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The effect of breathing exercises and mindset with or without cold exposure on mental and physical health in persons with a spinal cord injury—a protocol for a three-arm randomised-controlled trial

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STUDY DESIGN: A three-arm randomized controlled trial.
OBJECTIVES: To investigate the effects of the Wim Hof Method (WHM), with (WHM-C) and without cold exposure (WHM-NC), on mental and physical health in persons with chronic spinal cord injury (SCI).
SETTING: Rehabilitation centre (assessments and once-weekly intervention sessions) and home-based (daily intervention sessions).
METHODS: Sixty adults with chronic SCI will be randomised (1:1:1) to one of three groups: participants in the intervention groups (i.e., WHM-C and WHM-NC) will engage in a 7-week intervention, with one weekly practice session at the rehabilitation centre and a daily WHM session at home. WHM-NC will consist of breathing exercises and mindset, while participants in WHM-C will partake in breathing exercises, mindset and cold exposure. Participants allocated to usual care (UC) will not receive the WHM intervention. The primary outcome is mental health reported via the Mental Health Inventory (MHI)-5, while secondary outcomes include circulating inflammatory and metabolic marker concentration, pulmonary function, body composition, sleep quality, spasticity, chronic pain and psychological stress.
ETHICS AND DISSEMINATION: Ethics approval has been obtained from the medical ethics committee of the Máxima Medical Centre (Veldhoven, the Netherlands; identifier: w22.069). If shown efficacious in improving mental health, as well as physical health, in persons with chronic SCI, the low cost and accessibility of the WHM allows it to be directly implemented in SCI rehabilitation.
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INTRODUCTION

Spinal cord injury (SCI) is a medical condition that leads to decrements in mental and cardiometabolic health as well as physical function. Indeed, while improvements in acute clinical care have increased life expectancy, ageing with SCI remains associated with a plethora of comorbidities, including respiratory complications, chronic pain, increased cardiometabolic disease risk, chronic low-grade inflammation and deteriorated mental health [1, 2]. Thus, SCI requires a holistic care approach and interventions that target multiple body systems simultaneously.

Although exercise is widely accepted as an effective and holistic intervention to improve mental and physical health, persons with SCI encounter many barriers to engage in this activity [3]. Thus, for interventions to be widely adopted in SCI practice, they need to be accessible for individuals with a reduced physical capacity and limited access to specialised equipment. An intervention that does not require equipment and can be performed at home is the Wim Hof Method (WHM). The WHM combines breathing techniques, mindset and cold exposure. While its individual components are rooted in ancient traditions [4], little research into their combined effect on mental and physical health exists. Acutely, in able-bodied individuals, the WHM breathing exercises induce intermittent respiratory alkalosis and hypoxia, as well as an increase in plasma catecholamine concentrations and attenuated concentrations of pro-inflammatory mediators such as tumour necrosis factor (TNF)-α, interleukin (IL)-6, and IL-8 during experimental endotoxemia [5]; an effect that is further enhanced when the breathing exercises are compounded by cold exposure [6]. In addition, the breathing exercises and cold exposure require focus and attention (i.e., the mindset component of WHM); a type of mindfulness that when practiced repeatedly may help manage some of the complications commonly associated with SCI (e.g. chronic pain and perceived stress) [2, 7].

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Supporting the observed acute effects, long-term participation in the WHM improves quality of life (QoL) and markers of chronic low-grade inflammation in patients with active axial spondylarthritis [8], while also reducing depressive symptoms in individuals temporarily residing on the Antarctic [9] and when prescribed in an entirely remote fashion [4]. Our pilot work in a small sample of persons with SCI ($N = 10$) further suggests improvements in mental health and respiratory function following 4 weeks of daily WHM breathing exercises and mindset [10]. These preliminary findings are substantiated by the positive effects of individual components of the WHM, particularly mindset-related activities [7] and cold exposure [11]. Thus, the limited body of literature on the WHM to date suggests that it is safe and feasible in clinical populations and that it may have positive effects on mental and physical health. However, there remains a clear need for randomised-controlled trials (RCT), particularly in populations at risk for poor mental and physical health. Furthermore, it is yet unclear whether the positive health effects of the WHM are elicited by the breathing exercises and mindset alone, or whether the additional cold exposure is needed for these benefits to be accrued.

The present study will, therefore, investigate the effects of the WHM, with (WHM-C) and without cold exposure (WHM-NC), on mental and physical health in persons with chronic SCI through a three-arm RCT. The primary outcome is mental health, while secondary outcomes include inflammatory and metabolic markers, pulmonary function, body composition, sleep quality, spasticity, chronic pain and psychological stress. It is hypothesised that WHM-C results in a larger improvement in mental health compared with WHM-NC, and both interventions are more efficacious than usual care (UC).

METHODS

Participants and recruitment

Active participant recruitment will take place during outpatient rehabilitation visits at Reade Centre for Rehabilitation & Rheumatology (Amsterdam, the Netherlands). Enrolment of participants will be conducted by a rehabilitation professional. Ethics approval has been obtained from the medical ethics committee of the Máxima Medical Centre (Veldhoven, the Netherlands; identifier: w22.069), according to the Helsinki Declaration revised in 1983, and informed consent will be signed by all participants prior to any study procedures.

Inclusion criteria

The inclusion criteria for study participation are having a chronic SCI (time since injury ≥ 1 year) and being aged between 18 and 75 years.

Exclusion criteria

Exclusion criteria are a history of severe autonomic dysreflexia, insufficient mastery of the Dutch language, severe cognitive or communicative disorders, cardiac arrhythmias or disease, progressive disease, being or becoming pregnant during the study period, severe psychiatric illness or disorders, severe pulmonary disease, experience with (parts of) the WHM, being involved in another intervention which may have an effect on the outcome measures of the present study, and negative advice from a physician to participate in the WHM intervention based on the medical screening.

Study design

A three-arm RCT design will be used with two intervention groups (WHM-C and WHM-NC) and a UC group (Fig. 1). Following baseline assessments (T1), WHM-C and WHM-NC will engage in a 7-week intervention, while those allocated to UC will be asked to continue their daily life as usual. Post-intervention assessments (T2) will be made 3-10 days following the final WHM session.

Sample size determination

The power analysis is based on the anticipated difference in the selected primary outcome, i.e., the Mental Health Inventory (MHI)-5 [12]. Based on persons with total knee arthroplasty, the minimum clinically important difference (MCID) of the MHI-5 of is set at 4.4 [13]. The MHI-5 was administered in the WHM pilot study (4 weeks of daily breathing exercises and mindset, without cold exposure), following which it was improved by 7.3 points ($N = 11$; 69.1 ± 16.0 to 76.4 ± 11.4; MCID: 4.4; d: 0.71). Based on these data, a theoretical medium to large effect size of 0.25 (effect size f^2) was used. With an alpha set at 0.05, a total sample size of 54 is required to achieve a power of 0.9. Accounting for a 10% drop-out rate, the total sample size will be 60 persons ($N = 20$ in each group). Since a sample size

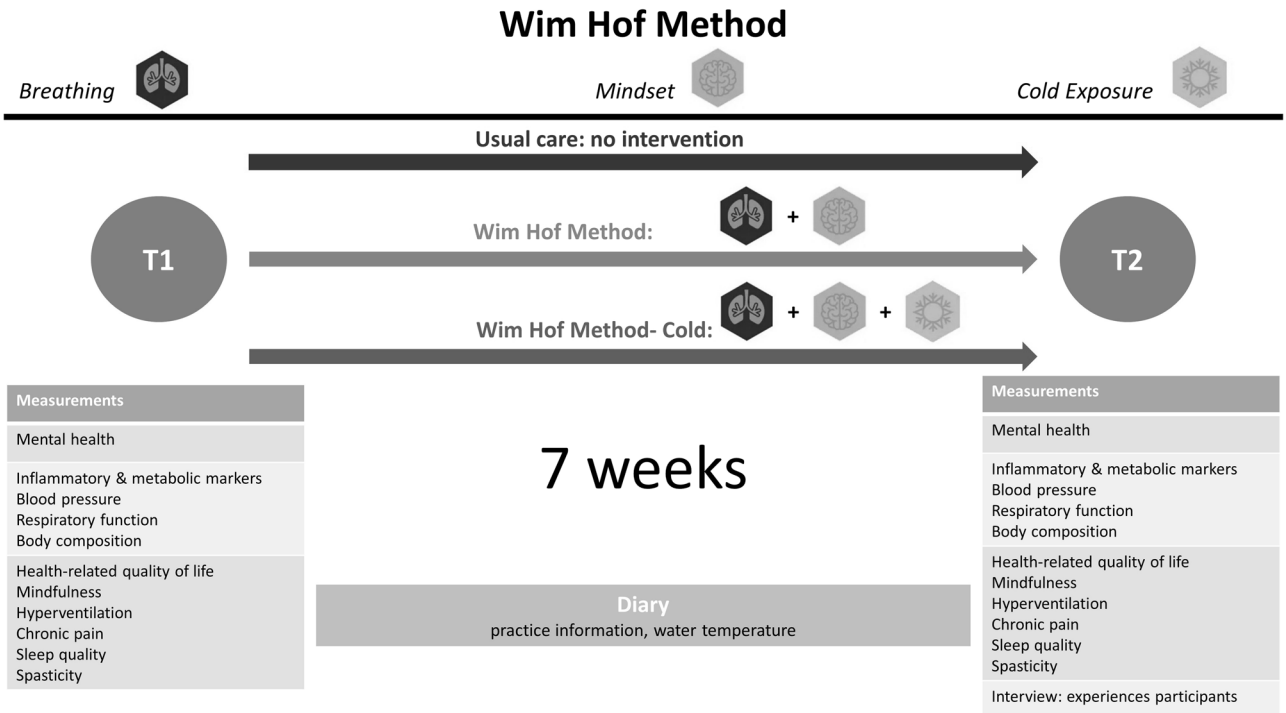

Fig. 1 Study design and outcome measures of the three-arm randomised-controlled trial.

calculation is inherently based on several assumptions, an interim analysis will be conducted after 40 participants have completed the study.

Randomisation, treatment allocation and blinding

Participants will be randomised by the Principal Investigator (SdG) to one of the three study groups with equal probability, stratified for level of injury (tetraplegia/paraplegia), using a web-based randomisation program (studyrandomizer.com) and a random permuted block algorithm with block sizes varying between 6 and 12. Breaking of the randomisation code will only occur in the event of unexpected serious adverse events associated with the intervention and after 40 participants have completed the study; the latter to verify whether the sample size calculation needs adjusting.

Blinding of participants to their group allocation is difficult to accomplish due to the obvious differences between conditions. However, to avoid motivational differences between participant groups, no explicit mention of expected intervention benefits will be communicated by the investigators. Furthermore, participants allocated to UC will be offered the WHM intervention after completion of the post-intervention assessments to promote study engagement. Pre- and post-intervention assessments will be performed by independent assessors.

Intervention groups

The WHM is based on three elements: breathing exercises, mindset, and cold exposure. Participants in WHM-NC will engage in breathing exercises and mindset, while WHM-C will include additional cold exposure (Table 1). Detailed instructions will be provided at the start of the intervention. Participants in WHM-NC and WHM-C will subsequently engage in a weekly group session led by a certified WHM instructor and will be asked to perform one daily WHM session at home. Participants are asked to fill out a diary following each WHM session, containing notes on the total session duration, their experience of the session and cold exposure, and water temperature (measured by a thermometer that they received from the researchers) if applicable. These notes will be monitored by the study team at each weekly group session. Furthermore, the participants are in a Whatsapp group with the therapists/instructors so if they have questions about their home sessions they can easily ask them. Group-based activities and activity monitoring are both widely used behaviour change techniques [14] and are anticipated to enhance intervention fidelity, in line with the high adherence rates found in our pilot work [10].

Breathing exercises

The WHM breathing technique consists of two exercises. First, participants need to inhale deeply through the nose or mouth, and exhale unforced through the mouth for an average of 30 breaths. Subsequently, the participant exhales deeply and holds their breath in an unforced manner until they feel a stimulus to inhale ("retention phase"). For safety reasons, participants will be instructed not to hold their breath longer than 3.5 min. Breath retention will be followed by a deep inhalation breath, which will be held for 15 s. Subsequently a new cycle of these breathing techniques begins. In total, 3 cycles will be performed during the first 3 weeks, and 4 cycles thereafter.

Mindset

The mindset will be trained during the breathing exercises and cold exposure. Commitment to focussing on the task without being distracted will be encouraged during the group sessions and required during the home-based sessions. Willpower, self-control and commitment are important parts of the WHM.

Gradual cold exposure

During the intervention period, the WHM-C participants expose themselves to cold in a gradual manner. During the first 14 days of the intervention, cold exposure will consist of washing with cold cloths. First, the non-paralyzed body parts will be washed with cold cloths and when this goes well, the paralyzed body parts will be washed similarly. After these 14 days, a cold shower will be taken for 30 s. Subsequently, these cold showers will be extended with 10 s each day until a final 2.5 min. The first cold shower will be taken under supervision of a health care professional at the rehabilitation centre. Detailed instructions for the home-based sessions with regards to water temperature and timing will also be provided during this session.

Usual care group

Participants allocated to UC will partake in the pre- and post-intervention assessments and will be requested to continue their daily life as usual during the 7 weeks in between.

Outcome measures

Primary outcome. Mental health will be assessed through the mental health subscale of the 36-Item Short Form Health Survey (SF-36), the MHI-5 [15].

Psychological outcomes. Overall health-related QoL will be assessed with the SF-36 [12], mindful attention awareness with the Mindful Attention Awareness Scale (MAAS) [16], experienced hyperventilation with the Nijmegen Hyperventilation Syndrome Questionnaire [17], chronic pain with the International Spinal Cord Injury Pain Basic Data Set [18], and sleep quality with the 9-item Pittsburgh Sleep Quality Index [19]. The hindrance participants perceive due to spasticity will be assessed for different aspects of daily living activities: sleeping, making transfers, washing and clothing, wheelchair manoeuvring and propulsion, and "other activities" [20]. Finally, an in-person exit-interview will be conducted to collect qualitative information on participants' experiences with the intervention.

Physical health outcomes. On the day prior to blood sample collection, participants will standardize their diet using a food diary and avoid exercise as well as the consumption of caffeine and alcohol. Following an overnight fast and 15 min of seated rest, a blood sample will be collected from an antecubital vein. Plasma will be stored at −80 °C until batch analysis. The circulating concentration of IL-6, CRP, glucose, triglycerides, total cholesterol, low-density lipoprotein (LDL)-cholesterol and high-density lipoprotein (HDL)-cholesterol will be determined by a specialised laboratory facility at the Amsterdam University Medical Centre.

Blood pressure will be assessed in triplicate through an automated arterial pressure monitor. The following pulmonary parameters will be measured using a standardised protocol: forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV1), forced inspiratory volume in 1 sec (FIV1), peak expiratory flow (PEF) and peak inspiratory flow (PIF) [21].

Body mass will be measured to the nearest 0.1 kg, while body composition will be measured in a supine position by bio-impedance analysis. Newly developed prediction equations specific to SCI will be used to determine % fat mass and % lean body mass [22].

Table 1. Frequency and doses of the intervention components.

	WHM-C	WHM-NC	UC
Breathing exercises (times x week $^{-1}$)	7	7	0
Breathing exercises week 1–3 (dose)	3 cycles	3 cycles	N/A
Breathing exercises week 4–7 (dose)	4 cycles	4 cycles	N/A
Cold exposure (times x week $^{-1}$)	7	0	0
Cold exposure week 1–2 (dose)	Cold cloths	N/A	N/A
Cold exposure week 3–4 (dose)	30 s – 150 s	N/A	N/A
Cold exposure week 5–7 (dose)	150 s	N/A	N/A
Group session (times x week $^{-1}$)	1	1	0

WHM-C Wim Hof Method with cold exposure, *WHM-NC* Wim Hof Method without cold exposure, *UC* usual care.

Statistical analyses

Using the 25th version of SPSS, a regression analysis will be performed with the difference in change of the outcome measures between baseline and post-intervention assessments as dependent variable and the groups (two dummy variables with UC as reference and in a second regression analysis WHM-NC as reference) as independent variables. Any drop-outs occurring during the study will be examined and included in the study based on the intention to treat principle.

DISCUSSION

The strengths of the current study are the accessibility of the intervention, which can largely be performed at home, as well as the multidisciplinary test battery and the large sample size relative to the field of SCI research. Limitations include the lack of blinding to the intervention, while its home-based nature may negatively affect internal validity. Furthermore, although the three groups will be stratified by lesion level and the most relevant health conditions in relation to participant safety are used as exclusion criteria, using additional characteristics such engaging in high levels of physical activity, having diabetes or taking anti-depressant medication could have reduced the variability within- and between groups. In conclusion, the present three-arm RCT will form an important contribution towards the development of accessible preventative health interventions suitable for persons with SCI. If shown efficacious, its low cost and scalability would allow it to be readily implemented in clinical practice.

DATA AVAILABILITY

The de-identified datasets generated during and/or analysed during the current study will be available from the corresponding author on reasonable request.

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AUTHOR CONTRIBUTIONS

SV, FE, MvdB, VvdS, EvB, LvO, WA, HD, TJ and SdG were responsible for designing the study. SH and SdG were responsible for writing the manuscript. FE, MvdB, VvdS, EvB, LvO, WA, HD and TJ provided feedback on/revised the product.

COMPETING INTERESTS

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ADDITIONAL INFORMATION

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