



UHASSELT

KNOWLEDGE IN ACTION

Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de kinesitherapie

Masterthesis

The effect of exercise therapy on cardiac autonomic functioning in persons with chronic non-specific low back pain: a preliminary analysis of RCT data

Luna Meers

Lauren Smets

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie, afstudeerrichting revalidatiewetenschappen en kinesitherapie bij musculoskeletale aandoeningen

PROMOTOR :

Prof. dr. Annick TIMMERMANS

BEGELEIDER :

De heer Timo MEUS

COPROMOTOR :

dr. Jonas VERBRUGGHE



UHASSELT

KNOWLEDGE IN ACTION

www.uhasselt.be

Universiteit Hasselt

Campus Hasselt:

Martelarenlaan 42 | 3500 Hasselt

Campus Diepenbeek:

Agoralaan Gebouw D | 3590 Diepenbeek

2024
2025



Faculteit Revalidatiewetenschappen

master in de revalidatiewetenschappen en de
kinesithérapie

Masterthesis

The effect of exercise therapy on cardiac autonomic functioning in persons with chronic non-specific low back pain: a preliminary analysis of RCT data

Luna Meers

Lauren Smets

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesithérapie,
afstudeerrichting revalidatiewetenschappen en kinesithérapie bij musculoskeletale aandoeningen

PROMOTOR :

Prof. dr. Annick TIMMERMANS

BEGELEIDER :

De heer Timo MEUS

COPROMOTOR :

dr. Jonas VERBRUGGHE

Table of contents

| | |
|---|----------|
| Research context | 1 |
| Abstract | 3 |
| <i>Background:</i> | 3 |
| <i>Objectives:.....</i> | 3 |
| <i>Methods:.....</i> | 3 |
| <i>Results:.....</i> | 3 |
| <i>Conclusion:.....</i> | 3 |
| <i>Keywords:.....</i> | 3 |
| Introduction | 5 |
| Methods | 7 |
| <i>Study design</i> | 7 |
| <i>Subjects</i> | 7 |
| <i>Inclusion and exclusion criteria</i> | 7 |
| <i>Procedure</i> | 8 |
| <i>Power analysis and sample size</i> | 8 |
| <i>Intervention.....</i> | 9 |
| Cardiopulmonary exercise test (CPET) | 9 |
| HIT | 10 |
| MIT | 12 |
| <i>Outcome measures</i> | 12 |
| HRV | 12 |
| Time domain | 14 |
| Frequency domain | 14 |
| <i>Data analysis.....</i> | 15 |

| | |
|--|-----------|
| Results | 17 |
| <i>HRV outcomes</i> | <i>17</i> |
| Discussion | 19 |
| <i>Relevance of the results</i> | <i>20</i> |
| <i>Strengths and limitations</i> | <i>20</i> |
| <i>Future directions</i> | <i>21</i> |
| Conclusion | 23 |
| Reference list | 25 |
| Appendix..... | 29 |

Research context

This study was completed as part of the physiotherapy and rehabilitation science degree program at the University of Hasselt, Belgium. It was part of an ongoing doctoral study by Timo Meus conducted in the research group of Prof. dr. Annick Timmermans. The research was embedded within two projects: the TechnoHIT-trial (project number: T000822N), funded by the Research Foundation Flanders (FWO-TBM), and HIT-BACK-HEART (grant number: BOF23DOC40), funded by Hasselt University and the Special Research Fund (BOF).

Recruitment and interventions were conducted at the University Hospital of Antwerp and Virga Jessa Hospital in Hasselt.

This thesis is situated within the field of rehabilitation in chronic musculoskeletal pain, with a specific focus on individuals with chronic non-specific low back pain (CNSLBP). This population frequently experiences pain, increased functional limitations, and a significant socioeconomic burden. Furthermore, a reduced heart rate variability (HRV) is shown, indicating dysregulation of cardiac autonomic function. HRV reflects the balance between sympathetic and parasympathetic nervous system activity and is considered a marker of cardiac autonomic function. Research suggests that exercise therapy can help improve symptoms, functionality, and HRV in individuals with musculoskeletal disorders. This study specifically examined the effect of high- and low-intensity exercise therapy on HRV in individuals with CNSLBP.

Given the progressive increase in functional limitations within this population over time, it is crucial to identify appropriate interventions that can effectively support the rehabilitation process while concurrently addressing cardiac autonomic function. Therefore, the relevance of this study lies in gaining more insight into how different exercise intensities influence cardiac autonomic function in this population, which is essential for the development of effective treatments. Furthermore, it could contribute to a more personalized rehabilitation approach and provide a deeper understanding of optimal treatment strategies for this population.

The research question was determined by the students in consultation with the supervisor. Both students contributed by assisting with the research, helping out with the interventions, conducting an in-depth literature review on the topic, collecting and processing the statistical data, and writing the thesis. All components were carried out in collaboration by both students.

Abstract

Background: Chronic non-specific low back pain (CNSLBP) is a common musculoskeletal condition with a substantial socioeconomic burden. Evidence suggests that dysregulation of the autonomic nervous system may contribute to its persistence, reflected by reduced heart rate variability (HRV) in affected individuals. Exercise therapy could improve autonomic function by increasing parasympathetic activity and reducing sympathetic dominance. However, limited research has examined the effects of different exercise intensities on HRV in individuals with CNSLBP.

Objectives: To compare the effects of high-intensity training (HIT) versus moderate-intensity training (MIT) on cardiac autonomic functioning in individuals with CNSLBP.

Methods: In this double-blind, randomized clinical trial, CNSLBP patients were assigned to either HIT ($n = 2$) or MIT ($n = 3$). Both groups followed a 12-week program of cardiorespiratory training, resistance exercises, and core strength training. Primary outcomes included HRV time and frequency domain measures (i.e. heart rate (HR), root mean square of successive differences (RMSSD), low-frequency power (LF), high-frequency power (HF), and LF/HF ratio).

Results: After 12 weeks, no significant differences were found between HIT and MIT groups ($p > .05$). Still, HR increased moderately in HIT (63.04 ± 5.90 to 67.37 ± 6.02 bpm, $g = 0.53$), and RMSSD in MIT (22.76 ± 3.39 to 30.38 ± 15.40 ms, $g = 0.50$). The LF/HF ratio increased in both groups, most notably in MIT (0.82 ± 0.45 to 3.40 ± 5.06 , $g = 0.52$).

Conclusion: First preliminary results show varying impacts of HIT and MIT on HRV measures in patients with CNSLBP. However, larger studies are recommended to confirm these findings.

Keywords: chronic low back pain, high-intensity training, moderate-intensity training, heart rate variability

Introduction

Low back pain is the most common musculoskeletal disorder and the leading cause of work disability and healthcare costs worldwide (Hartvigsen et al., 2018). Between 1990 and 2015, disability related to low back pain increased by 54%, with the greatest rise observed in low- and middle-income countries due to limited access to rehabilitation services (Cieza et al., 2021; Hartvigsen et al., 2018). Approximately 80% of cases are categorized under chronic non-specific low back pain (CNSLBP), indicating a pain that persists for 12 weeks or more with no clear structural or pathoanatomical cause (Deyo, 2002; Maher et al., 2017; van Tulder et al., 2006). The multifaceted etiology of CNSLBP is accentuated by the various physiological (e.g., muscle size, composition, coordination), psychological (e.g., depression, anxiety, catastrophizing), and social factors (e.g., compensation, work satisfaction, education, physical workloads), all of which contribute to pain and disability among individuals within this population (Hartvigsen et al., 2018). Increased attention is necessary to understand the underlying physiological mechanisms that may contribute to the persistence of CNSLBP. One such mechanism might also be the dysregulation of the autonomic nervous system, which can be evaluated through heart rate variability (HRV) (Rampazo É et al., 2024).

HRV represents the variability in the time between heartbeats (Rampazo É et al., 2024). Moreover, lower HRV frequently signifies autonomic dysfunction and may be assessed for implications on health deterioration, whereas elevated HRV typically denotes autonomic regulation inherent to a healthy individual (Vanderlei et al., 2009). Lower HRV has been demonstrated in a variety of chronic pain conditions, including complex regional pain syndrome (Terkelsen et al., 2012), whiplash-associated disorders (Koenig et al., 2016), neck pain (Hallman & Lyskov, 2012), and low back pain (Bandeira et al., 2021). For instance, patients with chronic neck-shoulder pain showed altered autonomic regulation, which was reflected in the changes in ambulatory HRV (Hallman & Lyskov, 2012). This suggested that the persistence of chronic musculoskeletal pain was influenced by both increased sympathetic tone and decreased parasympathetic activation (Hallman & Lyskov, 2012). Furthermore, compared to healthy controls, patients with CNSLBP exhibited a significant reduction in HRV, lower parasympathetic activation, and consequently, a predominance of sympathetic nervous system activity (Bandeira et al., 2021).

Exercise therapy is recommended in 71% of the guidelines for patients with CNSLBP and is associated with lower costs and more beneficial effects (Miyamoto et al., 2019; Oliveira et al., 2018). In addition, it has been shown that high-intensity interval training (HIIT) and moderate-intensity continuous training (MICT) affect HRV in inactive adults (Alansare et al., 2018). Moreover, this study stated that a HIIT training program had superior effects on improving HRV compared to MICT (Alansare et al., 2018). Furthermore, high-intensity training (HIT), including cardiorespiratory intervals, general resistance exercises, and core muscle training, has been shown to be more effective than moderate-intensity training (MIT) in reducing disability, enhancing exercise capacity, and back strength (Verbrugghe et al., 2019). Considering the autonomic dysregulation observed in CNSLBP, interventions positively influencing HRV could hold therapeutic potential. Exercise therapy affects HRV by increasing vagal modulation and reducing sympathetic tone, which may help restore autonomic balance (Routledge et al., 2010).

While moderate- to high-intensity aerobic training and whole-body resistance exercise training improved HRV in women with fibromyalgia (Figuerola et al., 2008; Sañudo et al., 2015), there is still very little research available on the impact of a structured exercise program on cardiac autonomic function among individuals suffering from CNSLBP. Therefore, the main objective of this study was to examine the effects of exercise therapy on cardiac autonomic functioning, specifically comparing HIT to MIT, focusing on HRV in individuals suffering from CNSLBP, under the hypothesis that HIT will lead to greater improvements in HRV compared to MIT.

Methods

Study design

This study used data from a double-blinded, multicenter randomized clinical trial ([NCT06491121](#)). The study protocol received ethical approval by FAGG ('consolidated opinion Federal Agency for Medicine and Health Products (AMHP) (Ref. CIV-23-12-045154) and by the medical ethical committees of University Hospital Antwerp, Virga Jessa Hospital, University of Hasselt, and the University of Antwerp (Van Eetvelde et al., 2024).

Subjects

Individuals with CNSLBP were recruited for this preliminary analysis of a larger multicenter longitudinal clinical trial. Recruitment took place at the University Hospital of Antwerp (UZA) and Virga Jessa Hospital in Hasselt (VJZH) under the supervision of rehabilitation physicians Prof. Dr. Stassijns from UZA and Prof. Dr. Kempeneers from Jessa Hospital Hasselt (VJZH), along with the associated MDs in their clinical teams. Eligible participants for the study were informed about the research. Interested individuals received a study flyer and approval form from the attending physician to facilitate subsequent contact via the participants preferred method (email and/or phone). Within two to seven days, the investigators reached out to these potential participants, addressed their initial inquiries, reviewed the inclusion criteria, and provided informed consent documentation, available in digital and hard copy formats per the participants preference. Participants who signed and returned the informed consent within a two-week period were subsequently contacted for potential enrollment in the study.

Inclusion and exclusion criteria

All inclusion and exclusion criteria can be found in Table 1. Dutch-speaking adult participants, aged 18-65 years old, who experienced CNSLBP for more than 12 weeks were included. This may involve fluctuating pain levels and periods of remission, spanning from the lower rib margins to the buttock creases, with an unspecified nociceptive source (Dionne et al., 2008; Maher et al., 2017; Stanton et al., 2010; van Tulder et al., 2006). Participants were excluded from the study if a musculoskeletal or chronic disorder other than CNSLBP interfered with completing the study protocol.

Table 1
Inclusion and Exclusion Criteria

| Inclusion | Exclusion |
|--|--|
| 18-65 years old | Spinal fusion surgery |
| Speak Dutch | Interfering musculoskeletal and/or chronic disorder aside from CNSLBP |
| CNSLBP for > 12 weeks | Severe comorbidities (e.g., paresis, sensory disturbances by neurological causes, diabetes mellitus, rheumatoid arthritis) |
| ≥ 20% on the MODI | Pregnancy |
| Own a working smartphone (iOS and Android) | Ongoing compensation claims |
| | Inability to attend regular therapy appointments |

Note. Abbreviations: CNSLBP = Chronic Non-Specific Low Back Pain; MODI = Modified Oswestry Disability Index

Procedure

Participants were not informed about which group they were allocated to. However, they were informed about the study's objective. A web-based online tool called Castor (EDC, 2024) was used to randomize participants. Due to the study design, blinding the physiotherapists who were providing the treatment was impossible. Therefore, a rater cross-over assessment protocol was implemented to minimize bias and to ensure that blinding was achieved among the assessors.

Power analysis and sample size

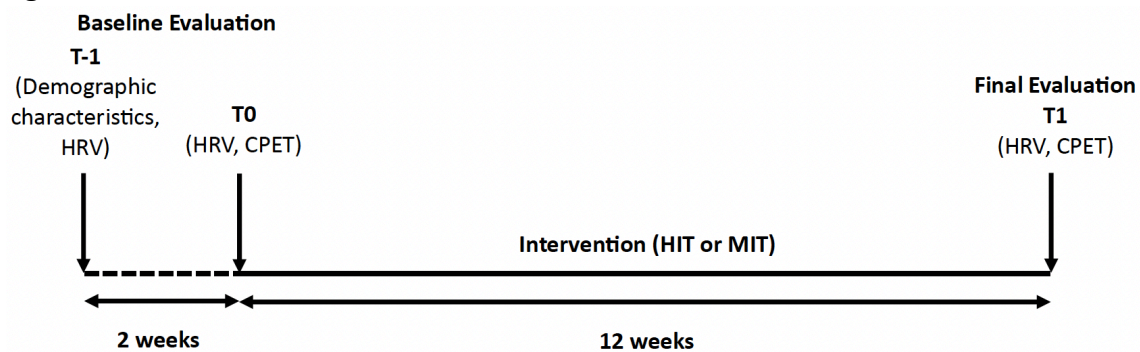
A power analysis was conducted to determine the minimum required sample size for detecting a statistically significant difference in root mean square of successive differences (RMSSD) between the HIT and MIT groups following a 12-week intervention in individuals with CNSLBP. The calculation was performed using JMP Pro 17 (SAS Institute Inc., Cary, NC, 2022-2023), with a significance level of $\alpha = 0.05$ and a power of $\beta = 0.80$. A moderate effect size was assumed based on previous studies showing that aerobic and resistance training can improve HRV in individuals with chronic musculoskeletal pain or low baseline HRV (Bandeira

et al., 2021; Hautala et al., 2006; Routledge et al., 2010; Sañudo et al., 2015). These findings supported using structured exercise interventions to improve HRV in clinical populations. The power analysis indicated that 101 participants (50 in HIT, 51 in MIT) were required to achieve sufficient statistical power.

Intervention

Participants followed a 12-week supervised exercise program, consisting of 24 sessions lasting 1.5 hours each, twice a week, conducted by physiotherapists at UZA or Jessa, following a HIT or MIT protocol (Verbrugghe et al., 2019), as shown in Figure 1.

Figure 1



Timeline of the Study

Note. The exercise program had a duration of 12 weeks. Three clinical evaluations were conducted during the study, two at baseline and one after 12 weeks.

Abbreviations: HRV = Heart Rate Variability; CPET = Maximal Cardiopulmonary Exercise Test; HIT = High-Intensity Training; MIT = Moderate Intensity Training.

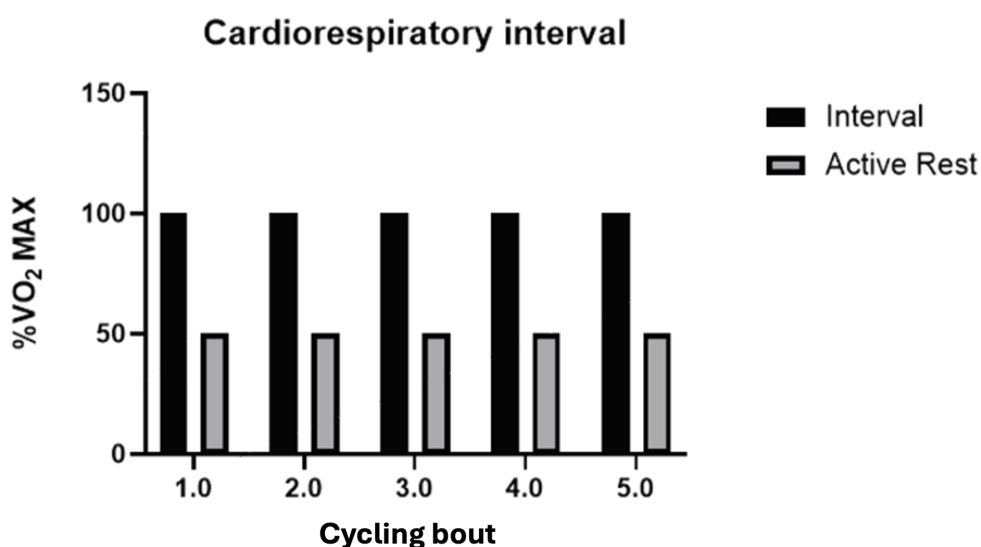
Cardiopulmonary exercise test (CPET)

A CPET was taken at baseline (T0) and after 12 weeks (T1) to individualize the HIT and MIT training protocol and evaluate changes in aerobic capacity (Herdy et al., 2016). The test was completed on a cycle ergometer (eBike Basic, General Electric GmbH, Germany) with a low workload that gradually increased every minute (30W+15W/min). The maximal oxygen uptake (VO₂max) and maximal workload through cycling time (min.) were evaluated through breath-by-breath gas exchange analysis (MetaMax3B, Cortex, Germany) and heart rate monitoring (H10, Polar Electro, Finland). A respiratory exchange ratio (RER) threshold of 1.10 was used to assess the maximum effort's appropriate validity.

HIT

Participants allocated to the HIT group conducted cardiorespiratory interval, general resistance, and core strength training at high intensity for 12 weeks, with biweekly sessions. The cardiorespiratory training involved intervals on a cycle ergometer, consisting of five maximal one-minute workload bouts (110 RPM at 100% VO₂ max) alternated with one minute of active rest (75 RPM at 50% VO₂ max, based on CPET) as described in Figure 2. The workload increased by 10 seconds every two sessions, while active rest duration remained consistent (Figure 3). The general resistance training included three upper body and three lower body exercises (Figure 4) performed on fitness equipment at intensities exceeding 80% of one repetition maximum (1RM) and were performed at least eight repetitions. When the participants performed more than 10 repetitions for two consecutive sessions, the workload was increased by 5%. The core muscle strength training comprised six static core exercises and progressions (Figure 5), enabling the loading of core muscles at intensities surpassing 60% of maximum voluntary contraction (MVC). The participants were required to perform a set of 10 repetitions, alternating between a 10-second hold and a five-second rest. As the participants progressed and maintained a stable posture for two consecutive sessions, the static hold was increased to 12 seconds, and more demanding postures were introduced.

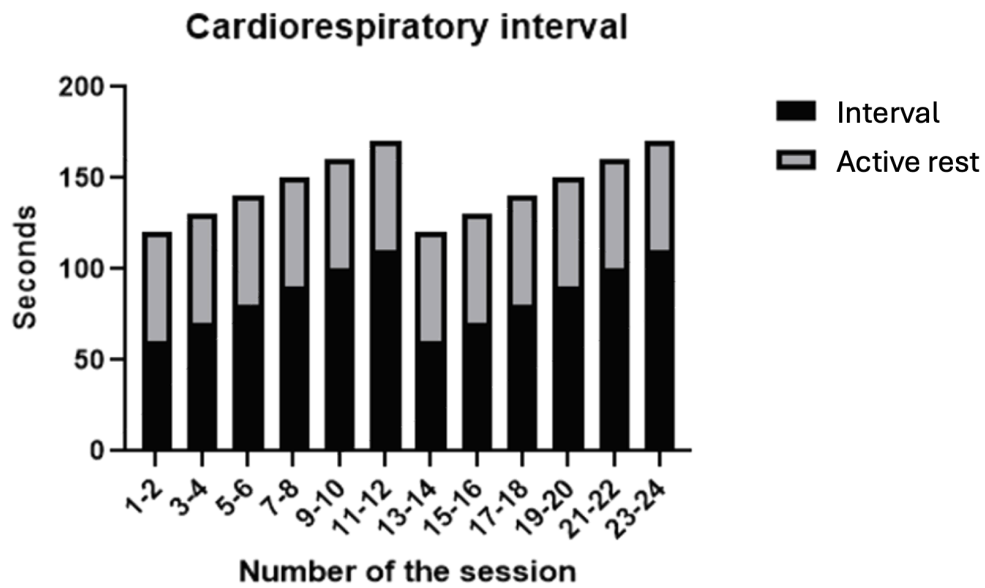
Figure 2



HIT Session

Note. Five cycling bouts (one-minute maximum workload and one-minute active rest) were done in each session.

Figure 3



HIT Protocol

Note. A total of 24 HIT-interval sessions were done. The resistance increased by 5% between sessions 12 and 13.

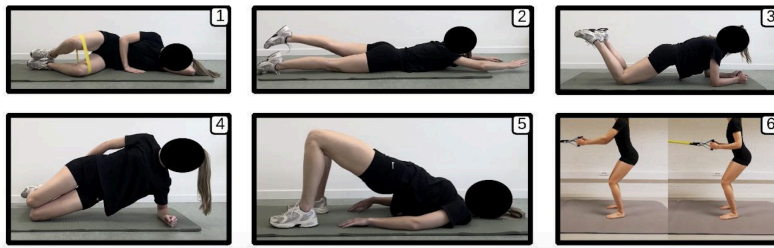
Figure 4



General Resistance Exercises

Note. 1: leg extension; 2: chest press; 3: leg press; 4: leg curl; 5: arm curl; 6: vertical traction.

Figure 5



Core Muscle Exercises

Note. 1: glute clam; 2: lying diagonal back extension; 3: adapted knee plank; 4: adapted knee side plank; 5: glute bridge; 6: elastic band shoulder retraction with hip hinge.

MIT

Participants allocated to the MIT group performed a 12-week, biweekly program similar to the HIT group but at a lower intensity. The cardiorespiratory training involved a continuous protocol on a cycle ergometer lasting 14 minutes (90 RPM at 60% of VO₂ max, based on CPET), with duration increasing by one minute and 40 seconds every two sessions. The general resistance training mirrored the protocol described in the HIT group, except exercise intensity was set at 60% of one repetition maximum (1RM), and repetitions were performed 15 times. The workload progressed by 5% every two weeks. The core muscle strength training aligned with the HIT protocol, except for the exercise intensity that was set below 60% of maximum voluntary contraction (MVC). Regarding the core exercises, each participant needed to complete one set of 10 repetitions, holding each repetition for 10 seconds. If the exercise was performed correctly, the static hold time was increased every six sessions. Moreover, the posture became more challenging when the core was steady for the required time during two consecutive sessions.

Outcome measures

Demographic characteristics, such as age, sex, and BMI, were collected at baseline (T-1).

HRV

HRV, defined as the fluctuation in time intervals between consecutive heartbeats, is a non-invasive and fast method for analyzing reliable and repeatable data regarding autonomic modulation of the heart rate (McCraty & Shaffer, 2015; Parati et al., 2006). To measure HRV at baseline (T-1 and T0) and after 12 weeks (T1), participants followed a standardized

protocol for 30 minutes in a quiet and low stimulus room with a controlled temperature of 20 to 24 degrees. The measurement period was standardized to account for the influences of circadian rhythms. First, the participants were asked about adhering to the researchers guidelines, sleep conditions, and general health conditions on the day of the test before any data was collected. Next, participants were asked to lay in supine position and breathe spontaneously for 14 minutes, after which beat-to-beat intervals (R-R) were recorded using a validated heart rate monitor (H10, Polar Electro, Finland) synchronized with a wristwatch (Ignite, Polar Electro, Finland) (Speer et al., 2020). Participants were asked not to talk or fall asleep during the measurement. If this did occur, the researcher noted down the time period when it happened during the measurement. To ensure accurate results, as described in Table 2, it was important that participants were well-hydrated and avoided consuming caffeine, nicotine, soft drinks, energy drinks, or chocolate on the day of the measurement. In addition, 48 hours before the measurement, participants were not allowed to consume alcohol or engage in any intense physical activity that exceeded 70% of their maximum heart rate.

Table 2
Heart Rate Variability Conditions

| Conditions |
|---|
| Well-hydrated |
| No caffeine, nicotine, soft drinks, energy drinks, chocolate ^a |
| No alcohol or intense physical activity (70% maximum heart rate) ^b |
| No talking or sleeping ^c |

Note. Conditions for participants.

^aThe day of the measurement. ^b48 hours before the measurement. ^cDuring the measurement.

HRV analysis was conducted using Kubios HRV Scientific software (Kubios Oy, Kuopio, Finland). Raw electrocardiogram (ECG) data from each 14-minute recording were imported into the software, with only data from minute seven onward included in the analysis. Recordings shorter than 14 minutes were excluded to ensure data quality. Artifact correction was applied using the "Custom" correction mode, with correction levels ranging between 0%

and 0.5%. HRV can be divided into two analyses: linear and nonlinear (Francesco et al., 2012), this study only used linear HRV outcome measurements.

Time domain

The extracted linear HRV parameters included time domain measures such as mean heart rate (HR), mean R-R interval, and RMSSD (Catai et al., 2020). RMSSD reflects on parasympathetic nervous system activity and quantifies the short-term fluctuations in R-R intervals by calculating the square root of the mean squared differences between successive R-R intervals (Shaffer & Ginsberg, 2017). Under appropriate measurement conditions, the RMSSD is considered a reliable and valid parameter of parasympathetic activity (Laborde et al., 2017; Nunan et al., 2010; Sandercock et al., 2005).

Frequency domain

The frequency domain measures included low-frequency power (LF), high-frequency power (HF), and the LF/HF ratio. These parameters are typically presented together to analyze the interaction between the sympathetic and parasympathetic branches of the autonomic nervous system (ANS), as well as their potentially distinct patterns of activity (Burr, 2007; Catai et al., 2020). Frequency domain values can be expressed in either absolute or relative power (Shaffer & Ginsberg, 2017). Expressing LF and HF in normalized units (n.u.) emphasizes the balanced and regulated functioning of both autonomic branches and reduces the influence of total power variations on the individual LF and HF components (Burr, 2007). HF (0.15-0.4Hz) is mainly associated with parasympathetic activity and strongly correlates with the RMSSD time domain measure. A lower HF power is commonly linked with stress and anxiety (Burr, 2007; Kleiger et al., 2005; Shaffer & Ginsberg, 2017). In addition, LF (0.04-0.15Hz) is mainly associated with sympathetic activity but is also seen as an indicator of overall modulation from both the sympathetic and parasympathetic branches (Burr, 2007). Furthermore, the LF/HF ratio is frequently used as an index to evaluate the sympathovagal balance, a higher LF/HF ratio usually indicates more stress and a lower LF/HF ratio indicates a more relaxed state (Burr, 2007).

Data analysis

Longitudinal data acquisition was conducted using the Castor Electronic Data Capture (EDC) platform (v2022.1, Castor EDC, Amsterdam, Netherlands), a cloud-based clinical data management system to guarantee complete data traceability and compliance with good clinical practice standards. Statistical analysis was performed in JMP Pro 17.0 (SAS Institute Inc., Cary, NC, 2022-2023). The significance level was set at $p > .05$.

Preprocessing involved deriving the baseline metrics through the mean aggregation of T-1 and T0 measurements. Subsequent values were then calculated for all HRV outcome variables (mean HR, RMSSD, LF, HF, and LF/HF ratio) across both intervention groups. Next, the difference between the final evaluation (T1) and the baseline average was calculated for both the HIT and MIT groups. Assumptions were checked and confirmed for all, except one outcome measure (mean R-R). When applicable, a two-sample t-test and exact rank-sum test ($n < 10$ in both groups) were performed (see Appendix).

Hedges g was calculated for each HRV outcome within both training groups to evaluate the magnitude of the intervention effects. The effect size was defined as the difference between the post-intervention mean (T1) and the baseline mean (averaged from T-1 and T0), divided by the pooled standard deviation of the two time points. The pooled standard deviation was computed as the square root of the mean variance of both measurements. To correct for potential bias in small samples, a correction factor was applied to Cohen's d to obtain an unbiased estimate of the effect size. This approach provided a standardized measure of change, allowing for comparison across variables with different units. Interpretation of Hedges g followed conventional thresholds, with values of 0.2 considered small, 0.5 medium, and 0.8 or above indicating a large effect (Cohen, 1988; Ellis, 2010)

Results

Five females with CNSLBP were enrolled in this study and subsequently assigned to respective groups (HIT; $n = 2$, MIT; $n = 3$). The mean age was 36.4 years ($SD = 8.85$), and the mean BMI was 25.95 kg/m^2 ($SD = 5.35$). Participants baseline and demographic characteristics are presented in Table 3.

Table 3
Participants Baseline and Demographic Characteristics

| | HIT ($n = 2$) | MIT ($n = 3$) |
|-------------------------|------------------|------------------|
| Sex (male/female) | 0/2 | 0/3 |
| Age (y) | 36.5 ± 3.5 | 36.3 ± 14.2 |
| Height (cm) | 167.5 ± 10.6 | 167.0 ± 12.1 |
| Weight (kg) | 73.5 ± 23.3 | 71.5 ± 6.1 |
| BMI (kg/m^2) | 25.8 ± 5.0 | 26.1 ± 5.7 |

Note. Values are presented as mean \pm SD.

Abbreviations: BMI = Body Mass Index; HIT = High Intensity Training; MIT = Moderate Intensity Training

HRV outcomes

The comparative analysis of HRV data between the HIT and MIT intervention groups revealed no statistically significant intergroup difference from PRE to POST. Table 4 summarizes the time domain (mean R-R, SDNN, RMSSD), frequency domain (LF, HF, LF/HF ratio) parameters assessed at baseline and post-intervention, and the effect size.

Table 4*HRV Data in Time and Frequency Domain*

| | HIT (<i>n</i> = 2) | | | MIT (<i>n</i> = 3) | | | <i>p</i> -value | |
|------------------|-----------------------|----------------|-----------------|-----------------------|-----------------|-----------------|-----------------|---------------|
| | PRE (Mean T-1, T0) | POST (T1) | Hedges <i>g</i> | PRE (Mean T-1, T0) | POST (T1) | Hedges <i>g</i> | T-test | Exact test |
| Time domain | | | | | | | | |
| HR (bpm) | 63.04 ± 5.90 | 67.37 ± 6.02 | 0.53 | 68.05 ± 6.70 | 68.12 ± 10.16 | 0.01 | .730 | .800 |
| R-R (ms) | 896.10 ± 77.88 | 955.97 ± 89.43 | 0.52 | 887.62 ± 90.79 | 893.21 ± 125.08 | 0.04 | / | .800 |
| RMSSD (ms) | 26.23 ± 2.38 | 28.24 ± 6.64 | 0.29 | 22.76 ± 3.39 | 30.38 ± 15.40 | 0.50 | .628 | .800 |
| Frequency domain | | | | | | | | |
| LF (n.u.) | 62.28 ± 10.86 | 62.86 ± 31.11 | 0.02 | 41.55 ± 17.64 | 51.51 ± 33.69 | 0.27 | .373 | .300 |
| HF (n.u.) | 37.70 ± 10.84 | 37.10 ± 31.09 | 0.02 | 58.35 ± 17.69 | 48.46 ± 33.69 | 0.27 | .374 | .700 |
| LF/HF ratio | 2.32 ± 1.35 | 3.15 ± 3.48 | 0.23 | 0.82 ± 0.45 | 3.40 ± 5.06 | 0.52 | .340 | .300 |

Note. Values are presented as mean ± SD. Hedges *g* indicates the effect size, where 0.2 is considered small, 0.5 medium, and 0.8 large.

Abbreviations: HIT = High Intensity Training; MIT = Moderate Intensity Training; HR = Heart Rate; R-R = beat-to-beat interval; RMSSD = Root Mean Square of Successive Differences; LF (n.u.) = Low Frequency power in normalized units; HF (n.u.) = High Frequency power in normalized units; LF/HF ratio = Ratio of low-frequency to high-frequency power

Discussion

The main objective of this study was to investigate the effects of exercise therapy, specifically HIT compared to MIT, on cardiac autonomic functioning in individuals with CNSLBP. Contrary to the hypothesis, the results indicated no significant difference between the HIT and MIT groups in HRV (mean R-R, RMSSD, LF, HF, LF/HF ratio). However, both groups showed a slight increase in RMSSD and a decrease in the LF/HF ratio, suggesting a potential improvement in parasympathetic activity and sympathovagal balance. Nevertheless, these changes were not statistically significant. Given the small sample size, these preliminary findings should be interpreted with caution. This study provides an initial indication, rather than drawing firm conclusions about the effect of training intensity on HRV in individuals with CNSLBP.

Previous studies have shown that both HIT and MIT can influence HRV in various populations such as women with fibromyalgia and inactive adults, with HIT often leading to more significant improvements in cardiac autonomic function (Alansare et al., 2018; Sañudo et al., 2015). For instance, research showed that HIT can enhance HRV by improving cardiovagal modulation with a predominance of parasympathetic indices in women with fibromyalgia (Sañudo et al., 2015). Additionally, as previously stated, a HIIT training program had superior effects on improving HRV compared to MICT in inactive adults (Alansare et al., 2018). Despite the structured design and individually prescribed exercise interventions, our preliminary study sample found no significant difference between HIT and MIT groups regarding HRV improvement. This inconsistency may be attributed to differences in exercise intervention characteristics or variations in the populations studied. Several studies have demonstrated that a multidimensional exercise approach, combining aerobic, resistance, and flexibility training, can positively influence HRV in individuals with musculoskeletal conditions. For instance, Janse van Rensburg et al. (2012) reported significant improvements in HRV in women with rheumatoid arthritis (RA) following a multidimensional exercise intervention. Similarly, Park and Lee (2020) observed increased HRV in individuals with chronic low back pain after a multimodal program that included not only exercises but also hot packs, transcutaneous electrical nerve stimulation (TENS), and ultrasound therapy. Furthermore, systematic reviews supported the effectiveness of such multimodal programs in improving autonomic regulation across broader musculoskeletal populations (Bandeira et al., 2021; Rampazo et al., 2024). In line with this methodology, our study also implemented a

multidimensional exercise intervention, but no significant changes in HRV were observed in our sample. Further investigation of the specific contribution of multidimensional exercise interventions and the intensity is needed in people with CNSLBP.

Relevance of the results

Even though there were no clear differences between HIT and MIT regarding HRV outcomes, these results still provide valuable insights for CNSLBP rehabilitation. Cardiac autonomic dysfunction has been linked to chronic pain persistence and disability (Bandeira et al., 2021). The small but consistent trends in HRV improvements in both groups, reflected by small to moderate effect sizes, suggested that exercise therapy could benefit cardiac autonomic function in this population. Although the clinical relevance of these improvements remains to be established, these findings aligned with the broader consensus that exercise, particularly aerobic and resistance training, positively affected autonomic regulation and overall well-being (Miyamoto et al., 2019; Oliveira et al., 2018). Although no differences were found between training intensities in this preliminary analysis, it is too early to rule out the potential role of intensity. Further analyses with a larger sample size as part of the full RCT are needed to confirm and refine these findings.

Strengths and limitations

First, a strength of this study is that the structured 12-week exercise program, with both HIT and MIT protocols, allows for a detailed comparison of their effects on HRV in individuals with CNSLBP. Including both training modalities ensures that any observed differences can be attributed to intensity rather than exercise content. Second, the use of CPET-based exercise prescriptions allowed for personalized training loads. Third, standardized HRV measurement protocols, such as controlled measurement conditions, validated equipment, and fixed measurement durations, enhanced the reliability and reproducibility of the HRV data. These methodological choices align with recommendations in the literature for obtaining high-quality cardiac data (Catai et al., 2020; Laborde et al., 2017). Finally, including multiple HRV parameters (time and frequency domain) enables a more comprehensive analysis of cardiac autonomic functioning, capturing both parasympathetic and sympathetic activity. This multifaceted approach strengthens the interpretability and clinical relevance of the findings.

However, several limitations must be acknowledged. First, the small sample size ($n = 5$) significantly restricted the statistical power, making it difficult to interpret or generalize the current findings. Second, while participants were blinded to their group allocation, the physiotherapists delivering the intervention were not, introducing a potential source of bias. Third, the study did not account for confounding factors, such as psychological stress, medication use, or variations in baseline fitness levels, all of which could have influenced HRV responses (Catai et al., 2020). Fourth, only HRV was included as an outcome measure in this study, whereas pain and functional disability may also have played an important role in individuals with CNSLBP. Finally, the study's reliance on short-term outcomes left uncertainty regarding the long-term effects on cardiac autonomic function and clinical improvements.

Future directions

Future research with larger sample sizes, longer intervention durations, and consideration of potential confounding factors, such as psychological stress, medication use, or variations in baseline fitness levels, is needed to gain a deeper understanding of HIT's long-term effects and underlying mechanisms compared to MIT on HRV in individuals with CNSLBP.

Conclusion

Similar effects observed in both a multidimensional HIT and MIT intervention consisting of cardiorespiratory interval, general resistance, and core strength training may suggest comparable impacts on HRV in CNSLBP patients. However, no significant results were found for either the time or frequency domain parameters. These preliminary results underline the need for larger studies with longer durations to confirm these findings.

Reference list

- Alansare, A., Alford, K., Lee, S., Church, T., & Jung, H. C. (2018). The Effects of High-Intensity Interval Training vs. Moderate-Intensity Continuous Training on Heart Rate Variability in Physically Inactive Adults. *Int J Environ Res Public Health*, 15(7). <https://doi.org/10.3390/ijerph15071508>
- Bandeira, P. M., Reis, F. J. J., Sequeira, V. C. C., Chaves, A. C. S., Fernandes, O., & Arruda-Sanchez, T. (2021). Heart rate variability in patients with low back pain: a systematic review. *Scand J Pain*, 21(3), 426-433. <https://doi.org/10.1515/sjpain-2021-0006>
- Burr, R. L. (2007). Interpretation of normalized spectral heart rate variability indices in sleep research: a critical review. *Sleep*, 30(7), 913-919. <https://doi.org/10.1093/sleep/30.7.913>
- Catai, A. M., Pastre, C. M., Godoy, M. F., Silva, E. D., Takahashi, A. C. M., & Vanderlei, L. C. M. (2020). Heart rate variability: are you using it properly? Standardisation checklist of procedures. *Braz J Phys Ther*, 24(2), 91-102. <https://doi.org/10.1016/j.bjpt.2019.02.006>
- Cieza, A., Causey, K., Kamenov, K., Hanson, S. W., Chatterji, S., & Vos, T. (2021). Global estimates of the need for rehabilitation based on the Global Burden of Disease study 2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*, 396(10267), 2006-2017. [https://doi.org/10.1016/s0140-6736\(20\)32340-0](https://doi.org/10.1016/s0140-6736(20)32340-0)
- Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed., pp. 413–414). Routledge.
- Deyo, R. A. (2002). Diagnostic evaluation of LBP: reaching a specific diagnosis is often impossible. *Arch Intern Med*, 162(13), 1444-1447; discussion 1447-1448. <https://doi.org/10.1001/archinte.162.13.1444>
- Dionne, C. E., Dunn, K. M., Croft, P. R., Nachemson, A. L., Buchbinder, R., Walker, B. F., Wyatt, M., Cassidy, J. D., Rossignol, M., Leboeuf-Yde, C., Hartvigsen, J., Leino-Arjas, P., Latza, U., Reis, S., Gil Del Real, M. T., Kovacs, F. M., Oberg, B., Cedraschi, C., Bouter, L. M.,... Von Korff, M. (2008). A consensus approach toward the standardization of back pain definitions for use in prevalence studies. *Spine (Phila Pa 1976)*, 33(1), 95-103. <https://doi.org/10.1097/BRS.0b013e31815e7f94>
- Ellis, P. D. (2010). *The Essential Guide to Effect Sizes*. <https://doi.org/10.1017/cbo9780511761676>
- Figueroa, A., Kingsley, J. D., McMillan, V., & Panton, L. B. (2008). Resistance exercise training improves heart rate variability in women with fibromyalgia. *Clin Physiol Funct Imaging*, 28(1), 49-54. <https://doi.org/10.1111/j.1475-097X.2007.00776.x>
- Francesco, B., Maria Grazia, B., Emanuele, G., Valentina, F., Sara, C., Chiara, F., Riccardo, M., & Francesco, F. (2012). Linear and nonlinear heart rate variability indexes in clinical practice. *Comput Math Methods Med*, 2012, 219080. <https://doi.org/10.1155/2012/219080>
- Hallman, D. M., & Lyskov, E. (2012). Autonomic regulation, physical activity and perceived stress in subjects with musculoskeletal pain: 24-hour ambulatory monitoring. *Int J Psychophysiol*, 86(3), 276-282. <https://doi.org/10.1016/j.ijpsycho.2012.09.017>

- Hartvigsen, J., Hancock, M. J., Kongsted, A., Louw, Q., Ferreira, M. L., Genevay, S., Hoy, D., Karppinen, J., Pransky, G., Sieper, J., Smeets, R. J., & Underwood, M. (2018). What low back pain is and why we need to pay attention. *Lancet*, 391(10137), 2356-2367. [https://doi.org/10.1016/s0140-6736\(18\)30480-x](https://doi.org/10.1016/s0140-6736(18)30480-x)
- Hautala, A. J., Kiviniemi, A. M., Mäkilä, T. H., Kinnunen, H., Nissilä, S., Huikuri, H. V., & Tulppo, M. P. (2006). Individual differences in the responses to endurance and resistance training. *Eur J Appl Physiol*, 96(5), 535-542. <https://doi.org/10.1007/s00421-005-0116-2>
- Herdy, A. H., Ritt, L. E., Stein, R., Araujo, C. G., Milani, M., Meneghelo, R. S., Ferraz, A. S., Hossri, C., Almeida, A. E., Fernandes-Silva, M. M., & Serra, S. M. (2016). Cardiopulmonary Exercise Test: Background, Applicability and Interpretation. *Arq Bras Cardiol*, 107(5), 467-481. <https://doi.org/10.5935/abc.20160171>
- Janse van Rensburg, D. C., Ker, J. A., Grant, C. C., & Fletcher, L. (2012). Effect of exercise on cardiac autonomic function in females with rheumatoid arthritis. *Clin Rheumatol*, 31(8), 1155-1162. <https://doi.org/10.1007/s10067-012-1985-5>
- Kleiger, R. E., Stein, P. K., & Bigger, J. T., Jr. (2005). Heart rate variability: measurement and clinical utility. *Ann Noninvasive Electrocardiol*, 10(1), 88-101. <https://doi.org/10.1111/j.1542-474X.2005.10101.x>
- Koenig, J., De Koning, M., Bernardi, A., Williams, D. P., Nijs, J., Thayer, J. F., & Daenen, L. (2016). Lower Resting State Heart Rate Variability Relates to High Pain Catastrophizing in Patients with Chronic Whiplash-Associated Disorders and Healthy Controls. *Pain Pract*, 16(8), 1048-1053. <https://doi.org/10.1111/papr.12399>
- Laborde, S., Mosley, E., & Thayer, J. F. (2017). Heart Rate Variability and Cardiac Vagal Tone in Psychophysiological Research - Recommendations for Experiment Planning, Data Analysis, and Data Reporting. *Front Psychol*, 8, 213. <https://doi.org/10.3389/fpsyg.2017.00213>
- Maher, C., Underwood, M., & Buchbinder, R. (2017). Non-specific low back pain. *Lancet*, 389(10070), 736-747. [https://doi.org/10.1016/s0140-6736\(16\)30970-9](https://doi.org/10.1016/s0140-6736(16)30970-9)
- McCraty, R., & Shaffer, F. (2015). Heart Rate Variability: New Perspectives on Physiological Mechanisms, Assessment of Self-regulatory Capacity, and Health risk. *Glob Adv Health Med*, 4(1), 46-61. <https://doi.org/10.7453/gahmj.2014.073>
- Meesen, R., & Nysen, R. (2022). *Wetenschappelijke vorming (WV2)* (p. 222). Acco.
- Miyamoto, G. C., Lin, C. C., Cabral, C. M. N., van Dongen, J. M., & van Tulder, M. W. (2019). Cost-effectiveness of exercise therapy in the treatment of non-specific neck pain and low back pain: a systematic review with meta-analysis. *Br J Sports Med*, 53(3), 172-181. <https://doi.org/10.1136/bjsports-2017-098765>
- Nunan, D., Sandercock, G. R., & Brodie, D. A. (2010). A quantitative systematic review of normal values for short-term heart rate variability in healthy adults. *Pacing Clin Electrophysiol*, 33(11), 1407-1417. <https://doi.org/10.1111/j.1540-8159.2010.02841.x>
- Oliveira, C. B., Maher, C. G., Pinto, R. Z., Traeger, A. C., Lin, C. C., Chenot, J. F., van Tulder, M., & Koes, B. W. (2018). Clinical practice guidelines for the management of non-specific low back pain in primary care: an updated

- overview. *Eur Spine J*, 27(11), 2791-2803.
<https://doi.org/10.1007/s00586-018-5673-2>
- Parati, G., Mancia, G., Di Rienzo, M., & Castiglioni, P. (2006). Point: cardiovascular variability is/is not an index of autonomic control of circulation. *J Appl Physiol* (1985), 101(2), 676-678; discussion 681-672.
<https://doi.org/10.1152/japplphysiol.00446.2006>
- Park, D., & Lee, K. S. (2020). The Comparison of the Effect of Thoracic Flexibility Exercise and Lumbar Stabilization Exercise on Pain and Heart Rate Variability of Patients with Chronic Low Back Pain. *International Journal of Advanced Nursing Education and Research*, 5(1), 25–30.
<https://doi.org/10.21742/ijaner.2020.5.1.03>
- Rampazo É, P., Rehder-Santos, P., Catai, A. M., & Liebano, R. E. (2024). Heart rate variability in adults with chronic musculoskeletal pain: A systematic review. *Pain Pract*, 24(1), 211-230. <https://doi.org/10.1111/papr.13294>
- Routledge, F. S., Campbell, T. S., McFetridge-Durdle, J. A., & Bacon, S. L. (2010). Improvements in heart rate variability with exercise therapy. *Can J Cardiol*, 26(6), 303-312. [https://doi.org/10.1016/s0828-282x\(10\)70395-0](https://doi.org/10.1016/s0828-282x(10)70395-0)
- Sandercock, G. R., Bromley, P. D., & Brodie, D. A. (2005). The reliability of short-term measurements of heart rate variability. *Int J Cardiol*, 103(3), 238-247.
<https://doi.org/10.1016/j.ijcard.2004.09.013>
- Sañudo, B., Carrasco, L., de Hoyo, M., Figueroa, A., & Saxton, J. M. (2015). Vagal modulation and symptomatology following a 6-month aerobic exercise program for women with fibromyalgia. *Clin Exp Rheumatol*, 33(1 Suppl 88), S41-45.
- Shaffer, F., & Ginsberg, J. P. (2017). An Overview of Heart Rate Variability Metrics and Norms. *Front Public Health*, 5, 258.
<https://doi.org/10.3389/fpubh.2017.00258>
- Speer, K. E., Semple, S., Naumovski, N., & McKune, A. J. (2020). Measuring Heart Rate Variability Using Commercially Available Devices in Healthy Children: A Validity and Reliability Study. *Eur J Investig Health Psychol Educ*, 10(1), 390-404.
<https://doi.org/10.3390/ejihpe10010029>
- Stanton, T. R., Latimer, J., Maher, C. G., & Hancock, M. J. (2010). How do we define the condition 'recurrent low back pain'? A systematic review. *Eur Spine J*, 19(4), 533-539. <https://doi.org/10.1007/s00586-009-1214-3>
- Terkelsen, A. J., Mølgaard, H., Hansen, J., Finnerup, N. B., Krøner, K., & Jensen, T. S. (2012). Heart rate variability in complex regional pain syndrome during rest and mental and orthostatic stress. *Anesthesiology*, 116(1), 133-146.
<https://doi.org/10.1097/ALN.0b013e31823bbfb0>
- Vanderlei, L. C., Pastre, C. M., Hoshi, R. A., Carvalho, T. D., & Godoy, M. F. (2009). Basic notions of heart rate variability and its clinical applicability. *Rev Bras Cir Cardiovasc*, 24(2), 205-217.
<https://doi.org/10.1590/s0102-76382009000200018>
- van Eetvelde, J. S., Timmermans, A. A. A., Coninx, K., Kempeneers, K., Meeus, M., Marneffe, W., Meus, T., Meuwissen, I., Roussel, N. A., Stassijns, G., & Verbrugghe, J. (2024). Technology supported High Intensity Training in chronic non-specific low back pain (the Techno-HIT trial): study protocol of a

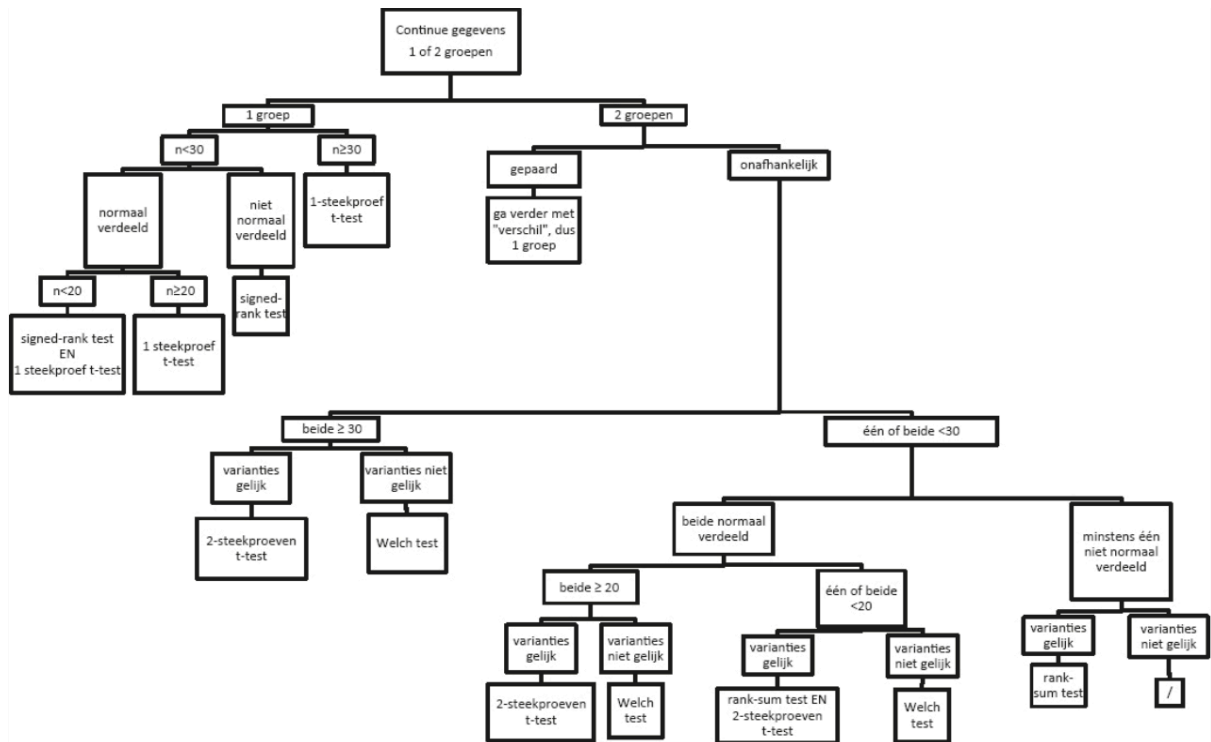
randomised controlled trial. *BMJ Open Sport Exerc Med*, 10(4), e002180.
<https://doi.org/10.1136/bmjsem-2024-002180>

van Tulder, M., Becker, A., Bekkering, T., Breen, A., del Real, M. T., Hutchinson, A., Koes, B., Laerum, E., & Malmivaara, A. (2006). Chapter 3. European guidelines for the management of acute nonspecific low back pain in primary care. *Eur Spine J*, 15 Suppl 2(Suppl 2), S169-191.

<https://doi.org/10.1007/s00586-006-1071-2>

Verbrugghe, J., Agten, A., Stevens, S., Hansen, D., Demoulin, C., B, O. E., Vandenabeele, F., & Timmermans, A. (2019). Exercise Intensity Matters in Chronic Nonspecific Low Back Pain Rehabilitation. *Med Sci Sports Exerc*, 51(12), 2434-2442. <https://doi.org/10.1249/mss.0000000000002078>

Appendix Decision Tree



Note. This decision tree illustrates the different steps that were taken for the statistical analysis. Reprinted from *Wetenschappelijke vorming (WV2)* (p.222), by R. Meesen and R. Nysen, 2022, Acco.