre for Health Care Research, University hospital Copenhagen, Rigshospitalet, University College

	Copenhagen, Department of Nursing and Nutrition, and the NeuroScience Centre, Rigshospitalet.
Secondary sponsor(s)	
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Public title	Health promotion and cardiovascular risk reduction in people with spinal cord injury - physical activity, healthy diet and maintenance after discharge: study protocol for a national cohort study followed by a clinical intervention study.
Scientific title	Health promotion and cardiovascular risk reduction in people with spinal cord injury - physical activity, healthy diet and maintenance after discharge: study protocol for a prospective national cohort study followed by a pre-post intervention study.
Countries of recruitment	Denmark
Health condition(s) or problem(s) studied	Spinal Cord Injury and the cardiovascular risk factor, including weight gain and consequences of an inactive lifestyle during and after the primary rehabilitation.
Intervention(s)	A controlled pre-post multi modal pragmatic clinical intervention study, with 6-months of follow up containing “new usual care” consisting of a uniform and systematic institutional strategy incorporating targeted strategic patient education about cardiovascular risk factors, physical activity and a healthy diet lifestyle starting early in the primary rehabilitation process.
	Comparator: A historic control conducted as a national prospective cohort study before “new usual care”
Key inclusion and	Inclusion criteria: All patients who are 18 years or older, and with a Spinal Cord Injury (SCI) within the last 12 months and admitted at Clinic for Spinal Cord

exclusion criteria	Injuries, are included regardless of etiology to the SCI, neurological level or completeness of the lesion if informed consent is retrieved.
	Exclusion criteria: Exclusion criteria for VO2peak test in the study includes motor complete SCI at C4 level or above, and assisted ventilatory function. Other exclusion criteria are the presence of decubitus, severe spasticity or musculoskeletal problems considered at risk of aggravation during testing or preventing completion of the VO2peak test.
Study type	Interventional. The study consists of a primary study designed as a controlled pre-post clinical intervention study and a historic control conducted as a prospective cohort study.
	Allocation: The intervention in the primary study is a part of new standard care. Therefore randomization or blinding is not appropriate.
	Primary purpose: prevention
Date of first enrolment	November 2017
Target sample size	160
Recruitment status	Recruiting
Primary outcome(s)	Oxygen uptake measured as VO2peak.
Key secondary outcomes	Body Mass Index, Body composition (determined by Dual energy x-ray absorptiometry), metabolic profile consisting of CRP as a marker for inflammation, lipid profile describing Total cholesterol, Triglycerides, HDL cholesterol, and LDL cholesterol and Hemoglobin A1c as a marker for carbohydrate metabolism, and blood pressure (BP).
Ethics Review	The project is approved by the Committees on Health Research Ethics in the Capital Region of Denmark on 10.07.2018 (Journal-nr.: H-18018325)
Completion data	June 2020
IPD sharing statement	Data can be accessed by request to the corresponding author after publications related to the Ph.D project are made.

The annual incidence of traumatic spinal cord injury (SCI) in Denmark is 10-15 per million [1], while nontraumatic SCI has accounted for approximately 60% of all newly injured patients admitted to the two SCI centers in Denmark in recent years. SCI is a life-changing event that may affect all bodily functions below the level of the lesion, requiring highly specialized interdisciplinary rehabilitation aiming at the

highest possible level of independent functioning and resulting in significant costs to affected individuals and society. Rehabilitation at the Clinic for Spinal Cord Injuries in Eastern Denmark (CSCI) generally includes functional training, strength training, cardiovascular exercise and fine motor training of the upper extremities. In addition, circulation, respiration, thermoregulation, bowel and bladder function, skin integrity, pain and spasticity are continually assessed and addressed, and aids are provided to compensate for functional losses, including communication aids and splinting. Counseling to address social and economic issues, sexual function and psychological issues is provided.

Over the long term, SCI and resulting impairments predispose affected individuals to increased cardiovascular risk and premature cardiovascular death; a clinical practice guideline addressing cardiometabolic disease after SCI was recently published [2]. However, targeted patient education addressing long-term cardiovascular risk, based on individualized face-to-face interaction between patients and health care professionals and aiming at a core clinical outcome, is not systematically integrated into early stages of specialized SCI rehabilitation at CSCI, even though an opportunity may exist to target the link between injury-related immediate impacts on functionality and long-term health consequences [3 4]. Similarly, health promotion education and activities related to body mass index (BMI), diet, smoking, alcohol intake and physical activity (PA) are not systematically provided, and assessment of physical capacity, metabolic profile and body composition is not a part of standard care. A systematic approach may ensure that all patients at CSCI receive information and knowledge related to health promotion and the risk of cardiovascular disease, which may support patient adaptation and adherence to recommended PA and healthy diet.

As a result, cardiovascular risk factors, including weight gain and the consequences of an inactive lifestyle during and after primary rehabilitation, are the focus of the current study.

The course of overweight

The prevalence of overweight in people with SCI is conservatively estimated at 66%. Overweight has been found to be one of the most common cardiometabolic risk factors among people with SCI, increasing the cardiovascular risk profile of wheelchair-dependent people with paraplegia [5], [6] [7 8]. Energy expenditure decreases significantly after sustaining a SCI and remains low. Although body fat and body weight decrease in the acute injury phase, they increase in the subacute phase, and a loss of lean body mass in the lower extremities and trunk has been observed during the first year after injury [9]. BMI increases gradually during the first years after discharge from primary rehabilitation [10]. Obese people with SCI achieve a lower level of functioning during primary rehabilitation than do those of normal weight [11]. Overweight in people with SCI is associated with increased risk of depression [12]. Nutritional education delivered by a dietician or lifestyle coach has been found promising [13-15], although it is often not offered in a clinical setting [16]. Increased knowledge about weight management among clinicians is recommended, but weight management is often not prioritized in rehabilitation settings. Clinicians have called for evidence-based knowledge and clinical guidelines [16 17].

Impact of physical activity on health and fitness

In the general population, PA is associated with beneficial effects on diseases contributing to the metabolic syndrome, and its beneficial effect increases when it is combined with diet therapy [18]. Similar effects of

PA among people with SCI have been described; numerous studies have reported the positive effects of PA intervention programs in people with both acute and chronic SCI on physical capacity, strength and functional performance, including the effect of exercise interventions on cardiometabolic health [19 20]. Evidence-based exercise guidelines for cardiometabolic health in people with SCI recommend a minimum of 30 minutes of moderate to vigorous aerobic exercise three times weekly to reduce cardiovascular risk factors [21]. The long-term effect increases when PA is combined with behavioral interventions [22]. However, not all people with SCI are able to participate in PA intervention programs or maintain PA. Rates of participation in leisure time PA and in sports activities after discharge from primary rehabilitation are low among people with SCI [23 24]. Intra- and extrapersonal factors influence participation in PA, including self-efficacy related to being physically active [25]. PA alone is insufficient to induce weight loss in people with SCI [2]. Therefore, a broader approach to cardiovascular risk reduction may be appropriate, and a combination of several interventions is required to promote a physically active lifestyle and weight loss [26]. Examples of key intervention components are autonomy in relation to decision-making and behavioral interventions comprising goal setting and feedback via physical assessments [26 27].

Although the separate or combined effects of PA, diet and behavioral interventions have been investigated previously in people with SCI with generally positive results, this study will investigate the effect of educational and behavioral interventions related to PA and diet in a subacute clinical rehabilitation setting. The study will investigate implementation of recommendations from the recent clinical practice guideline for identification and management of cardiometabolic risk after SCI, including assessments of physical capacity, body composition, bodyweight, dyslipidemia and impaired fasting glucose, as well as PA and diet [2]. Feedback on these assessments and goal setting will be part of the patient education delivered by clinical staff across settings during primary rehabilitation.

To the best of our knowledge, only a single study has investigated outcomes related to cardiovascular risk factors following PA and behavioral interventions during subacute inpatient rehabilitation using outcomes related to cardiovascular risk factors, but this study only included wheelchair users [28 29]. The current study will contribute to existing knowledge by consecutively enrolling all patients, aged 18 years or older, with a new SCI who are admitted to CSCI, regardless of mobility status, and by evaluating the implementation of evidence-based guidelines for identification and management of cardiometabolic risk after SCI in a clinical setting.

Objectives

This study will investigate the effect of a systematic approach to incorporating targeted patient education about cardiovascular risk factors, PA and a healthy diet early in the primary rehabilitation process, compared to a historical control group.

STUDY DESIGN

The primary study comprises a primary study designed as a controlled pre-post pragmatic intervention study with 6 months of follow up. A prospective national cohort study provides a historical control (Fig 1).

Substudies

BMI is considered a high-risk determinant due to the impact of overweight on the cardiovascular risk profile and level of functioning among wheelchair-dependent people with SCI [5], [6] [7 8]. A prospective representative longitudinal survey of BMI conducted before the controlled intervention in collaboration with SCI Center of Western Denmark serves as a historical control (substudy 1). Additional outcome measures will be collected at CSCI during the survey period, including measures of PA, physical capacity and body composition. Two substudies of test-retest reliability of a VO2peak test (substudy 2) and a multisensor accelerometer (substudy 3) will be performed. VO2peak and accelerometry are considered valid methods to measure the effect, amount and intensity of PA at discharge from primary SCI rehabilitation. Both will be collected repeatedly during the primary study and serve as individual motivational components in education and communication, as well as outcome measures. Assessing test-retest reliability of the two procedures is essential.

METHODS AND ANALYSIS

The SPIRIT reporting guidelines are used in the reporting of the clinical trial [30].

Patient involvement

A user panel consisting of six patients (three women and three men aged 23 to 78 years), including both recently injured people and those who had been living with SCI for some time, was established and involved in the early phase of study protocol development. All participants were hospitalized at CSCI when they participated in semi-structured focus group interviews about their perceptions of health promotion practices in the clinical setting [31]. The interview focused on both the existing level of information about increased risk of overweight and cardiovascular disease after SCI and education about diet and PA as a way of reducing those risks. Data were analyzed using constant comparative analysis [32]. The user panel recommended more information in the early phase of rehabilitation about cardiovascular risk, PA and diet and more support and guidance about appropriate diet and being physically active, which is the primary aim of the project. The study results will be disseminated to project participants.

Participants and eligibility criteria

Inpatients who are aged 18 years or older, injured with SCI within the last 12 months and admitted at CSCI are recruited and consecutively included after providing informed consent, regardless of SCI etiology (i.e., traumatic or non-traumatic), neurological level or completeness[1] of the lesion. In substudy 1, all newly injured people with SCI admitted at the SCI Centre of Western Denmark are also included. Substudy 1

[1] The completeness of the injury is graded according to the ASIA Impairment Scale (AIS). AIS is used to determine the degree of motor and sensory function below the level of the SCI. A complete or incomplete injury is defined as absence or presence of sensory and motor function in the most caudal sacral segments. A = sensory and motor complete; B = sensory incomplete without motor function > 3 levels below the motor level of injury on both sides of the body; C = motor incomplete, with preserved motor function below the level of injury and where > 50% of the key muscles below the injury level have a degree < 3 by manual muscle test (MMT); D = motor incomplete with preserved motor function below the level of injury and where > 50% of key muscles below the injury level have a degree > 3 by MMT; E = normal sensory and motor function in all segments.

serves as a historical control group, and the intervention in the primary study is part of a new standard of care. Therefore, randomization, blinding and sample size calculation are not appropriate.

Exclusion criteria for the VO2peak test include motor complete SCI (AIS A and B) at cervical (C)4 level or above and a need for artificial ventilation. Other exclusion criteria are the presence of decubiti, severe spasticity or musculoskeletal problems at risk of exacerbation or aggravation during testing or preventing completion of the test.

Substudy 3 includes a convenience sample of 20 patients with the goal of ensuring variation in age, gender, neurological level and completeness of SCI.

Primary study: A systematic interdisciplinary multimodal intervention that facilitates physical activity, healthy diet and maintenance after discharge through strategic patient education as part of usual care, with the aim of decreasing cardiovascular risk

This pre-post study includes all patients aged 18 years or older with a new SCI who are admitted at CSCI during a period of 12 to 18 months. The study includes follow up 6 months after discharge from primary rehabilitation.

Approximately 70 patients with a new SCI are admitted to CSCI annually; but due to expected missing data , complete data sets from admission through follow up may be fewer.

Intervention

The intervention is based on recommendations in a recently released clinical practice guideline for the identification and management of cardiometabolic risk after SCI and conclusions from a meta- synthesis by Williams et al. and a systematic review by Greaves et al. [2 26 27]. A combination of several interventions is most effective at promoting a physically active lifestyle and weight loss after SCI. Crucial intervention components are autonomy in relation to decision-making about PA, support and follow up from health care professionals and mentors with SCI, information about adapted PA and behavioral interventions comprising goal setting and feedback from, for example, physical tests. Greaves et al. recommend group sessions, individual sessions and interdisciplinary interventions in the clinical setting that focus on maintaining PA and healthy diet [26].

The intervention will be integrated into usual care during the project period, and all newly injured patients will receive all multimodal components as appropriate to individual circumstances, such as level of injury. At discharge, the patient will describe adherence to the intervention and document participation in targeted education elements on a checklist. Similarly, health care professionals will use a checklist to document adherence to interventions at the start, midpoint and end of the study period. Medical records and schedules for goal-setting meetings will also be reviewed to monitor health care professionals' adherence to the interventions. Rehabilitation of the physical level of functioning and physical capacity (e.g., physiotherapy) will occur as part of usual care and is a mandatory core component of highly specialized SCI rehabilitation. However, decisions about PA made by the patient during rehabilitation may be integrated into the rehabilitation program to achieve his or her goals for PA during and after the rehabilitation period.

A central part of the intervention is to create a standardized approach to targeted strategic patient education of patients about cardiovascular risk factors, PA and a healthy diet by systematizing the existing clinical setting and treatment interventions.

In the process of reorganizing the institutional approach to addressing cardiovascular risks, *pre-education* of interdisciplinary health care personnel and peers with SCI is mandatory to clarify their roles in relation to targeted patient education. Pocket cards with evidence-based recommendations related to PA, diet and BMI in people with SCI are provided to all health care professionals and peers with SCI and will also illustrate the timeline for systematic targeted approaches during primary rehabilitation (Fig. 2)

Patients receive information and instructions about PA and healthy diet through patient education based on principles that include individualized face-to-face interaction between patients and health care professionals while working towards a specific health-related outcome [33]. The interventions begin at the outset of primary SCI rehabilitation and are integrated into usual care at predetermined time points (e.g., DXA scan, VO2peak, metabolic profile with feedback early after admission to rehabilitation and goal setting meetings about PA and diet within 6 weeks after admission) throughout the entire rehabilitation continuum, with the goal of secondary and tertiary cardiovascular prevention.

Representatives of all the health care professions generally carry out education of patients and their relatives in a variety of educational settings [34 35], with a focus on clarifying the importance of PA and a healthy diet. Patient education involves training sessions [36] and feedback on physiological outcome measures and tests that also serve as motivational tools. Additionally, goal-setting meetings, tools for shared decision making [37] [26] [38] and use of mentors with SCI are also integrated as components supporting decision making about PA and healthy diet. BMI and diet are evaluated 3 months after discharge in an outpatient setting (see appendix for a more detailed description of the strategic interventions).

All components are offered to patients as a mandatory part of the intervention, ensuring that information and patient education are provided and decisions about PA and healthy diet are made. However, patients individually determine the extent to which they engage in making decisions and setting goals about PA and healthy diet. Interdisciplinary health care professionals respect the decisions and autonomy of patients who choose not to set goals or make decisions about PA and healthy diet.

Several outcome measures used to evaluate the intervention at admission, discharge and at follow up 6 months after discharge are also motivational components of the intervention: BMI, body composition measured by dual- energy X-ray absorptiometry (DXA), physical capacity (VO2peak), PA (Actiheart multisensor accelerometer) and blood samples describing metabolic profile.

Substudy 1. Prospective national survey of body mass index among people with SCI

This study includes all patients with a new SCI hospitalized at CSCI or SCI Center of Western Denmark during a period of 10 months; 100 patients are expected to participate. Data on BMI, level of functioning (Spinal Cord Injury Independence Measure III [SCIM III]) and neurological status (International Standards for Neurological Classification of SCI [ISNCSCI] are collected at both centers. Patients with an SCI within the last 12 months who are admitted for rehabilitation several months after injury are also included in the prospective survey. Data on BMI at the time of injury are collected for all patients at admission to primary rehabilitation from the patient's medical record. At CSCI, BMI every 6 weeks, quality of life (QoL SCI),

depression (PHQ-2), amount of PA (Leisure Time Physical Activity Questionnaire for people with Spinal Cord Injury [LTPAQ-SCI]) and self- assessed ability to be physically active (ESES) will be collected at admission, discharge and follow up 6 months after discharge. Measures of physical capacity (VO2peak) and body composition (DXA) are also obtained at discharge. Data from this substudy serve as a historical control for the Intervention study.

Substudy 2. Test-retest reliability of VO2peak testing

This study includes all patients participating in substudy 1 who are able to perform the VO2peak test at discharge from primary rehabilitation. Patients are randomized to a test session of either intra- or interrater reliability. Due to the complexity of SCI, four pre-defined exercise protocols are used to reach criteria for VO2peak, defined as a respiratory exchange ratio (RER) > 1.0 [39]. As a starting point, people with an incomplete SCI, as defined by ISNCSCI, will use a seated cross-trainer (NuStep T5XR®), which has software incorporating both a standard and a modified test protocol. The standard protocol starts at 50 watts (W) with 25W incremental increases every 2 minutes in the first three stages, 30 W increments thereafter and 115 steps per minute (SPM). The modified protocol starts at 25W with 15W increments every 2 minutes and 80 SPM. The equipment and modified protocol are reliable in people with traumatic brain injury and has been validated in healthy persons [40 41]. In people with an incomplete SCI, the equipment is safe and involves a large amount of muscle mass [42]. People with an ISNCSCI-defined complete SCI, very de-conditioned patients or those with an incomplete SCI but a poor ISNCSCI lower extremity motor score that may hinder reaching VO2peak on the seated cross trainer will use an arm-cranking ergometer (SCI FIT Pro1®). Test protocols used on the SCI FIT ergometer are established from the most common protocols for people with tetra- and paraplegia during rehabilitation reported in a recent systematic review [39]. The study protocols are designed as stage protocols starting at 5 W with an increase every minute of 5W for people with tetraplegia and 10W for people with paraplegia and 60 revolutions per minute.

If predefined criteria for VO2peak are not reached during test 1, a more suitable protocol to reach VO2peak is chosen for test 2 and will be retested at test 3. However, this is not possible if the protocol designed for people with tetraplegia is used. The test-retest study takes place at discharge, with 48 hours to 5 days between tests occurring at the same time of the day. Participants refrain from caffeine, alcohol and intensive physical exercise on the day of testing, as well as tobacco smoking two hours before testing. Bladder emptying occurs immediately before testing.

In the intervention study, the four exercise protocols are used to ensure that a true VO2peak is reached during the rehabilitation process. VO2peak is highly dependent on the level and completeness of the SCI and the testing equipment; for instance, a patient may be initially tested on the protocol designed for people with a complete tetraplegia and later tested on the non-modified standard protocol in the seated cross trainer due to neurological recovery and improvement in functional level.

Substudy 3. Test-retest reliability of a multisensor accelerometer

This study includes a convenience sample of 20 patients ensuring a representative sample of individuals with para- and tetraplegia, complete and incomplete SCI, age and gender. The equipment used for monitoring the amount and intensity of PA consists of sensors registering acceleration and heart rate and is

placed on the thorax of the participant with two surface electrodes. The sensor can be dismantled from the thorax without removing the adhesive part of the surface electrodes, making it possible to easily reattach the sensor and resume monitoring after e.g. sleeping or bathing. Data are expressed as total and daily physical activity energy expenditure (kcal/min) and the time spent in different activity intensities on the basis of metabolic equivalents. The equipment has been previously used among wheelchair-dependent people with SCI, although its reliability in an inpatient setting has not been assessed [43]. Precision is higher when the equipment is calibrated to individual participants using measures of energy expenditure and corresponding heart rate during rest and during exercise testing, covering a range of submaximal and maximal intensities. The equipment software uses these data to estimate energy expenditure using branched model equations [44]. This method will also take into account compromised cardiac sympathetic innervation in individuals with an injury above T6. In this study, individual calibration is based on activity performed during the VO2peak test (substudy 2), with resting metabolic rate measured before testing for 10 minutes following a rest period of 20 minutes [45 46]. In order to reliably measure total energy expenditure (kcal/min) and the amount and intensity of PA patients are instructed to wear the equipment for 48 hours. They are informed to take off the sensor (not the adhesive part) when bathing, but if they experience discomfort or skin irritation related to the equipment they can as well remove the adhesive part of the electrode. If they have impaired or absent sensation, they are recommended to take off the equipment when sleeping, and to check for skin irritation regularly, alternatively asking a nurse for help if they are not able to do this themselves. A period of 48 hours with sampling epochs every 15 seconds and a minimum wear-time of 80% is aimed for, and considered an appropriate wear time as described by Nightingale et al [47]. However, data from recordings with < 80% wear time will be analyzed as well. To ensure comparability, test-retest procedures are performed over a period of two weeks on identical days of the week .

Outcome measures

Outcome measures evaluating the intervention comprise the following.

Primary outcome

Oxygen uptake Is measured as VO2peak during a maximal exercise test and is the gold standard for measuring aerobic capacity. For people with SCI, several test protocols have been used [36].

Secondary outcomes

Objective PA is measured in a subsample of the historical control cohort and participants in the intervention study with a multisensor device (Actiheart®) recording accelerations and heart rate. It has been previously used for wheelchair users with SCI, and individual calibration is important to get the most accurate data [47]. Evidence-based exercise guidelines for cardiometabolic health in people with SCI recommend a minimum of 30 minutes of moderate to vigorous aerobic exercise three times weekly [21]

Bodyweight is measured as BMI, which is the most widely used outcome measure for body weight in people with SCI. BMI is not sensitive enough to distinguish between fat mass and lean body mass or overweight in people with SCI. Overweight among adults with SCI is defined as ≥ 22kg/m^2 [48] [2]. BMI is

already collected as part of usual care, and data for BMI every 6 weeks until discharge will be included in the project.

Body composition is determined by dual energy X-ray absorptiometry (DXA), which is the gold standard for assessing obesity and body composition. Among adults with SCI, men with >22% body fat and women with >35% body fat should be classified as obese [2].

Metabolic profile consists of C-reactive protein (CRP) as a marker for inflammation and lipid profile including total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C), which are included in the international SCI Endocrine and Metabolic Function Basic Data Set. Triglycerides should not be ≥ 150 mg/dL (1.7 mmol/L). HDL-C should not be < 40 mg/dL (1.03 mmol/L) in men or < 50 mg/dL (1.29 mmol/L) in women [2]. LDL-C should not be > 3.0 mmol/l [49]. Hemoglobin A1c (HbA1c) serves as a marker for carbohydrate metabolism and is included in the International SCI Endocrine and Metabolic Extended Data Set [50 51]. Criteria for a diagnosis of prediabetes include HbA1c 5.7-6.4% (39-47 mmol/mol) and criteria for a diagnosis of diabetes include HbA1c > 6.5% (> 48 mmol/mol) [2]. As approved by the Committees on Health Research Ethics in the Capital Region of Denmark, blood samples will not be stored after analysis.

Blood pressure (BP) is measured by sphygmomanometry. Criteria for a diagnosis of hypertension in people with SCI vary with injury level, severity and etiology. BP should not exceed 130/85 mm Hg.

Level of functioning is determined by the SCIM III, which is a valid and reliable outcome measure designed to assess level of functioning in people with SCI in clinical care and research [52] [53 54] [55].

Neurologic status is determined by the ISNCSCI and is the most widely used classification in people with SCI [56 57].

Depression is measured by the Patient Health Questionnaire-2 (PHQ-2), which is a generic measure of depression. Among people with SCI, a cut-off score of 3 is associated with sensitivity of 83.3% and specificity of 95.7% [58].

Quality of life is measured by the International SCI Quality of Life Basic Data Set (QoL SCI), which consists of three questions about satisfaction with life in general and physical and mental health. It is a valid outcome measure with good internal consistency [59] [60].

Self-reported PA is measured by the Leisure Time Physical Activity Questionnaire for people with SCI (LTPAQ-SCI), which is a self-administered questionnaire about leisure time PA, including amount and intensity during the past 7 days. Reliability and validity of self-reported activity are satisfactory in moderate and high intensity levels [61]. An additional question concerning PA outside of leisure time PA (i.e., PA as part of rehabilitation) is included in substudy 1. The question is designed to be similar to the original questions and is scored using the same intensity scale. During the intervention study, a version of LTPAQ-SCI adjusted to a Danish context will be used. This version is approved by the developers of the original LTPAQ-SCI and includes active transportation and active physiotherapy.

Self-assessed ability to be physically active is measured by the Exercise Self Efficacy Scale for people with SCI (ESES). It is an outcome measure developed for assessing self-efficacy related to PA in people with SCI

and consists of 10 questions on a 0-4 response scale. ESES is reliable with high internal consistency (Cronbach`s alpha 0.94) and satisfactory content validity in the form of face and construct validity [62].

Shared decision making related to patient decision aids for PA and healthy diet is measured by the 9-item Shared Decision Making Questionnaire (SDM-Q-9), which assesses the process of shared decision making between health care professionals and the patient from the patient's perspective. SDM-Q-9 consists of nine statements, which can be rated on a six-point scale from 0 to 5, with higher scores indicating greater shared decision making. All items are summed to yield a raw total score of 0 to 45. SDM Q-9 is only used at discharge.

Varied and healthy diet in an appropriate amount is measured by the Nordic monitoring of diet, PA and overweight (NORMON) developed in a Nordic collaboration and commonly used for monitoring [63]. The questionnaire explores how frequently 16 food indicators, several of which are recommended in the Nordic national nutritional recommendations, have been consumed over the previous 12 months. NORMON also includes questions related to alcohol intake, smoking and PA. The questionnaire was validated in 2009 against existing questionnaires about diet [64]. In this study, a modified version of the questionnaire will ask patients to recall their dietary habits over the previous month.

Statistics

All data collected at admission, discharge and follow up are continuous and are reported descriptively. In the intervention study, differences in the primary and secondary outcomes between baseline and follow up will be analyzed using analysis of covariance. The same approach will be used between baseline and follow up in the historic control study. Likewise differences between the intervention study and the historic control is analyzed using analysis of covariance. Due to the small sample size, participants in the intervention study and historic control will not be matched but participants will be compared to each other controlling for ISNCSCI classification, gender and functional level. a. Linear regression is used to measure the strength and association between BMI and DXA results and the association between the psychometric variables e.g. QoL and depression compared to VO2peak and BMI. Ordinal regression analysis is made for ordinal data e.g. ESES. Missing data are analyzed as intention to treat without imputation, but dropout analysis is made for primary outcomes. In substudies 3 and 4, the reliability of the outcome measures are analyzed by paired t-test, Pearson´s product-moment correlation and coefficient of variation or intraclass correlation coefficient between the test-retest sessions. .

Ethics and dissemination

The project is approved by the Committees on Health Research Ethics in the Capital Region of Denmark on 10.07.2018 (Journal-nr.: H-18018325). During the intervention period, all newly injured patients who are admitted for rehabilitation at CSCI are offered treatment and tests included in the intervention as a mandatory part of usual care to the extent they are able to participate, which may vary with the level of lesion and completeness of SCI. Because the intervention is a part of usual care and comprises a standardized approach to patient education, no data monitoring or interim analysis is planned. Informed consent is obtained to analyze the data generated during the project. The intervention in the project is closely related with the content of the present rehabilitation, and the risk of pain and discomfort is considered modest. During the VO2peak test, special attention is paid to potential symptoms of autonomic

dysreflexia (AD) in people with SCI above T5-6. In case of AD, the exercise test is stopped and relevant actions are initiated. It is assumed that any risks are surpassed by therapeutic gains, i.e. expected reductions in the risk of cardiovascular disease and mortality. Any unintended events related to the intervention are reported according to existing regional procedures, and compensation is covered by the normal procedures for unintended harm during hospitalization. The study is reported to the Danish Data Protection Agency and is registered at Clinicaltrials.gov (See World Health Orgainzation Trial Registration Data Set (Version 1.3.1) (Table 1). Positive and negative results will be submitted to relevant scientific journals related to SCI for publication.

Data statement section

All patient data are stored in a secure web-based database (Redcap) with limited access and ID code, to which data are transferred directly or by an encrypted USB stick. Patients are assigned unique identification numbers, which is the only identifier exported from Redcap during data analysis. Data are stored until December 31, 2027, after which paper material is shredded, data files are deleted and the Redcap database is no longer accessible. The principal investigator has access to all trial data. Data can be accessed upon request to the corresponding author after reports related to the Ph.D. project are published. No data monitoring committee is established.

DISCUSSION

This study will investigate the effectiveness of a systematic institutional strategy incorporating individualized patient education and testing about cardiovascular risk factors, PA and a healthy diet lifestyle early after SCI diagnosis during primary rehabilitation, compared to a historical control group. Our findings will be discussed in light of recent studies suggesting that an interdisciplinary multimodal approach in prevention of cardiovascular risks among people with SCI with a focus on diet, PA and behavioral interventions is beneficial [23] [65] [66] [13 25] [14]. Crucial components of the intervention are autonomy in relation to decision-making and support and follow up from health care professionals and mentors with SCI. A qualitative meta-synthesis concluded that timely information about PA and its benefits in relation to SCI and behavioral interventions using goal setting and motivational feedback through physical tests might be important patient-activating tools [27]. This is consistent with a recent systematic review by Greaves et al. [26], who also strongly recommended that interventions in the clinical setting contain both group sessions and individual sessions as well as interdisciplinary interventions that focus on maintaining PA and healthy diet [26]. These elements are incorporated into the intervention investigated in this study.

Several of the outcome measures used to evaluate the intervention are components of the intervention, as recommended in the clinical guideline for identification and management of cardiometabolic risk after SCI [2]. Outcome measures also serve as individual motivational tools. The primary outcome measure is VO2peak, for which a significant positive relationship exists with some cardiometabolic markers in people with SCI, such as lipid profiles and fasting insulin levels [61]. Consequently, physical activity that increases physical capacity may also reduce the risk of cardiovascular disease [67]. Physical capacity measured as VO2peak is positively associated with functional independence [68], less physical strain during activities of daily living [69] and life satisfaction [70] among people with SCI, although other measures of physical capacity have an important and, in some cases, stronger impact on functional independence [68].

Among people with SCI, several test protocols have been used for assessing VO2peak [36]. In this study, four exercise protocols make VO2peak testing feasible for clinical physiotherapists who, although trained in using the testing equipment, are inexperienced in determining the appropriate workload during VO2peak testing, which is difficult due to the complexity of a SCI. If predefined criteria for VO2peak are not reached, a more suitable protocol is selected. The protocol and equipment used in the study are identical at admission and discharge. If a patient's neurological and functional level has improved to the point where a different protocol and equipment will more accurately measure VO2peak, an additional test at discharge will be performed on a separate day. Data from both tests will be evaluated and the new protocol will be repeated at follow up 6 months after discharge. This approach to testing VO2peak in a clinical setting has, to the best of our knowledge, not been described previously

Secondary outcome measures include PA. Objective PA will be measured by the Actiheart accelerometer, which has previously been used for wheelchair users with SCI in laboratory and outpatient settings [47]. In this study, it will be used in an inpatient setting and among people with SCI and some ambulatory function, which has not been previously described. As a measure of self-reported PA, a validated Danish version of the Leisure Time Physical Activity Questionnaire for people with Spinal Cord Injury will be used. This version has been adapted to a Danish context in close collaboration with the developers of the original questionnaire; PA-related active transportation, such as hand biking or wheeling to work or school, as well as active physiotherapy exercises are included, as both are common PA for people with SCI in Denmark.

The primary study is possible due to the average length of stay during initial rehabilitation at CSCI, which is 85 and 86 days, respectively, for people with incomplete tetra- and paraplegia and 110 and 123 days, respectively, for people with complete tetra- and paraplegia (Fin Biering-Sørensen: Data from Clinic for Spinal Cord Injuries, Denmark, 2014). The study is highly dependent on adherence by interdisciplinary health care professionals and patients to the new intervention. Health care professionals' adherence to the intervention is both supported and measured by a process inspired by a prospective effect and process evaluation for complex trials, in which at least 75% must agree that a specific element of strategic patient education has become a part of routine clinical practice before it is considered implemented [71]. This evaluation is repeated every 6-8 weeks throughout the intervention period. Similarly, perceived barriers to implementation are also evaluated every 6-8 weeks throughout the intervention period. Interdisciplinary coordination meetings occurring three times weekly facilitate the implementation of all interventions.

Patient adherence may be challenging; in one report, patients missed an average of 2.5 hours weekly of rehabilitation [72]. Patient adherence to the intervention is described at discharge by the patient, who will document participation in targeted education elements using a checklist. However, a 2016 study found that the most important factor facilitating participation in clinical studies was the possibility of learning more about SCI and health, which is a clear potential in the intervention study [73]. A review by Van Wyk et al. emphasizes that patient education is an important part of the interdisciplinary rehabilitation of people with SCI and recommend an individualized approach and the use of different settings in which the patient can receive the education [29].

Author Contributions

Nicolaj Jersild Holm has been primarily responsible for writing the protocol. Tom Møller (head supervisor), Fin Biering-Sørensen and Lone Schou (co-supervisors) have all contributed to the development of the

protocol and study design, as well as feedback, supervision and contributions to the text writing. Lis Adamsen has read and commented on several of the protocol drafts and contributed ideas for ensuring adherence of participants during the intervention. Line Dalsgaard has, in particular, contributed critical insights into the clinical setting and workflows involved in the project and the initial development and writing of the protocol. All authors approved the final version of the manuscript.

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Competing interest statement

The authors have no conflicts of interest.

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Figure 1. Timeline for all sub studies and used outcome measures. Figure A and B illustrates the prospective historic control study and the intervention study respectively.

Figure 2. Timeline illustrated on the pocket card for systematic targeted approaches during primary rehabilitation within 2, 4 and 6 weeks after admission (AA) and during the last 4 and 2 weeks before discharge (BD) and at follow up 6 months after discharge. **PA:** Physical activity; **VO2peak**: peak oxygen uptake; **BMI:** Body Mass Index; **DXA:** Dual- energy X-ray Absorptiometry.

Fig. A

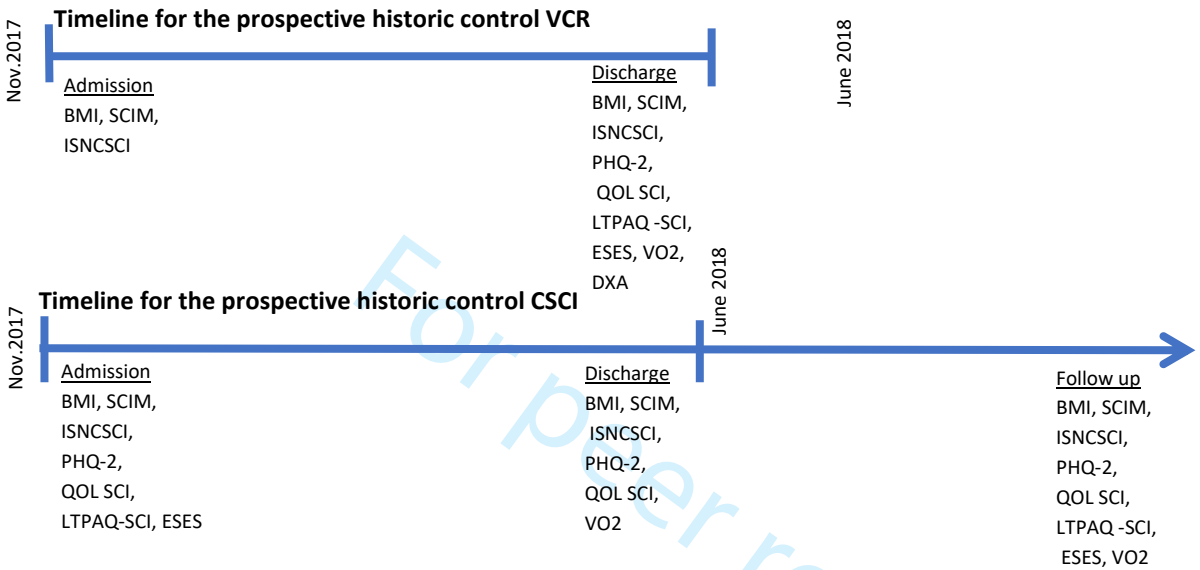
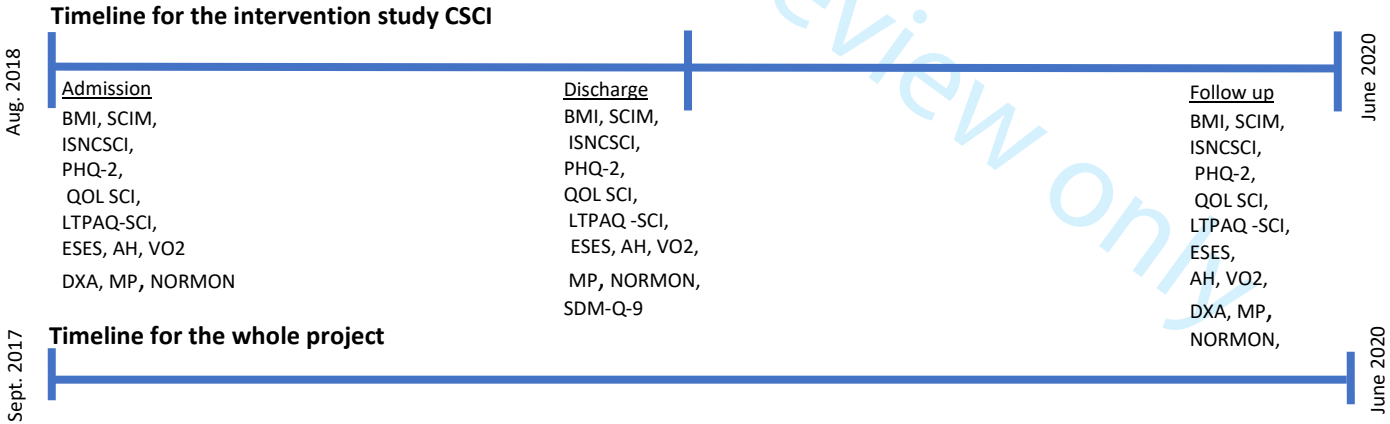
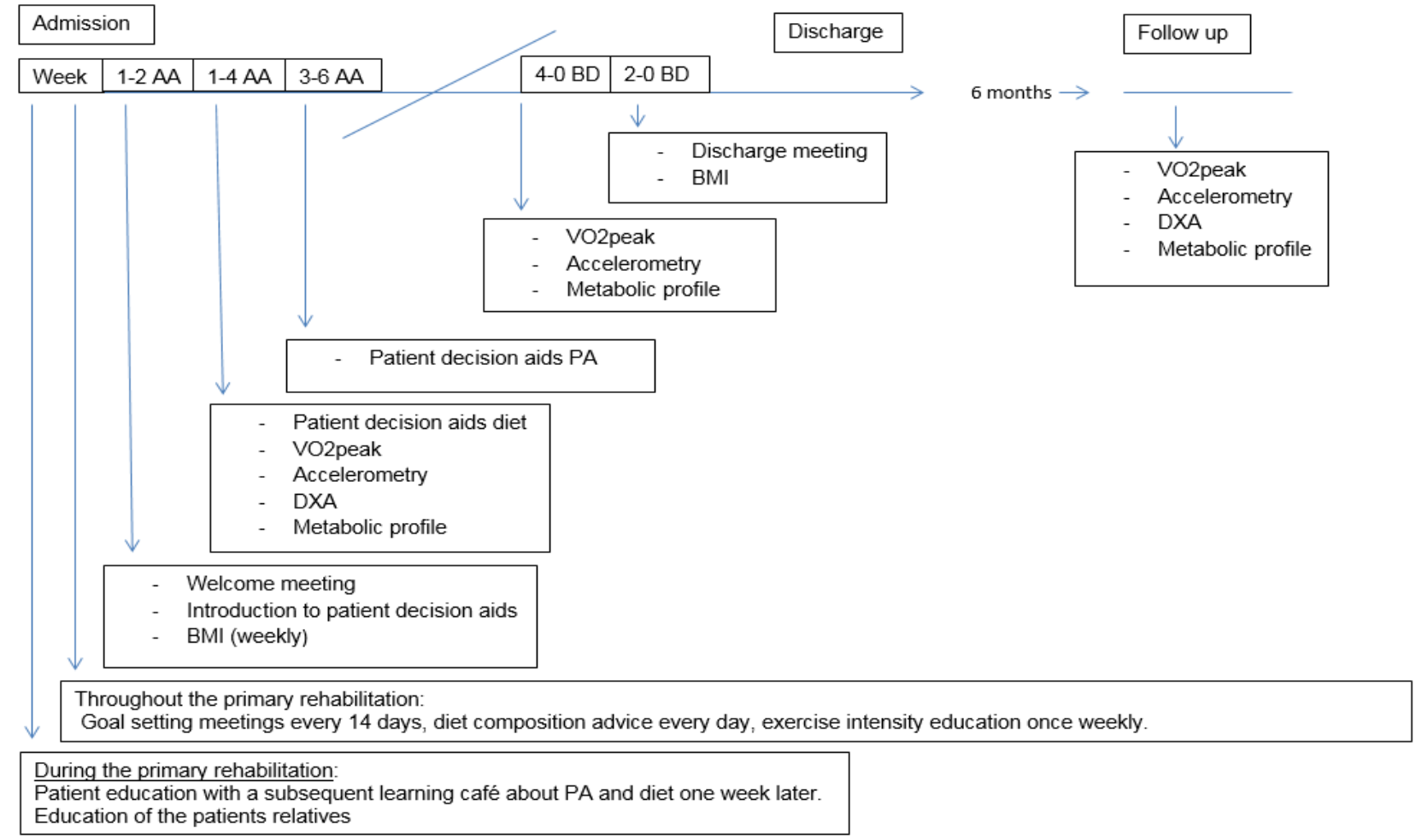


Fig. B



VCR: Center for Spinal Cord Injury, Western Denmark **; CSCI:** Clinic for Spinal Cord Injuries, Eastern Denmark; **BMI:** Body Mass Index**; SCIM**: Spinal Cord Injury Independence Measure; **ISNCSCI**: International Standards for Neurological Classification of Spinal Cord Injury; **PHQ-2**: Patient Health Questionnaire- 2; **QOL SCI**: International SCI Quality of Life Basic Data Set; **LTPAQ-SCI**: Leisure Time Physical Activity Questionnaire for people With Spinal Cord Injury; **ESES**: Exercise Self Efficacy Scale **;AH Actiheart (accelerometer); VO2peak**:peak oxygen uptake **;DXA**; Dual- energy X-ray Absorptiometry **MP**: Metabolic profile;**; NORMON: Nordic monitoring of diet, physical activity and overweight; SDM-Q-9: 9-item Shared Decision Making Questionnaire**


Admission
Week
1-2 AA
1-4 AA
3-6 AA
Discharge
4-0 BD
2-0 BD
6 months
Follow up
- Discharge meeting
- BMI
- VO2peak
- Accelerometry
- Metabolic profile
- VO2peak
- Accelerometry
- DXA
- Metabolic profile
- Patient decision aids PA
- Patient decision aids diet
- VO2peak
- Accelerometry
- DXA
- Metabolic profile
- Welcome meeting
- Introduction to patient decision aids
- BMI (weekly)
Throughout the primary rehabilitation:
Goal setting meetings every 14 days, diet composition advice every day, exercise intensity education once weekly.
During the primary rehabilitation:
Patient education with a subsequent learning café about PA and diet one week later.
Education of the patients relatives

Appendix: Strategic interventions

	Strategic interventions	Scope/ Content	Procedure	Health care staff	Process
Information and education in group sessions	Pre- education of all health care professionals and peers with SCI	To prepare a uniform and systematic approach and clarifying the roles of each profession in relation to the targeted patient education, an evidence-based pre-education of the inter-disciplinary health care personnel and peers with SCI is performed about cardiovascular risk, PA and healthy diet.	Pre-education is performed by stakeholders, as one session just before the intervention start-up. Pocket cards with evidence based basic recommendations related to PA and healthy diet in people with SCI are provided to all professions and peers with SCI.	All health care professionals at the clinic, and all peers from the peer corps.	The pre-education is performed multiple times until all health care professionals have attended the pre-education.
	Patient education + session about diet and PA	To Inform the patients about SCI in general, including specific evidence based information about cardiovascular risk and overweight as a mandatory part, facilitating patients discussing healthy diet and PA	Patient education is performed face- to-face as a group session. Afterwards the patients discuss PA and healthy diet. Interdisciplinary health care professionals facilitates the session from evidence based information in the patient decision aids material.	Patient education: Medical doctors. Session about diet and PA: Interdisciplinary health care professionals.	Once
	Education of relatives	To inform the relatives about SCI in general, including specific evidence based information about cardiovascular risk and overweight and the benefits of healthy diet and PA as a mandatory element.	The session last a full day with face-to-face information and discussion about several aspects related to SCI and the role as a relative.	Interdisciplinary+ invited relatives to former patients sharing their experiences about being a relative to a person with SCI	Once
	Admission meeting	A group setting where patients and relatives are informed about the scope of the rehabilitation and consequences of a SCI.	Information face- to-face about cardiovascular risk and overweight and the benefits of healthy diet and PA is provided	Interdisciplinary team	Once

	Discharge meeting	A group setting where the patient and relatives are informed about the discharge in general, and how to manage consequences of the SCI in a new context after discharge	Information face- to-face about how to transfer the achieved knowledge and behaviors related to PA and healthy diet to a new context and information about the risk of low PA and gaining weight after discharge is provided.	Interdisciplinary team	Once
	Diet composition advice	Recommendations about the diet composition at lunch servings is presented, based on the national nutrition guidelines.	Servings take place in a dining room. Visual material with diet composition recommendations is available and a plate model for inspiration is presented, with 200-300 gram of vegetables.	Kitchen staff	Every day
	Exercise intensity education	Education about evidence based exercise amount and intensity for reducing cardiovascular risk and how to monitor intensity by using ratings of perceived exertion	The education is delivered by trained physiotherapists during group sessions of wheelchair skills training and cardiovascular exercise sessions.	Physiotherapist	Once weekly
Motivational physiologic outcome measures and face-to-face feedback	BMI	BMI is assessed as part of existing routines and the patient is informed about the course of BMI. Serves as motivational tool.	Information is delivered to the patient face to face, in a private setting, with no other agendas. Evidence based actions related to BMI are discussed if relevant. Physiotherapists makes sure that the patient is up to date with total weight of the wheelchair and cushion before assessment	Nurses + Physiotherapists.	BMI and feedback is performed every week throughout the rehabilitation
	VO2peak	VO2peak serves as a marker of physical capacity and the patient is informed about the test result and the course of physical capacity. Serves as motivational tool.	Information is delivered to the patient face to face, in a private setting, with no other agendas. Evidence based actions related to physical capacity are discussed if relevant.	Physiotherapists	Measurement and subsequently feedback at: Admission Discharge Follow up

	Accelerometry	Accelerometry serves as a marker of amount and intensity of PA and the patient is informed about the result and the course of PA. Serves as motivational tool.	Information is delivered to the patient face to face, in a private setting, with no other agendas. Evidence based actions related to are discussed if relevant	Physiotherapists	Measurement and subsequently feedback at: Admission Discharge Follow up
	DXA	DXA serves as a marker of body composition (percentage lean mass and fat mass) and the patient is informed about the result and the course of body composition. Serves as motivational tool.	Information is delivered to the patient face to face, in a private setting, with no other agendas. Evidence based actions to change body composition are discussed if relevant	Medical doctors	Measurement and subsequently feedback at: Admission Follow up
	Metabolic profile	Metabolic profile serves as a biomarker for diabetes and atherosclerotic disease and the patient is informed about the result and the course of measurements. Serves as motivational tool.	Information is delivered to the patient face to face, in a private setting, with no other agendas. Evidence based actions related to metabolic disease are discussed if relevant	Medical doctors	Measurement and subsequently feedback at: Admission Discharge Follow up
Goalsetting and action planning (lifestyle changes)	Introduction to patient decision aids for diet and PA and a brochure about food, weight and health for people with SCI	A setting in the early rehabilitation phase, where the decision aids and brochure are provided to the patient. The structure and goal of the two decision aids is introduced. The brochure supports the aim and rationale of the two decision aids.	A private setting between the patient and nurse face-to-face with no other agendas. From the time of introduction until the first goal setting meetings about diet and PA, the patient may read the information coupled to the recommendations for diet and PA.	Nurses + Physiotherapists	Once
	Goal setting using patient decision aids for diet and PA	Consists of two different patient decision aids. They are evidence-based tools describing several options, recommendations and consequences of choices, and creates the basis for the decision process. The aim is	The tool consists of written information material. The decision process together with the health care professionals, takes place face to face, in a private setting, with no other agendas. If requested by the	Interdisciplinary team	A continuous process until a decision is made by the patient. The tools for diet and PA are introduced at the

	to help the patient consider each option in relation to his/her overall life situation and make a choice that fits the patient well.	patient, peers with SCI are accessible, ready to share their own experiences related to PA and diet.		***goalsetting meetings*** approx. 4 and 5 weeks after admission respectively.
Goal setting meetings	A setting with the patient where goals for the rehabilitation are defined including goals related to PA and healthy diet.	Previous goals are evaluated and new goals are defined for the next 14 days. Asking the patient about goals for PA and healthy diet is mandatory.	Interdisciplinary team	Every 14 days
Follow up 3 months after discharge.	Follow up in an outpatient setting on the course of BMI and healthy diet.	The follow-up is a face-to-face interaction based on the patient decision aids for diet	Nurses	Once

Interdisciplinary team: Medical doctor, nurse, physiotherapist, occupational therapist, social worker, psychologist.

SCI: Spinal Cord Injury; PA: Physical Activity; BMI: Body Mass Index; DXA: Dual-energy X-ray Absorptiometry

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

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Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

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		Reporting Item	Page Number
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	3
Protocol version	#3	Date and version identifier	2
Funding	#4	Sources and types of financial, material, and other support	13
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	13

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	13
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	13
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	N/A
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	3-4
Objectives	#7	Specific objectives or hypotheses	5
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	5
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	5

Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	6
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	7-9
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	N/A Decisions related to the intervention are made by the clinical staff
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	12-13
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	7
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	9
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	7
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical	7

		assumptions supporting any sample size calculations	
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	6
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	N/A due to consecutive enrollment
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	N/A due to consecutive enrollment
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N/A due to consecutive enrollment
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N/A due to consecutive enrollment
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N/A due to consecutive enrollment
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	9

Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	13
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	11
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	11
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	11
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	-
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	11
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	N/A The trial evaluates elements in standard care which are not terminated.

Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	11
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	N/A
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	3
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	3
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	3
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N/A
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	11
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	13
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	11
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	11

Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	3
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	13
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	11
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	3
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	9