

# Journal Pre-proof

Changes in health-related quality of life, motivation for physical activity, the levels of anxiety and depression after individualized aerobic training in subjects with metabolic syndrome

Jurate Zupkauskiene, Ieva Lauceviciene, Petras Navickas, Ligita Ryliskyte, Roma Puronaite, Jolita Badariene, Aleksandras Laucevicius

PII: S1109-9666(22)00057-4

DOI: <https://doi.org/10.1016/j.hjc.2022.04.003>

Reference: HJC 690

To appear in: *Hellenic Journal of Cardiology*

Received Date: 11 December 2021

Revised Date: 4 April 2022

Accepted Date: 12 April 2022

Please cite this article as: Zupkauskiene J, Lauceviciene I, Navickas P, Ryliskyte L, Puronaite R, Badariene J, Laucevicius A, Changes in health-related quality of life, motivation for physical activity, the levels of anxiety and depression after individualized aerobic training in subjects with metabolic syndrome, *Hellenic Journal of Cardiology*, <https://doi.org/10.1016/j.hjc.2022.04.003>.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2022 Hellenic Society of Cardiology. Publishing services by Elsevier B.V. All rights reserved.



**Changes in health-related quality of life, motivation for physical activity, the levels of anxiety and depression after individualized aerobic training in subjects with metabolic syndrome**

Jurate Zupkauskiene <sup>1</sup>, Ieva Lauceviciene <sup>2</sup>, Petras Navickas <sup>1,3</sup>, Ligita Ryliskyte <sup>1</sup>, Roma Puronaite <sup>4</sup>, Jolita Badariene <sup>1</sup>, Aleksandras Laucevicius <sup>1,3</sup>

<sup>1</sup> Clinic of Cardiac and Vascular Diseases, Faculty of Medicine, Vilnius University, 08661 Vilnius, Lithuania

<sup>2</sup> Department of Rehabilitation, Physical and Sports Medicine, Faculty of Medicine, Vilnius University, 03101 Vilnius, Lithuania

<sup>3</sup> State Research Institute Center for Innovative Medicine, 08410 Vilnius, Lithuania

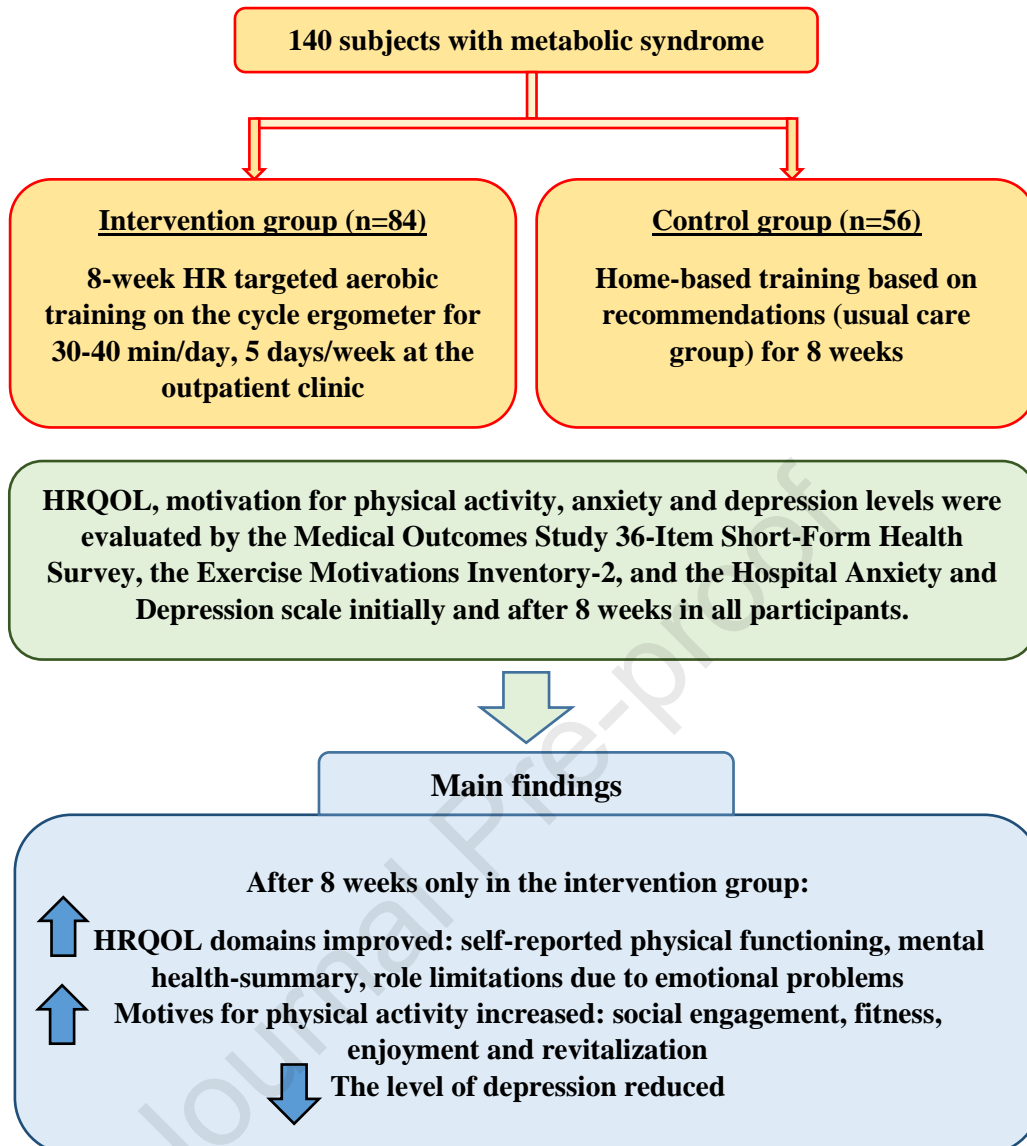
<sup>4</sup> Institute of Data Science and Digital Technologies, Faculty of Mathematics and Informatics, Vilnius University, 08412 Vilnius, Lithuania

Corresponding author:

Jurate Zupkauskiene, MD, Clinic of Cardiac and Vascular Diseases, Faculty of Medicine, Vilnius University, Santariskiu st. 2, 08661 Vilnius, Lithuania. Tel.: (+370) 5236 5307.

Email: jurate.balsyte@gmail.com

Declarations of interest: none



## Abstract

### Background

Numerous studies associate metabolic syndrome (MetS) with poor life quality, depression, and anxiety. Aerobic exercise training has proven its value in promoting health among subjects with MetS. We aimed to evaluate the changes in health-related quality of life (HRQOL), motivation for physical activity, and the levels of anxiety and depression in subjects with MetS after individualized aerobic training.

### Methods

A total of 140 subjects with MetS ( $53.2 \pm 6.8$ -years, 55%-female) were analyzed after the random assignment to the intervention ( $n=84$ ) or the control group ( $n=56$ ). Only the intervention group participated in the 8-week HR targeted aerobic training program, which consisted of exercises on a cycle ergometer for 30-40 min/day, 5 days/week. In all study participants HRQOL, motivation for physical activity, anxiety and depression levels were evaluated by the Medical Outcomes Study 36-Item Short-Form Health Survey, the Exercise Motivations Inventory-2, and the Hospital Anxiety and Depression scale before and after 8 weeks.

### Results

After 8 weeks, self-reported physical functioning significantly increased only in the intervention group ( $p=0.01$ ). The scores of mental health-summary and role limitations due to emotional problems also improved in subjects with MetS, who participated in the aerobic training program ( $p<0.001$ ,  $p=0.009$ , respectively). The scores for social engagement motive, enjoyment and revitalization motive, and fitness motive to exercise increased ( $p=0.003$ ,  $p<0.001$ ,  $p=0.023$ , respectively), whereas the level of depression reduced only in the intervention group ( $p=0.021$ ).

### Conclusions

The 8-week individualized aerobic training had a positive effect on HRQOL, motivation for physical activity, and the level of depression in subjects with MetS.

### Keywords

aerobic exercise; metabolic syndrome; physical functioning; psycho-emotional state; health-related life quality; motivation

## Abbreviations

MetS, metabolic syndrome; HRQOL, health-related quality of life; CPET, cardiopulmonary exercise test; HR, heart rate; VO<sub>2</sub>, oxygen uptake; AT, anaerobic threshold; BP, blood pressure; BMI, body mass index; CRF, cardiorespiratory fitness; VE, maximal minute ventilation; VO<sub>2</sub> max, maximal oxygen uptake; WR, work rate; VCO<sub>2</sub> - carbon dioxide output; VT<sub>1</sub>, first ventilatory threshold; VT<sub>2</sub>, second ventilatory threshold; HADS, the Hospital Anxiety and Depression Scale; SF-36, the Medical Outcomes Study 36-Item Short-Form Health Survey; EMI-2, the Exercise Motivations Inventory 2.

## 1. Introduction

Studies cumulatively foreground the prognostic significance of metabolic syndrome (MetS)<sup>1-3</sup>. It is a cluster of the risk factors that comprise abdominal obesity, dyslipidemia, impaired glucose tolerance, and arterial hypertension with a prevalence of 20-25% among the adult population worldwide<sup>4,5</sup>. MetS increases by 1.53 to 2.18 the relative risk of cardiovascular disease, by 1.27 to 1.6 the risk of all-cause mortality<sup>1-3</sup>, and leads to 5-fold greater risk for type 2 diabetes<sup>6</sup>.

The evaluation of psycho-emotional conditions in patients suffering from cardiometabolic diseases is of great importance. Depressive and anxiety disorders are more common in subjects with MetS than those without MetS<sup>7</sup>. By contrast, the prevalence of MetS among psychiatric inpatients was found to be 29.4%<sup>8</sup>. Some studies pointed out the link between MetS and depression, but not anxiety<sup>9,10</sup>, while a recent meta-analysis revealed that there is a positive association between MetS and anxiety<sup>11</sup>. In addition, it was demonstrated that both depression and anxiety are linked to MetS, which leads to a poor prognosis of MetS subjects<sup>12</sup>. Health-related quality of life (HRQOL) is just as important because it reflects on a person's physical and mental health and also independently predicts mortality in type 2 diabetes patients<sup>13</sup>. To add, it has been shown that the fear associated with obesity, hypertension, diabetes, and cardiovascular disease affects cardiometabolic patients and deteriorates their HRQOL<sup>14</sup>.

An increase in physical activity by applying exercise programs is an effective way to improve HRQOL<sup>15</sup>, as well as cardiometabolic health and fitness status<sup>16</sup>. Exercise training, and specifically aerobic exercise, has proven its value in promoting health among subjects with MetS<sup>17</sup> and was shown to be superior compared to standard home-based training<sup>18</sup>. However,

very few publications that demonstrate the positive effect of aerobic exercise on HRQOL in subjects with MetS were found<sup>19–21</sup>. Moreover, there are very few studies that show the influence of physical activity on reducing the levels of anxiety and depression among MetS subjects<sup>19,22</sup>. Finally, it is also worth emphasizing that motivation is a key factor for daily physical activity or sustained training<sup>23</sup>, therefore understanding the motives for physical activity is crucial for developing new exercise interventions for better involvement and health promotion<sup>23</sup>.

Individualized aerobic exercise prescription by performing incremental cardiopulmonary exercise test (CPET) and directly evaluating the functional capacity of the patient is the gold standard<sup>24</sup>. This approach is physiologically comprehensive and can maximize the benefits of aerobic exercise training<sup>24</sup>. Heart rate (HR) at anaerobic threshold (AT) is one of the CPET physiological parameters useful for aerobic exercise training prescription and monitoring<sup>25</sup>. Heart rate (HR) is widely used for exercise prescription because of its linear relationship with workload and VO<sub>2</sub> (oxygen uptake) increase during incremental exercise<sup>24,26</sup>. There has already been an attempt at demonstrating the effect of the HR targeted aerobic exercise training program on cardiometabolic risk markers<sup>18,27,28</sup>. Moreover, there are several studies that analyzed the impact of HR-based exercise programs on various subjective outcomes, such as HRQOL and work ability in subjects with MetS<sup>20,27–29</sup>. However, we have not found any available publication on the complex assessment of HRQOL, motivation for physical activity, and the levels of anxiety and depression in subjects with MetS before and after the HR targeted aerobic training program.

The purpose of this study was to assess the changes in HRQOL, motivation for physical activity, and the levels of anxiety and depression in subjects with MetS after the 8-week individualized, HR targeted, aerobic training program.

## **2. Methods**

### **2.1. Study Design and Eligibility Criteria**

The prospective study was carried out between 2018 and 2020 at the outpatient clinic "InMedica" and Vilnius University Hospital Santaros Klinikos, Lithuania. All individuals included in the study were participants of the Lithuanian High Cardiovascular Risk (LitHiR) primary prevention program<sup>30</sup>. The study participants were male (40–55 years) and female (50–65 years) with MetS, which was defined according to the National Cholesterol Education

Programme (NCEP ATP III) criteria<sup>5</sup>. At least three of the following five criteria are required for MetS diagnosis: hypertriglyceridemia (triglycerides  $\geq 1.7$  mmol/l); high-density lipoprotein cholesterol  $\leq 1.03$  mmol/l for men or  $\leq 1.29$  mmol/l for women; abdominal obesity (waist circumference  $> 102$  cm for men and  $> 88$  cm for women); elevated blood pressure (BP) (systolic BP  $\geq 130$  mm Hg and/or diastolic BP  $\geq 85$  mm Hg or current use of antihypertensive drugs); elevated fasting plasma glucose  $\geq 5.6$  mmol/l<sup>5</sup>. All recruited participants were age and sex matched. They were divided into the intervention and control (usual care) groups manually by the study researcher using a 1:1 random sampling method. Patients with overt cardiovascular disease or type 2 diabetes were excluded from the study.

## 2.2. Clinical Assessment

All study participants were investigated at baseline and after 8 weeks. Their anthropometric parameters, such as body mass index (BMI), waist circumference, clinical data, such as BP, HR at rest, venous blood sampling for blood lipids and glucose were assessed at rest, between 7 AM and 12 PM after overnight fast and abstinence from caffeine and at least 2 hours after smoking. Blood pressure was measured in a sitting position using oscillometric devices in accordance with the 2018 European Society of Cardiology / European Society of Hypertension guidelines<sup>31</sup>. Arterial hypertension was defined as systolic BP  $\geq 140$  mm Hg and/or diastolic BP  $\geq 90$  mm Hg<sup>31</sup> or the use of antihypertensive drugs was present. BMI was calculated by dividing the body weight in kilograms by the square of the body height in meters. Obesity was defined as BMI of  $\geq 30$  kg/m<sup>2</sup>; overweight, as BMI of 25 – 29.9 kg/m<sup>2</sup>; and normal weight, as BMI of  $< 25$  kg/m<sup>2</sup><sup>31</sup>.

We assessed cardiorespiratory fitness (CRF) in all study participants by performing an incremental CPET on the cycle ergometer, which was set to a ramp mode from 15 to 30 W/min. The workload was chosen individually according to the participant's anticipated physical capacity, gender, age, body mass, and self-reported physical activity status. After 2 minutes of cycling without resistance, the workload was constantly increased until the participants refused to continue exercise because of fatigue or other withdrawal symptoms. The exercise protocol lasted approximately 8–12 minutes. During the test, BP and electrocardiogram were maintained. Gas exchange analysis was performed using a dedicated SensorMedics metabolic cart (Vmax ENCORE 229). Ventilatory equivalents for O<sub>2</sub> (VE/VO<sub>2</sub>, where VE – maximal minute ventilation, VO<sub>2</sub> - oxygen uptake) and CO<sub>2</sub> (VE/VCO<sub>2</sub>, where VCO<sub>2</sub> - carbon dioxide output) as a function of work rate (WR) were used

as criteria for the establishment of the first ventilatory threshold (VT1) and the second ventilatory threshold (VT2). VT1 was identified at the point when VE/VO<sub>2</sub> ratio inverted its trend in the presence of a still decreasing or constant VE/VCO<sub>2</sub>, also as the nadir of the VE/VO<sub>2</sub> versus WR relationship<sup>24</sup>. VT2 was identified at the point where the VE/VCO<sub>2</sub> ratio inverted its trend, also as the nadir of the VE/VCO<sub>2</sub> versus WR relationship<sup>24</sup>. VT2 was considered as AT<sup>32</sup>. Training HR was obtained between VT1 and VT2 and was used for the exercise intensity prescription during our aerobic training program. HR registered at VT1 was taken as a level for the initial training and HR registered at VT2 or AT was the target HR for the training<sup>25</sup>. The CRF of the patient was described by maximal oxygen uptake (VO<sub>2</sub> max ml/kg/min). AT was described as % of predicted VO<sub>2</sub> max. The respiratory exchange ratio (VCO<sub>2</sub>/VO<sub>2</sub>) greater than 1 was taken as a criterion of maximal effort.

### 2.3. Motivational Consultation and Questionnaires

At the beginning of the study and after 8 weeks all individuals participated in the motivational consultation, which lasted about 20 minutes and was supervised by a rehabilitation specialist and cardiologist. During the first motivational consultation, participants in both groups received detailed recommendations on the reduction of cardiovascular risk, including standard recommendations for physical activity and home-based training. During the first and the second motivational consultation, the following questionnaires were applied for all participants in person to evaluate their levels of anxiety and depression, HRQOL, and motivation for physical activity: the Hospital Anxiety and Depression Scale (HADS), the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), and the Exercise Motivations Inventory 2 (EMI-2). These questionnaires were selected because they are validated, widely used, and translated into Lithuanian language.

The HADS questionnaire comprises seven items related to anxiety and seven related to depression<sup>33</sup>. Scoring for each item ranges between 0 and 3. A person can score between 0 and 21 for either anxiety or depression: 8-10 scores indicate mild, 11-14 scores - moderate, and 15-21 scores - severe anxiety or depression.

The SF-36 is a multidimensional questionnaire designed to assess the condition of general health and quality of life<sup>34</sup>. The questionnaire consists of 36 questions that reflect the main eight domains of HRQOL: physical functioning, role limitations due to physical health problems (role-physical), bodily pain, assessment of general health and change in reported health, vitality, social functioning, mental health, role limitations due to emotional problems



(role-emotional); and two summarized measurements of physical and mental health that combine these different areas. This questionnaire evaluates well-being over the last 4 weeks. Each domain is scored from 0 to 100 (100 points show the best estimate).

The EMI-2 is a questionnaire which is used to assess the influence of the person's motivation on undertaking physical exercise training<sup>35</sup> and comprises 51 statements, fourteen subscales, and five groups of motives: psychological motives (enjoyment and revitalization) - 4 subscales, interpersonal motives (social engagement) - 3 subscales, health motives - 3 subscales, body-related motives (appearance/weight) - 2 subscales, and fitness motives - 2 subscales. The questionnaire is appropriate not only for physically active persons but also for non-exercisers. In response to each statement, the participants had to choose an answer on a six-step scale from 0 points ("not at all true for me") to 5 points ("very true for me").

#### 2.4. Intervention

Only the intervention group participated in the individualized, HR targeted, aerobic training program, which consisted of exercises on a cycle ergometer for 30-40 min/day, 5 days/week for 8 weeks (40 individual sessions in total). The aerobic training protocol was developed based on the standard recommendations for incremental aerobic exercise<sup>24,26</sup> and was adapted for untrained subjects with MetS.

Each aerobic exercise training session consisted of 3 phases: warm-up, exercise training, cool-down. The warm-up phase lasted 10 minutes. For the first 5 minutes of warm-up, exercise intensity was set to 25 W, and for the next 5 minutes it was gradually increased until the training HR was reached. During the exercise training phase, the intensity of exercise was maintained at such a level that the training HR remained constant. The cool-down phase also lasted 10 minutes. The exercise intensity was gradually reduced to 25 W for the first 5 minutes, and a constant exercise intensity of 25 W was maintained for the last 5 minutes. The pedalling frequency throughout each session was 60 rpm.

During the first 2 weeks of the individualized aerobic training program, the duration of the exercise training phase was increased from 30 minutes to 40 minutes (every 2 sessions for 2 minutes) and the intensity of exercise was maintained at HR for initial training (HR registered at VT1 during CPET). During the third and fourth week, the intensity of exercise was gradually increased up to the target HR which has been individually estimated at VT2 or AT during CPET. For the remaining 4 weeks of the individualized aerobic training program, the exercise intensity was maintained at the target HR. To adjust exercise intensity and monitor

HR, we used the Ergoline Rehabilitation System-2 (ERS-2), which enabled us to control the load of the cycle ergometer, so that the patient's HR would be at a targeted level during the exercise training phase. Targeted HR was carefully monitored and maintained at all times and the deviation from the target HR was insignificant. The Borg Perceived Exertion 6 to 20 scale was used to evaluate the effort of the patient to exercise during each session<sup>36</sup>.

The HR targeted aerobic training program was designed to be implemented into clinical practice. The program was carried out at the outpatient clinic and was supervised by a team of rehabilitation specialists and cardiologists.

## 2.5. Statistics

Statistical analysis was performed by SPSS Statistics 20 and R package "corrplot"<sup>37</sup>. The sample size was calculated to provide at least 80% power at the 5% significance level to detect least the medium effect (Cohen  $d = 0.5$ ) between group differences on the change in scores. A sample of 64 individuals per group was required. However, since some individuals from the control and intervention group were lost during follow-up, we checked that the power was sufficient to detect  $d = 0.5$ . Post-hoc analysis showed that the power still exceeds 80% (the achieved power is 82%).

Data were checked for normality using the Shapiro–Wilk test. Descriptive statistics are presented as mean  $\pm$  standard deviation for the continuous variables and as counts and frequencies for the categorical variables. Independent samples t-test or Mann-Whitney U test was used to compare between-group data at baseline when appropriate. A linear multiple regression was conducted where the outcome (e.g., physical functioning at 8-weeks) is regressed against the group (i.e., intervention vs control) and the baseline score for other covariates (age, sex and total cholesterol at baseline) are controlled for. In addition, to assess improvement within groups, a paired t-test or the Wilcoxon signed-rank test was used to compare baseline to 8 weeks in the treatment group and the control group. The McNemar test was used to compare changes of anxiety and depression levels within groups. The calculated Cohen's  $d$  effect sizes were plotted as a heatmap<sup>38</sup>. In all comparisons, values of  $p < 0.05$  were considered statistically significant.

## 3. Results

### 3.1. Descriptive statistics

Initially, a total of 170 participants were included to the study (the mean age  $53.3 \pm 6.9$  years, 55% female). Out of 170 individuals, 30 (17.65%) of the participants missed the second appointment: 1 from the intervention group and 29 from the control group. The main reasons for withdrawing from the study, especially in the control group, were lack of time, willingness to participate, and exacerbation of comorbidities. Data on the missing participants were not included in further analysis. Correspondingly, at baseline and after 8 weeks, 140 participants were investigated: 84 from the intervention group and 56 from the control group. The mean age of 140 individuals was  $53.2 \pm 6.8$  years (in the intervention group –  $53.9 \pm 6.4$  years and in the control group –  $52.1 \pm 7.1$  years) and 55% of them were female.

All participants were not sufficiently physically active: they indicated exercising less than the recommended 30 minutes of moderate aerobic physical activity 5 times/week. 98.6% of the participants reported to have poor CRF. Abdominal obesity was present in 81.4%, arterial hypertension - in 91.3%, dyslipidemia – in 97.6%, and elevated fasting glucose – in 62.7% of cases. More detailed characteristics of the study participants are presented in Table 1.

**Table 1.** Baseline characteristics of the participants.

	Intervention group (n = 84)	Control group (n = 56)	<i>p</i> value between the groups
<b>Age (years)</b>	$53.9 \pm 6.4$	$52.1 \pm 7.1$	0.133
<b>Sex</b>			
Female (%)	50 (59.52)	27 (48.21)	0.188
Male (%)	34 (40.48)	29 (51.79)	
<b>Assessment of BP</b>			
Systolic BP (mm Hg)	$132.73 \pm 13.01$	$133.78 \pm 15.32$	0.667
Diastolic BP (mm Hg)	$81.56 \pm 9.23$	$82.71 \pm 10.88$	0.511
Arterial hypertension (%)	79 (94.05)	49 (87.5)	0.222
<b>Assessment of blood lipids</b>			
T-Chol (mmol/l)	$6.41 \pm 1.40$	$5.86 \pm 1.24$	<b>0.012</b>
LDL-Chol (mmol/l)	$4.19 \pm 1.17$	$3.80 \pm 1.05$	<b>0.044</b>
TG (mmol/l)	$2.35 \pm 2.81$	$1.94 \pm 0.91$	0.231
HDL-Chol (mmol/l)	$1.19 \pm 0.30$	$1.15 \pm 0.29$	0.41
Dyslipidemia (%)	84 (100)	53 (94.64)	0.062
Fasting glucose (mmol/l)	$5.99 \pm 0.83$	$5.80 \pm 0.59$	0.34
Elevated fasting glucose (%)	54 (64.3)	34 (61.8)	0.768
<b>Assessment of obesity</b>			
Waist circumference (cm)	$102.18 \pm 9.13$	$104.98 \pm 9.10$	0.082
Abdominal obesity (%)	69 (81.9)	45 (80.4)	0.816
BMI (kg/m <sup>2</sup> )	$30.86 \pm 3.96$	$31.05 \pm 3.21$	0.769
<b>BMI categories</b>			
Normal (%)	4 (4.82)	1 (1.79)	
Overweight (%)	32 (38.55)	20 (35.71)	0.850

<b>Obese (%)</b>	48 (56.62)	35 (62.5)	
<b>Assessment of CRF</b>			
<b>VO2 max (ml/kg/min)</b>	22.28 ± 5.47	22.51 ± 4.61	0.637
<b>AT (% Predicted VO2 max)</b>	76.22 ± 17.63	77.98 ± 17.55	0.541
<b>Resting HR (bpm)</b>	63.57 ± 7.96	61.30 ± 8.04	0.173
<b>Self-reported CRF</b>			
<b>Bad (%)</b>	82 (97.6)	56 (100)	
<b>Satisfactory (%)</b>	1 (1.2)	0	
<b>Good (%)</b>	1 (1.2)	0	1
<b>Very good (%)</b>	0	0	
<b>Excellent (%)</b>	0	0	

Data are presented as mean ± SD or in absolute numbers (n) and percentage in parentheses (%). *p* value in bold denotes a statistically significant difference ( $p < 0.05$ ).

Abbreviations: BP, blood pressure; T-Chol, total cholesterol; LDL-Chol, low-density lipoprotein cholesterol; TG, triglycerides; HDL-Chol, high-density lipoprotein cholesterol; BMI, body mass index; CRF, cardiorespiratory fitness; VO2 max, maximal oxygen uptake; AT, anaerobic threshold; HR, heart rate.

At the baseline, there were no significant differences between the intervention and control groups according to the age, sex, main anthropometric parameters, MetS components, self-reported CRF (Table 1), and questionnaire scores, except for one domain from the EMI-2 questionnaire (ill-health avoidance motive,  $p = 0.02$ ).

### 3.2. The Evaluation of the Health-Related Quality of Life

According to the initial assessment of HRQOL with the SF-36 questionnaire, individuals in both groups assigned the lowest scores when rating their health changes during the last year, general health condition, and vitality status. Social functions, physical functioning, and role limitations due to emotional problems were rated with top scores (Table 2).

Males from both groups rated their physical functioning with higher scores than females ( $p = 0.002$  and  $p = 0.007$ , respectively). Younger participants in both groups evaluated their physical functioning better than older participants ( $p = 0.009$  in the intervention group and  $p = 0.012$  in the control group). In the intervention group, pain affected older participants more ( $p = 0.009$ ), and social functions were rated worse by females as well as by older participants ( $p = 0.003$  and  $p = 0.029$ , respectively).

**Table 2.** Changes in scores of the Medical Outcomes Study 36-Item Short-Form Health Survey domains from the baseline to the second measurement 8 weeks later.

Intervention group	<i>p</i> value between the groups *	Control group
--------------------	---	---------------

At baseline	After 8 weeks	Change	<i>p</i>		<i>p</i>	Change	At baseline	After 8 weeks
Physical health – summary				Physical health – summary				
73.57 ± 17.43	76.79 ± 17.43	3.22 ± 11.68	<b>0.020</b>	<b>0.031</b>	<b>&lt; 0.001</b>	8.76 ± 15.19	73.69 ± 15.29	82.45 ± 14.23
Physical functioning				Physical functioning				
81.58 ± 17.10	83.29 ± 17.10	1.71 ± 12.05	<b>0.010</b>	0.568	0.265	1.76 ± 8.12	85.99 ± 12.40	87.75 ± 9.40
Role-physical				Role-physical				
77.53 ± 33.87	80.91 ± 31.36	3.38 ± 28.54	0.373	0.161	0.051	15.24 ± 53.00	76.83 ± 34.64	92.07 ± 38.91
Bodily pain				Bodily pain				
76.79 ± 21.44	80.73 ± 27.08	3.94 ± 25.16	0.211	0.396	<b>0.004</b>	10.84 ± 21.01	70.73 ± 0.30	81.57 ± 18.36
General health				General health				
58.45 ± 15.07	62.23 ± 16.06	3.78 ± 12.13	<b>0.006</b>	0.192	<b>0.014</b>	6.92 ± 22.76	61.22 ± 14.00	68.14 ± 22.01
Mental health – summary				Mental health – summary				
74.43 ± 15.21	79.47 ± 13.73	5.03 ± 12.03	<b>&lt; 0.001</b>	0.299	0.108	2.67 ± 11.03	76.41 ± 16.12	79.08 ± 13.81
Vitality				Vitality				
62.37 ± 18.21	67.31 ± 14.43	4.94 ± 14.27	<b>0.002</b>	0.986	<b>0.036</b>	4.25 ± 12.38	64.38 ± 15.57	68.63 ± 15.02
Social functioning				Social functioning				
84.97 ± 17.26	86.23 ± 16.09	1.27 ± 16.94	0.496	0.729	0.779	0.00 ± 13.11	86.89 ± 15.80	86.89 ± 15.80
Role-emotional				Role-emotional				
78.06 ± 31.53	87.76 ± 23.37	9.70 ± 29.31	<b>0.009</b>	0.367	0.724	2.44 ± 28.27	83.74 ± 31.73	86.18 ± 26.85
Mental health				Mental health				
72.67 ± 14.51	75.85 ± 13.31	3.18 ± 11.66	<b>0.009</b>	0.820	<b>0.011</b>	5.00 ± 11.77	70.50 ± 14.57	75.50 ± 14.86
Change in reported health				Change in reported health				
42.53 ± 19.89	62.01 ± 21.69	19.48 ± 25.20	<b>0.0001</b>	<b>0.036</b>	<b>0.003</b>	10.26 ± 16.93	44.23 ± 17.64	54.49 ± 19.76

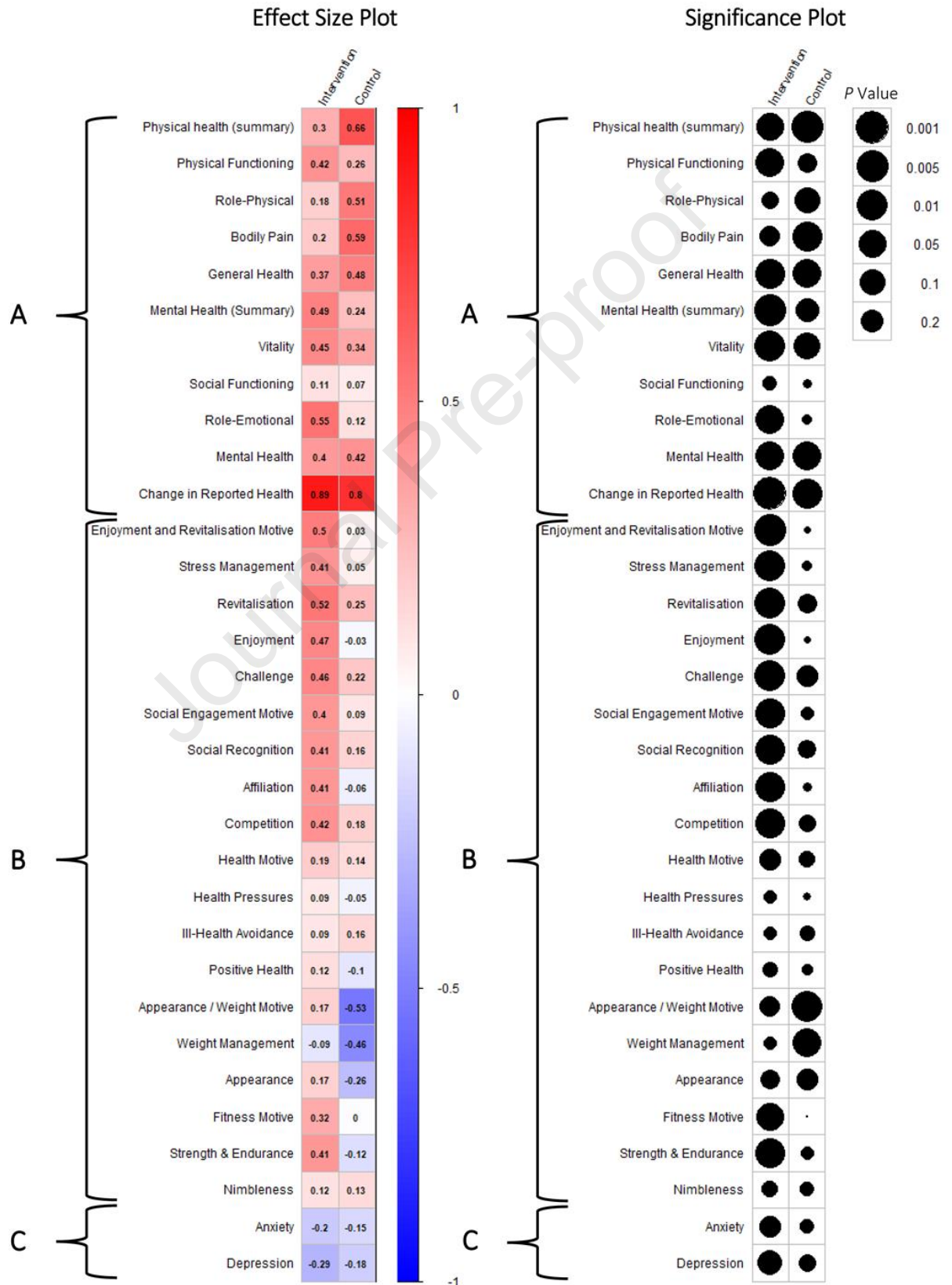
Data are presented as mean ± SD. *p* value in bold denotes a statistically significant difference ( $p < 0.05$ ). \* Linear multiple regression.

After 8 weeks, self-reported physical functioning statistically significantly increased only in the intervention group (an increase of 2.09%,  $p = 0.01$ ,  $d = 0.42$ ). There was no statistically significant improvement in physical functioning in the control group ( $p = 0.265$ ,  $d = 0.26$ ).

The score of mental health-summary and the score of role limitations due to emotional problems statistically significantly improved only in the intervention group by 6.77% and 12.43% respectively ( $p \leq 0.001$ ,  $d = 0.49$  and  $p = 0.009$ ,  $d = 0.55$ ). The domain of mental health-summary includes subdomains of vitality, role emotional, mental health, and social functioning. The summarized score of physical health, the scores of general health, vitality, mental health, and change in reported health improved in both groups (all  $p < 0.05$ ).

However, after the 8-week follow-up, there were significant between-group differences found in the summarized score of physical health ( $p = 0.031$ ) and the score of change in reported health ( $p = 0.036$ ). The domain of change in reported health had the largest positive effect size after 8 weeks ( $d = 0.89$  in the intervention group and  $d = 0.8$  in the control group). The

score indicating the decrease in bodily pain improved only in the control group by 15.33% ( $p = 0.004$ ,  $d = 0.59$ ). All changes in the SF-36 scores after 8 weeks with significance and effect sizes are presented in Table 2 and Figure 1, respectively.





**Figure 1.** A heatmap of effect sizes and significance plot comparing first and second visits within the intervention and control groups: (a) Health-related quality of life domains from the Medical Outcomes Study 36-Item Short-Form Health Survey, (b) Motives for physical activity from the Exercise Motivations Inventory 2, (c) The Hospital Anxiety and Depression Scale domains.

A higher value in the effect size plot (the Cohen's *d*) indicates an increase and a lower value indicates a decrease in the domain. In the effect size plot, shades of red are used for positive effect sizes, shades of blue - for negative effect sizes. The intensity of the color increases proportionally with the magnitude of the effect size. In the significance plot, the radius of the circles represents the value of statistical significance.

### 3.3. The Assessment of Motivation for Physical Activity

In the beginning, according to the scores of the EMI-2 questionnaire, in both groups, the most important motives for being physically active were health, appearance/weight, and fitness, while the least important were social engagement, enjoyment, and revitalization motives (Table 3).

**Table 3.** Changes in scores of the Exercise Motivations Inventory 2 motives from the baseline to the second measurement 8 weeks later.

Intervention group				<i>p</i> value between the groups *	Control group			
At baseline	After 8 weeks	Change	<i>p</i>		<i>p</i>	Change	At baseline	After 8 weeks
Enjoyment and revitalization motive					Enjoyment and revitalization motive			
2.97 ± 1.26	3.34 ± 1.12	0.37 ± 0.81	< 0.001	0.018	0.848	0.03 ± 0.83	2.98 ± 1.13	3.01 ± 1.20
Stress management					Stress management			
2.83 ± 1.37	3.14 ± 1.22	0.32 ± 0.98	0.002	0.138	0.743	0.04 ± 0.82	3.01 ± 1.20	3.05 ± 1.25
Revitalization					Revitalization			
3.92 ± 1.11	4.26 ± 0.89	0.34 ± 0.85	0.001	0.053	0.254	0.08 ± 0.86	3.78 ± 0.94	3.86 ± 1.03
Enjoyment					Enjoyment			
2.85 ± 1.47	3.32 ± 1.25	0.47 ± 1.11	0.001	0.007	0.864	-0.03 ± 1.13	2.80 ± 1.35	2.77 ± 1.33
Challenge					Challenge			
2.36 ± 1.49	2.75 ± 1.43	0.38 ± 0.93	0.001	0.362	0.177	0.19 ± 0.87	2.49 ± 1.41	2.68 ± 1.46
Social engagement motive					Social engagement motive			
1.85 ± 1.47	2.22 ± 1.41	0.37 ± 0.94	0.003	0.206	0.568	0.08 ± 0.94	2.16 ± 1.33	2.24 ± 1.46
Social recognition					Social recognition			
1.80 ± 1.56	2.17 ± 1.50	0.37 ± 1.06	0.004	0.887	0.300	0.19 ± 0.87	2.18 ± 1.49	2.39 ± 1.41
Affiliation					Affiliation			
1.88 ± 1.56	2.30 ± 1.45	0.41 ± 1.19	0.006	0.115	0.756	-0.01 ± 1.03	2.26 ± 1.37	2.25 ± 1.51
Competition					Competition			
1.75 ± 1.48	2.09 ± 1.44	0.35 ± 1.01	0.004	0.264	0.359	0.12 ± 0.82	2.00 ± 1.50	2.12 ± 1.61
Health motive					Health motive			

4.09 ± 0.78	4.15 ± 0.81	0.06 ± 0.73	0.177	0.878	0.421	0.39 ± 1.53	3.53 ± 1.53	3.92 ± 0.91
Health pressures			Health pressures					
3.39 ± 1.31	3.43 ± 1.30	0.04 ± 1.20	0.566	0.541	0.806	-0.05 ± 1.09	3.40 ± 1.39	3.35 ± 1.29
Ill-health avoidance			Ill-health avoidance					
4.46 ± 0.78	4.47 ± 0.83	0.01 ± 0.95	0.581	0.385	0.443	0.40 ± 1.61	3.75 ± 1.57	4.15 ± 0.86
Positive health			Positive health					
4.41 ± 0.72	4.46 ± 0.76	0.05 ± 0.81	0.470	0.306	0.667	-0.05 ± 0.78	4.26 ± 0.84	4.21 ± 0.80
Appearance / weight motive			Appearance / weight motive					
3.76 ± 1.00	3.80 ± 1.15	0.04 ± 0.82	0.222	<b>&lt; 0.001</b>	<b>0.002</b>	-0.93 ± 1.78	3.91 ± 1.05	2.98 ± 1.65
Weight management			Weight management					
4.27 ± 1.01	4.14 ± 1.15	-0.13 ± 0.88	0.564	<b>0.001</b>	<b>0.010</b>	-0.96 ± 1.92	4.23 ± 0.95	3.27 ± 1.76
Appearance			Appearance					
3.22 ± 1.30	3.39 ± 1.34	0.17 ± 1.05	0.251	0.245	0.185	-0.15 ± 0.93	3.43 ± 1.36	3.28 ± 1.20
Fitness motive			Fitness motive					
3.63 ± 1.13	3.89 ± 1.01	0.26 ± 0.94	<b>0.023</b>	0.099	0.986	-0.05 ± 0.84	3.63 ± 1.01	3.59 ± 1.07
Strength & endurance			Strength & endurance					
3.71 ± 1.22	4.05 ± 0.93	0.35 ± 0.99	<b>0.006</b>	<b>0.010</b>	0.558	-0.13 ± 0.98	3.75 ± 0.93	3.62 ± 1.06
Nimbleness			Nimbleness					
3.57 ± 1.24	3.65 ± 1.26	0.08 ± 1.10	0.435	0.969	0.539	0.07 ± 0.91	3.48 ± 1.29	3.55 ± 1.22

Data are presented as mean ± SD. *p* value in bold denotes a statistically significant difference ( $p < 0.05$ ). \* Linear multiple regression.

After 8 weeks, the most dominant motives to be physically active in both groups were health motives, especially ill-health avoidance and positive health (Table 3). In the intervention group, there was a statistically significant increase in the overall scores for the social engagement motive, the enjoyment and revitalization motive, and the fitness motive (respectively, by 20.12%, 12.41%, and 7.09%;  $p = 0.003$ ,  $p < 0.001$  and  $p = 0.023$ ;  $d = 0.4$ ,  $d = 0.5$  and  $d = 0.32$ ). The significant between-group difference was found in the overall scores for the enjoyment and revitalization motive ( $p = 0.018$ ). Only in the intervention group, statistically significant improvement was observed in the scores indicating the motives of stress management, revitalization, enjoyment, challenge, social recognition, affiliation, competition, strength & endurance (respectively, by 11.22%, 8.70%, 16.64%, 16.15%, 20.84%, 22.00%, 19.79% and 9.43%; all  $p \leq 0.006$ ). The significant between-group differences were found in the scores of enjoyment motive and strength & endurance motive (respectively,  $p = 0.007$  and  $p = 0.010$ ). The motive of revitalization had the largest positive effect in the intervention group ( $d = 0.52$ ). After 8 weeks, based on the level of scores, the least important motives for physical training in both groups remained social recognition and competition. Only in the control group the appearance/weight motive and the weight



management motive statistically significantly decreased (respectively, by 23.75% and 22.65%;  $p = 0.002$  and  $p = 0.01$ ). The between-group differences in the motives of appearance/weight and weight management were significant (respectively,  $p < 0.001$  and  $p = 0.001$ ). These motives also had the largest negative effects in the control group ( $d = -0.53$  and  $d = -0.46$ , respectively). The changes of the EMI-2 scores after 8 weeks are presented in more detail in Table 3 and Figure 1.

### 3.4. The Evaluation of the Levels of Anxiety and Depression

We evaluated the levels of anxiety and depression at baseline according to the scores of the HADS questionnaire (Table 4). In the beginning, symptoms of anxiety were present in 15.4% of the intervention group participants and 24.5% of the control group participants (Table 4). Depressive symptoms were observed in 11.5% of the intervention group participants and 1.9% of the control group participants at baseline (Table 4).

**Table 4.** The baseline scores from the Hospital Anxiety and Depression Scale.

Assessment of anxiety and depression	Intervention group (n = 84)	Control group (n = 56)	<i>p</i> value between the groups
<b>Anxiety (scores)</b>	5.21 ± 2.87	4.33 ± 3.34	0.151
<b>Depression (scores)</b>	3.40 ± 2.92	2.65 ± 2.40	0.188
<b>Anxiety</b>			
0–7 scores (%)	71 (84.6)	42 (75.5)	0.158
8–10 scores (%)	9 (10.3)	12 (20.7)	
11–14 scores (%)	4 (5.1)	1 (1.9)	
15–21 scores (%)	0	1 (1.9)	
<b>Depression</b>			
0–7 scores (%)	74 (88.5)	55 (98.1)	0.111
8–10 scores (%)	9 (10.2)	1 (1.9)	
11–14 scores (%)	1 (1.3)	0	
15–21 scores (%)	0	0	

Data are presented as mean ± SD or in absolute numbers (n) and percentage in parentheses (%). *p* value in bold denotes a statistically significant difference ( $p < 0.05$ ).

After 8 weeks in either group, there were no statistically significant changes in the scores of anxiety and depression (Table 5). All changes of anxiety and depression scores after 8 weeks are also presented with effect sizes in Figure 1. However, only in the intervention group, we observed significant reduction of depression level in 10.9% of the individuals ( $p = 0.021$ ) (Table 6). This improvement was obtained in 9 out of 10 intervention group participants with symptoms of depression at baseline.

**Table 5.** Changes of anxiety and depression scores from the Hospital Anxiety and Depression Scale between the baseline and the second measurement 8 weeks later.

Intervention group				<i>p</i> value between the groups *	Control group			
At baseline	After 8 weeks	Change	<i>p</i>		Change	At baseline	After 8 weeks	
Anxiety				0.907	Anxiety			
5.21 ± 2.87	4.83 ± 3.13	-0.39 ± 2.39	0.160		0.49	-0.15 ± 3.34	4.18 ± 3.04	
Depression				0.918	Depression			
3.40 ± 2.92	2.94 ± 2.45	-0.46 ± 1.95	0.073		0.38	-0.23 ± 2.40	2.43 ± 2.01	

Data are presented as mean ± SD. *p* value in bold denotes a statistically significant difference ( $p < 0.05$ ). \* Linear multiple regression.

**Table 6.** Changes (%) of anxiety and depression levels after 8 weeks according to the Hospital Anxiety and Depression Scale.

Sign	Intervention group (n = 84)	<i>p</i> value *	Control group (n = 56)	<i>p</i> value *
<b>Anxiety</b>				
Improved (%)	2.8		10.0	
Not changed (%)	84.9	0.109	82.5	0.796
Worsened (%)	12.3		7.5	
<b>Depression</b>				
Improved (%)	10.9		1.9	
Not changed (%)	87.7	<b>0.021</b>	98.1	1.000
Worsened (%)	1.4		0	

Data are presented as percentage in parentheses (%). *p* value in bold denotes a statistically significant difference ( $p < 0.05$ ). \* The McNemar test.

#### 4. Discussion

This study aimed to evaluate the changes in HRQOL, motivation for physical activity, and the levels of anxiety as well as depression before and after the 8-week individualized aerobic training program in subjects with MetS. This analysis demonstrated that the individualized, HR targeted, aerobic training program had a positive effect on life quality status, motivation for physical activity, and depressive symptoms.

It has been shown that some of the MetS components, including obesity, insulin resistance, and arterial hypertension, are associated with worse HRQOL<sup>39-41</sup>. Firstly, it ought to be noted

that several studies have concluded that MetS itself may be the cause of deteriorated life quality<sup>42-44</sup>. In addition, Tziallas et al. have found that subjects with MetS assigned significantly lower scores on all domains of the SF-36 questionnaire except for bodily pain in comparison with subjects without overt MetS<sup>45</sup>. Similarly, Jahangiry et al. have demonstrated that the most impaired HRQOL domains in subjects with MetS were role-physical, vitality, and mental health<sup>46</sup>. On the other hand, Vetter et al. reported that MetS itself was not associated with decreased HRQOL<sup>47</sup>. Authors suggested that depression, greater disease burden, and some of the individual components of MetS (such as obesity) may significantly affect HRQOL in this population<sup>47</sup>.

In our study, during the initial assessment of HRQOL with SF-36 questionnaire, all participants rated their health changes, general health condition, and vitality status with the lowest scores. However, after the 8-week individualized aerobic training program, the scores of physical functioning, mental health-summary, and role limitations due to emotional problems significantly improved. Some prospective studies have also found that aerobic exercise programs can improve HRQOL in cardiometabolic patients<sup>48,49</sup>. Megakli et al. have investigated 72 women with obesity and demonstrated that the 12-week aerobic and resistance exercise program improved HRQOL domains of physical functioning, vitality, bodily pain, mental health, and role-emotional<sup>48</sup>. Moreover, Myers et al. have shown that the 9-month exercise training program improved HRQOL domain of physical health-summary in sedentary patients with type 2 diabetes regardless of training modality<sup>49</sup>.

In relation to our study, some other studies have investigated subjects with MetS and demonstrated a positive effect of aerobic exercise training programs on their HRQOL<sup>19,20,27-29</sup>. Landaeta-Díaz et al. have found that the 12-week aerobic exercise training program combined with a hypocaloric Mediterranean diet had a greater effect on HRQOL than diet alone in subjects with MetS<sup>20</sup>. The aforementioned study demonstrated that, according to the SF-36 questionnaire scores, the domains of role-physical, bodily pain, and social functioning improved only after this combined intervention with aerobic exercise training program<sup>20</sup>. Another prospective study demonstrated that after the 6-month telemonitoring-supported physical activity intervention promoting aerobic exercises, subjects with MetS improved their HRQOL domains of physical functioning, general health, vitality, and mental health<sup>19</sup>. To add, Farinha et al. showed that a 15-week moderate intensity aerobic training program improved SF-36 questionnaire scores of physical functioning, role-physical, bodily pain, general health and social functioning in women with MetS<sup>29</sup>.

Although the role of motives for physical activity has already been evaluated in various studies<sup>50-52</sup>, most of these studies were conducted in terms of the general population. There are studies investigating motivation for physical activity in patients with type 2 diabetes<sup>53-55</sup>. Ferrand et al. highlighted sex differences in type 2 diabetes patients and demonstrated that females were more likely to indicate the importance of positive body image related to physical activity, whereas males were more likely to indicate the importance of health-promoting behaviors<sup>53</sup>. To add, Korkiakangas et al. showed that the motivation for physical activity in adults with high risk of type 2 diabetes was mostly related to weight management, social relationships, physical and mental well-being<sup>56</sup>. In our study participants with MetS at the beginning, however, the most important motives for being physically active were health, appearance/weight, and fitness, whereas the social engagement motive was the least important. According to Murer et al., subjects with MetS are usually motivated to improve their physical activity and to know about its positive effect<sup>57</sup>. However, we think that subjects with MetS need to be supported and advised on how to be physically active. We also think that the improvement of the objective parameters of physical fitness and cardiometabolic risk markers could serve as additional factors for higher motivation for physical activity. It was demonstrated that the increase of CRF parameter VO2 max improves mental health<sup>58</sup> and is associated with intrinsic motivation for physical activity<sup>59</sup>. The improvements in cardiometabolic risk markers and CRF parameters, including VO2 max, were actually observed after our 8-week HR targeted aerobic training program but the data will be presented in a future publication.

To the best of our knowledge, there are no studies assessing the motivation for physical activity in subjects with MetS by applying standardized questionnaires. We have found only one interview study that involved 20 patients having one or more MetS components and evaluated their experiences with physical activity prescription during regular, long-term follow-ups<sup>60</sup>. The study concluded that motivational consultation and individual adjustments increase physical activity<sup>60</sup>. Also, it was stated that the motivation for physical activity could be higher if cardiometabolic patients create their personal routines for physical activity, and experience positive effects on health<sup>60</sup>. In our study, subjects with MetS from the intervention group had to participate in a strict program with regular sessions of aerobic exercise. However, the intensity of aerobic exercise was individually tailored to each participant. Moreover, before and after the individualized aerobic training program, intervention group participants with MetS also attended motivational consultations, and we believe that this

contributed to our results in terms of motivation. We demonstrated that subjects with MetS, who participated in the supervised, HR targeted aerobic training program, improved their motivation for physical activity significantly more, compared to subjects with MetS, who only had home-based training dependent on recommendations. The improved motives for physical activity in our intervention group participants with MetS were social engagement, enjoyment and revitalization, and fitness. We think that regular, supervised aerobic exercise training sessions also help individuals to adapt to the required intensity of exercise, and it may potentially encourage their further self-training.

It is emphasized that some of the MetS components, including obesity, impaired glucose metabolism, and subclinical signs of atherosclerosis are linked to symptoms of depression or anxiety<sup>61-63</sup>. However, some studies have observed that MetS is associated with depression, but not anxiety<sup>9,10</sup>. Despite conflicting findings, it was concluded that anxiety and depression disorders are more prevalent in subjects with MetS than in the general population<sup>7</sup>. Therefore, effective strategies are needed to reduce anxiety and depression levels in subjects with MetS.

Although exercise training is an effective intervention to promote health in subjects with MetS<sup>17,64</sup>, the evidence for the exercise training effect on anxiety and depression in such population is scarce. Most of the studies, conducted in this regard, analyzed patients with type 2 diabetes and obesity, and the results are inconclusive<sup>65,66</sup>. Some studies demonstrated positive effect on depression and/or anxiety, while other studies reported no significant effect on psycho-emotional condition after exercise training programs in type 2 diabetes patients and obese individuals<sup>63,64</sup>.

There are very few studies investigating the effect of physical training on the indices of anxiety and depression in subjects with MetS<sup>19,22,27</sup>. Haufe et al. enrolled a total of 314 middle-aged subjects with MetS<sup>19</sup>. Authors have demonstrated the greater decrease of depression and anxiety severity in subjects with MetS, who participated in the 6-month telemonitoring-supported exercise training program, based on the HADS questionnaire<sup>19</sup>. Furthermore, the greatest benefit from this particular intervention was observed in individuals with MetS having mild to moderate severity of depression and anxiety at baseline<sup>19</sup>. In our study, however, there were no significant changes in the level of anxiety in subjects with MetS, who participated in the 8-week individualized aerobic training program. This result may be explained by the shorter duration of our exercise training program, compared to the program from the aforementioned study. In another recent study, after the 12-week

intervention of regular, low intensity exercise sessions and psychoeducation, women with MetS had significantly reduced de-pression and stress levels, compared to women without MetS<sup>67</sup>. Although it ought to be pointed out that there is no consensus on the optimal type, amount, duration and frequency of physical exercise in terms of influencing depression and anxiety. Aerobic exercises, either group or individual, are more frequently used to achieve this goal, with a duration of 4 to 20 weeks, a duration of 20 to 90 minutes, and a frequency of 3 to 5 times a week<sup>68</sup>.

Our study's particular contribution is the evaluation of the levels of anxiety and depression in subjects with MetS under the 8-week individualized, HR targeted, aerobic training program versus home-based training dependent on recommendations. In our study, we found that in subjects with MetS, who participated in the 8-week individualized aerobic training program, the level of depression reduced in 9 out of 10 individuals with depressive symptoms at baseline.

The present study has some potential limitations that should be acknowledged. First, because of the wide range of evaluated variables, we did not perform a separate analysis adjusting for all individual factors. Second, the overall evaluation period lasted for 8 weeks, and this study cannot evaluate the long-term impact of the individualized aerobic training program on HRQOL, motivation for physical activity, and the levels of anxiety and depression in subjects with MetS. In addition, the study cohort was very homogeneous in terms of age and clinical conditions, which limits the generalizability of our findings. Another limitation of this study is that 29 control group participants missed the second visit. Nevertheless, our prospective study pioneers in offering a complex psycho-emotional assessment of subjects with MetS before and after the individualized, HR targeted, aerobic training program. We think that the study results may be maintained with additional, regular training. The key is motivating individuals with MetS to continue with self-training in a similar mode to that in the clinic. To this end, additional telemonitoring is currently being investigated, which we hypothesize will help to maintain and hopefully improve the results obtained.

## **5. Conclusions**

Only intervention group individuals with MetS, who participated in the 8-week HR targeted aerobic training program, significantly improved their physical functioning and other HRQOL domains associated with mental health and emotional problems. In addition, the

overall scores for the social engagement motive, the enjoyment and revitalization motive, and the fitness motive to exercise increased only in the intervention group. Finally, in contrast to the control group, there was a significant reduction of depression level among intervention group participants after aerobic training. Our data foregrounds the importance of the individualized, HR targeted, aerobic training program in middle-aged subjects with MetS and its potential to improve their HRQOL, psycho-emotional state, and increase motivation for physical activity.

### **Author Contributions**

Conceptualization, A.L. and I.L.; formal analysis, R.P., I.L., J.Z.; writing—original draft preparation, J.Z. and P.N.; writing—review and editing, I.L., L.R., J.B., and A.L.; supervision, I.L., A.L.; resources and funding acquisition, A.L. All authors have read and agreed to the published version of the manuscript.

### **Funding**

The study was supported by the Gediminas Gruodis donation allocated in a public institution "Informeda" as well as by the European Union Fund as part of a project "Creation of Customized Physical Activity Effectiveness Evaluation Tool and Application Method" developed with the joint venture "InMedica".

### **Institutional Review Board Statement**

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Lithuanian Bioethics Committee (protocol code: PFAEV53, date of approval: 7 July 2017).

### **Informed Consent Statement**

Written informed consent was obtained from all participants involved in the study.

### **Data Availability Statement**

Not applicable.

### **Conflicts of Interest**

The authors declare no conflicts of interest.



## References

1. Galassi A, Reynolds K, He J. Metabolic syndrome and risk of cardiovascular disease: a meta-analysis. *Am J Med.* 2006;119(10):812-819. doi:10.1016/j.amjmed.2006.02.031
2. Gami AS, Witt BJ, Howard DE, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. *J Am Coll Cardiol.* 2007;49(4):403-414. doi:10.1016/j.jacc.2006.09.032
3. Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. *Diabetes Care.* 2005;28(7):1769-1778. doi:10.2337/diacare.28.7.1769
4. International Diabetes Federation. The IDF consensus worldwide definition of the metabolic syndrome. Last update 05/04/2017. Available from: <http://www.idf.org/metabolic-syndrome>. <http://www.idf.org/metabolic-syndrome>. <https://www.idf.org/e-library/consensus-statements/60-idfconsensus-worldwide-definition-of-the-metabolic-syndrome>. Published 2017. Accessed June 27, 2020.
5. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation.* 2002;106(25):3143-3421.
6. Ford ES, Li C, Sattar N. Metabolic syndrome and incident diabetes: current state of the evidence. *Diabetes Care.* 2008;31(9):1898-1904. doi:10.2337/dc08-0423
7. Butnorienė J, Steiblienė V, Saudargienė A, Bunevicius A. Does presence of metabolic syndrome impact anxiety and depressive disorder screening results in middle aged and elderly individuals? A population based study. *BMC Psychiatry.* 2018;18(1):5. doi:10.1186/s12888-017-1576-8
8. Teixeira PJR, Rocha FL. The prevalence of metabolic syndrome among psychiatric inpatients in Brazil. *Braz J Psychiatry.* 2007;29:330-336. doi:10.1590/S1516-44462007000400007
9. Butnorienė J, Bunevicius A, Norkus A, Bunevicius R. Depression but not anxiety is associated with metabolic syndrome in primary care based community sample. *Psychoneuroendocrinology.* 2014;40:269-276. doi:10.1016/j.psyneuen.2013.11.002
10. Skilton MR, Moulin P, Terra JL, Bonnet F. Associations between anxiety, depression, and the metabolic syndrome. *Biol Psychiatry.* 2007;62(11):1251-1257. doi:10.1016/j.biopsych.2007.01.012
11. Tang F, Wang G, Lian Y. Association between anxiety and metabolic syndrome: A systematic review and meta-analysis of epidemiological studies. *Psychoneuroendocrinology.* 2017;77:112-121. doi:10.1016/j.psyneuen.2016.11.025
12. Ortega Y, Aragonès E, Piñol JL, Basora J, Araujo A, Cabré JJ. Impact of depression and/or anxiety on the presentation of cardiovascular events in a cohort with metabolic syndrome. StreX project: Five years of follow-up. *Prim Care Diabetes.* 2018;12(2):163-171. doi:10.1016/j.pcd.2017.09.002
13. Kleefstra N, Landman GWD, Houweling ST, et al. Prediction of mortality in type 2 diabetes from health-related quality of life (ZODIAC-4). *Diabetes Care.* 2008;31(5):932-933. doi:10.2337/dc07-2072
14. Coffey JT, Brandle M, Zhou H, et al. Valuing health-related quality of life in diabetes. *Diabetes Care.* 2002;25(12):2238-2243. doi:10.2337/diacare.25.12.2238
15. Kaushal N, Langlois F, Desjardins-Crépeau L, Hagger MS, Bherer L. Investigating dose–response effects of multimodal exercise programs on health-related quality of life in older adults. *Clin Interv Aging.* 2019;14:209-217. doi:10.2147/CIA.S187534
16. Godoy-Izquierdo D, Guevara NML de, Toral MV, Galván C de T, Ballesteros AS, García JFG. Improvements in health-related quality of life, cardio-metabolic health, and fitness in postmenopausal women



- after a supervised, multicomponent, adapted exercise program in a suited health promotion intervention: a multigroup study. *Menopause*. 2017;24(8):938-946. doi:10.1097/GME.0000000000000844
17. Wewege MA, Thom JM, Rye KA, Parmenter BJ. Aerobic, resistance or combined training: A systematic review and meta-analysis of exercise to reduce cardiovascular risk in adults with metabolic syndrome. *Atherosclerosis*. 2018;274:162-171. doi:10.1016/j.atherosclerosis.2018.05.002
18. Slivovskaja I, Ryliskyte L, Serpytis P, et al. Aerobic Training Effect on Arterial Stiffness in Metabolic Syndrome. *Am J Med*. 2018;131(2):148-155. doi:10.1016/j.amjmed.2017.07.038
19. Haufe S, Kahl KG, Kerling A, et al. Employers With Metabolic Syndrome and Increased Depression/Anxiety Severity Profit Most From Structured Exercise Intervention for Work Ability and Quality of Life. *Front Psychiatry*. 2020;11:562. doi:10.3389/fpsy.2020.00562
20. Landaeta-Díaz L, Fernández J, Silva-Grigoletto MD, et al. Mediterranean diet, moderate-to-high intensity training, and health-related quality of life in adults with metabolic syndrome. *Eur J Prev Cardiol*. 2013;20(4):555-564. doi:10.1177/2047487312445000
21. Oh SH, Son SH, Kang SH, Kim DK, Seo KM, Lee SY. Relationship Between Types of Exercise and Quality of Life in a Korean Metabolic Syndrome Population: A Cross-Sectional Study. *Metab Syndr Relat Disord*. 2017;15(4):199-205. doi:10.1089/met.2016.0151
22. Chiang LC, Chiang SL, Tzeng WC, Lee MS, Hung YJ, Lin CH. Active Physical Activity Patterns Are Associated With Improved Quality of Life and Depression Status in Taiwanese Women With Metabolic Syndrome. *J Cardiovasc Nurs*. 2019;34(6):491-502. doi:10.1097/JCN.0000000000000602
23. Molanorouzi K, Khoo S, Morris T. Motives for adult participation in physical activity: type of activity, age, and gender. *BMC Public Health*. 2015;15:66. doi:10.1186/s12889-015-1429-7
24. Mezzani A, Hamm LF, Jones AM, et al. Aerobic exercise intensity assessment and prescription in cardiac rehabilitation: a joint position statement of the European Association for Cardiovascular Prevention and Rehabilitation, the American Association of Cardiovascular and Pulmonary Rehabilitation and the Canadian Association of Cardiac Rehabilitation. *Eur J Prev Cardiol*. 2013;20(3):442-467. doi:10.1177/2047487312460484
25. Mezzani A, Agostoni P, Cohen-Solal A, et al. Standards for the use of cardiopulmonary exercise testing for the functional evaluation of cardiac patients: a report from the Exercise Physiology Section of the European Association for Cardiovascular Prevention and Rehabilitation. *Eur J Cardiovasc Prev Rehabil*. 2009;16(3):249-267. doi:10.1097/HJR.0b013e32832914c8
26. Fletcher GF, Ades PA, Kligfield P, et al. Exercise standards for testing and training: a scientific statement from the American Heart Association. *Circulation*. 2013;128(8):873-934. doi:10.1161/CIR.0b013e31829b5b44
27. Reljic D, Frenk F, Herrmann HJ, Neurath MF, Zopf Y. Low-volume high-intensity interval training improves cardiometabolic health, work ability and well-being in severely obese individuals: a randomized-controlled trial sub-study. *Journal of Translational Medicine*. 2020;18(1):419. doi:10.1186/s12967-020-02592-6
28. Reljic D, Frenk F, Herrmann HJ, Neurath MF, Zopf Y. Effects of very low volume high intensity versus moderate intensity interval training in obese metabolic syndrome patients: a randomized controlled study. *Sci Rep*. 2021;11(1):2836. doi:10.1038/s41598-021-82372-4
29. Farinha JB, Dos Santos DL, Bresciani G, et al. Weight loss is not mandatory for exercise-induced effects on health indices in females with metabolic syndrome. *Biol Sport*. 2015;32(2):109-114. doi:10.5604/20831862.1134313
30. Laucevičius A, Rinkūnienė E, Skorniakov V, et al. High-risk profile in a region with extremely elevated cardiovascular mortality. *Hellenic J Cardiol*. 2013;54(6):441-447.
31. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of

- Cardiology (ESC) and the European Society of Hypertension (ESH). *European Heart Journal*. 2018;39(33):3021-3104. doi:10.1093/eurheartj/ehy339
32. Binder RK, Wonisch M, Corra U, et al. Methodological approach to the first and second lactate threshold in incremental cardiopulmonary exercise testing. *European Journal of Cardiovascular Prevention & Rehabilitation*. 2008;15(6):726-734. doi:10.1097/HJR.0b013e328304fed4
  33. Stern AF. The Hospital Anxiety and Depression Scale. *Occupational Medicine*. 2014;64(5):393-394. doi:10.1093/occmed/kqu024
  34. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*. 1992;30(6):473-483.
  35. Markland D, Ingledew DK. The measurement of exercise motives: Factorial validity and invariance across gender of a revised Exercise Motivations Inventory. *British Journal of Health Psychology*. 1997;2(4):361-376. doi:10.1111/j.2044-8287.1997.tb00549.x
  36. Williams N. The Borg Rating of Perceived Exertion (RPE) scale. *Occupational Medicine*. 2017;67(5):404-405. doi:10.1093/occmed/kqx063
  37. Wei T, Simko V. *R Package "Corrplot": Visualization of a Correlation Matrix (Version 0.84)*; 2017. <https://github.com/taiyun/corrplot>. Accessed February 13, 2021.
  38. Haarman BCMB, Riemersma-Van der Lek RF, Nolen WA, Mendes R, Drexhage HA, Burger H. Feature-expression heat maps--a new visual method to explore complex associations between two variable sets. *J Biomed Inform*. 2015;53:156-161. doi:10.1016/j.jbi.2014.10.003
  39. Schlotz W, Ambery P, Syddall HE, et al. Specific associations of insulin resistance with impaired health-related quality of life in the Hertfordshire Cohort Study. *Qual Life Res*. 2007;16(3):429-436. doi:10.1007/s11136-006-9129-5
  40. Søltøft F, Hammer M, Kragh N. The association of body mass index and health-related quality of life in the general population: data from the 2003 Health Survey of England. *Qual Life Res*. 2009;18(10):1293-1299. doi:10.1007/s11136-009-9541-8
  41. Zygmontowicz M, Owczarek A, Elibol A, Chudek J. Comorbidities and the quality of life in hypertensive patients. *Pol Arch Med Wewn*. 2012;122(7-8):333-340.
  42. Botosaneanu A, Ambrosius WT, Beavers DP, et al. Prevalence of metabolic syndrome and its association with physical capacity, disability, and self-rated health in Lifestyle Interventions and Independence for Elders Study participants. *J Am Geriatr Soc*. 2015;63(2):222-232. doi:10.1111/jgs.13205
  43. Frisman GH, Kristenson M. Psychosocial status and health related quality of life in relation to the metabolic syndrome in a Swedish middle-aged population. *Eur J Cardiovasc Nurs*. 2009;8(3):207-215. doi:10.1016/j.ejcnurse.2009.01.004
  44. Miettola J, Niskanen LK, Viinamäki H, Sintonen H, Kumpusalo E. Metabolic syndrome is associated with impaired health-related quality of life: Lapinlahti 2005 study. *Qual Life Res*. 2008;17(8):1055-1062. doi:10.1007/s11136-008-9386-6
  45. Tziallas D, Kastanioti C, Kostapanos MS, Skapinakis P, Elisaf MS, Mavreas V. The impact of the metabolic syndrome on health-related quality of life: a cross-sectional study in Greece. *Eur J Cardiovasc Nurs*. 2012;11(3):297-303. doi:10.1016/j.ejcnurse.2011.02.004
  46. Jahangiry L, Shojaezadeh D, Montazeri A, Najafi M, Mohammad K. Health-related Quality of Life Among People Participating in a Metabolic Syndrome E-screening Program: A Web-based Study. *Int J Prev Med*. 2016;7:27. doi:10.4103/2008-7802.174893
  47. Vetter ML, Wadden TA, Lavenberg J, et al. Relation of health-related quality of life to metabolic syndrome, obesity, depression and comorbid illnesses. *Int J Obes (Lond)*. 2011;35(8):1087-1094. doi:10.1038/ijo.2010.230

48. Megakli T, Vlachopoulos SP, Theodorakis Y. Effects of an Aerobic and Resistance Exercise Intervention on Health-Related Quality of Life in Women with Obesity. *Journal of Applied Biobehavioral Research*. 2016;21(2):82-106. doi:10.1111/jabr.12047
49. Myers VH, McVay MA, Brashear MM, et al. Exercise training and quality of life in individuals with type 2 diabetes: a randomized controlled trial. *Diabetes Care*. 2013;36(7):1884-1890. doi:10.2337/dc12-1153
50. Ingledew DK, Markland D, Strömmer ST. Elucidating the Roles of Motives and Gains in Exercise Participation. *Sport, Exercise, and Performance Psychology*. 2014;3(2):116-131. doi:https://doi.org/10.1037/spy0000004
51. Ruffault A, Bernier M, Juge N, Fournier JF. Mindfulness May Moderate the Relationship Between Intrinsic Motivation and Physical Activity: A Cross-Sectional Study. *Mindfulness*. 2016;7(2). doi:10.1007/s12671-015-0467-7
52. Teixeira PJ, Carraça EV, Markland D, Silva MN, Ryan RM. Exercise, physical activity, and self-determination theory: a systematic review. *Int J Behav Nutr Phys Act*. 2012;9:78. doi:10.1186/1479-5868-9-78
53. Ferrand C, Perrin C, Nasarre S. Motives for regular physical activity in women and men: a qualitative study in French adults with type 2 diabetes, belonging to a patients' association. *Health & Social Care in the Community*. 2008;16(5):511-520. doi:10.1111/j.1365-2524.2008.00773.x
54. Miquelon P, Castonguay A. Motives for Participation in Physical Activity and Observance of Physical Activity Recommendations among Adults with Type 2 Diabetes. *Can J Diabetes*. 2016;40(5):399-405. doi:10.1016/j.jcjd.2016.02.009
55. Sebire SJ, Toumpakari Z, Turner KM, et al. "I've made this my lifestyle now": a prospective qualitative study of motivation for lifestyle change among people with newly diagnosed type two diabetes mellitus. *BMC Public Health*. 2018;18:204. doi:10.1186/s12889-018-5114-5
56. Korkiakangas E, Taanila AM, Keinänen-Kiukaanniemi S. Motivation to physical activity among adults with high risk of type 2 diabetes who participated in the Oulu substudy of the Finnish Diabetes Prevention Study. *Health & Social Care in the Community*. 2011;19(1):15-22. doi:10.1111/j.1365-2524.2010.00942.x
57. Murer M, Schmied C, Battegay E, Keller DI. Physical activity behaviour in patients with metabolic syndrome. *Swiss Med Wkly*. 2012;142:w13691. doi:10.4414/smw.2012.13691
58. Siqueira CC, Valiengo LL, Carvalho AF, et al. Antidepressant Efficacy of Adjunctive Aerobic Activity and Associated Biomarkers in Major Depression: A 4-Week, Randomized, Single-Blind, Controlled Clinical Trial. *PLoS One*. 2016;11(5):e0154195. doi:10.1371/journal.pone.0154195
59. Thøgersen-Ntoumani C, Shepherd SO, Ntoumanis N, Wagenmakers AJM, Shaw CS. Intrinsic motivation in two exercise interventions: Associations with fitness and body composition. *Health Psychol*. 2016;35(2):195-198. doi:10.1037/hea0000260
60. Joelsson M, Lundqvist S, Larsson MEH. Tailored physical activity on prescription with follow-ups improved motivation and physical activity levels. A qualitative study of a 5-year Swedish primary care intervention. *Scandinavian Journal of Primary Health Care*. 2020;38(4):399-410. doi:10.1080/02813432.2020.1842965
61. Corica F, Corsonello A, Apolone G, et al. Metabolic syndrome, psychological status and quality of life in obesity: the QUOVADIS Study. *Int J Obes (Lond)*. 2008;32(1):185-191. doi:10.1038/sj.ijo.0803687
62. Hernandez R, Allen NB, Liu K, et al. Association of depressive symptoms, trait anxiety, and perceived stress with subclinical atherosclerosis: results from the Chicago Healthy Aging Study (CHAS). *Prev Med*. 2014;61:54-60. doi:10.1016/j.ypmed.2013.12.032
63. Timonen M, Laakso M, Jokelainen J, Rajala U, Meyer-Rochow VB, Keinänen-Kiukaanniemi S. Insulin resistance and depression: cross sectional study. *BMJ*. 2005;330(7481):17-18. doi:10.1136/bmj.38313.513310.F71

64. Myers J, Kokkinos P, Nyelin E. Physical Activity, Cardiorespiratory Fitness, and the Metabolic Syndrome. *Nutrients*. 2019;11(7):1652. doi:10.3390/nu11071652
65. van der Heijden MMP, van Dooren FEP, Pop VJM, Pouwer F. Effects of exercise training on quality of life, symptoms of depression, symptoms of anxiety and emotional well-being in type 2 diabetes mellitus: a systematic review. *Diabetologia*. 2013;56(6):1210-1225. doi:10.1007/s00125-013-2871-7
66. Carraça EV, Encantado J, Battista F, et al. Effect of exercise training on psychological outcomes in adults with overweight or obesity: A systematic review and meta-analysis. *Obesity Reviews*. 2021;22(S4):e13261. doi:10.1111/obr.13261
67. Morga P, Cieślik B, Sekułowicz M, Bujnowska-Fedak M, Drower I, Szczepańska-Gieracha J. Low-Intensity Exercise as a Modifier of Depressive Symptoms and Self-Perceived Stress Level in Women with Metabolic Syndrome. *Journal of Sports Science and Medicine*. 2021;20(2):222-228.
68. Wegner M, Helmich I, Machado S, Nardi AE, Arias-Carrion O, Budde H. Effects of exercise on anxiety and depression disorders: review of meta- analyses and neurobiological mechanisms. *CNS Neurol Disord Drug Targets*. 2014;13(6):1002-14. doi: 10.2174/1871527313666140612102841.