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Impact of Aerobic Training on Cardiometabolic Markers and Menopausal Symptoms: A Stratified Analysis by Multimorbidity

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Highlights

Public health relevance—How does this work relate to a public health issue?

- Postmenopausal women are frequently affected by cardiometabolic multimorbidity, a condition associated with increased cardiovascular risk, adverse body composition, and reduced quality of life.
- Effective non-pharmacological strategies are needed to improve health outcomes and support healthy aging in this growing population.

Public health significance—Why is this work of significance to public health?

- A 12-week aerobic training program improved climacteric symptoms and body composition regardless of cardiometabolic disease burden.
- Women with cardiometabolic multimorbidity showed greater improvements in cardiometabolic markers, particularly triglycerides and VLDL cholesterol.

Public health implications—What are the key implications or messages for practitioners, policy makers and/or researchers in public health?

- Aerobic exercise should be considered a key component of health promotion strategies for postmenopausal women with cardiometabolic conditions.
- Community- and healthcare-based exercise programs may provide substantial benefits for women living with cardiometabolic multimorbidity.

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Abstract

Cardiometabolic multimorbidity is highly prevalent among postmenopausal women and is associated with adverse metabolic outcomes and a greater burden of climacteric symptoms. This secondary analysis of a quasi-experimental controlled clinical trial investigated the effects of a 12-week aerobic training program on climacteric symptoms, menopause-related quality of life, body composition, and cardiometabolic biomarkers in postmenopausal

women with and without cardiometabolic multimorbidity. Forty-one postmenopausal women (50–70 years) were allocated to a single-cardiometabolic-condition group (SINGLE, n = 18) or a multimorbidity group (MULTI, n = 23) and completed supervised walking/jogging aerobic exercise three times per week at 65–75% of heart rate reserve. Climacteric symptoms, quality of life, anthropometric measures, body composition, and biochemical markers were assessed before and after the intervention. Generalized Estimating Equations (GEEs) with Bonferroni post hoc adjustment were used to compare group, time and group*time interactions with alpha of 5%. Significant group-by-time interactions were observed for the Menopause Rating Scale total score and psychological symptoms, as well as for the Cervantes Scale total score, indicating greater improvements among women with multimorbidity. The MULTI group demonstrated significant reductions in overall menopausal symptoms, psychological symptoms, and menopause-related quality of life scores following training. Body weight, triglycerides, and very-low-density lipoprotein cholesterol also decreased significantly only in the MULTI group, whereas several body composition parameters improved over time regardless of cardiometabolic burden. These findings indicate that aerobic training may be associated with improvements in menopausal symptoms, quality of life, body composition, and selected cardiometabolic markers in postmenopausal women, with some outcomes showing greater changes among women with cardiometabolic multimorbidity.

Keywords: postmenopause; multimorbidity; exercise training; body composition; cardiometabolic risk factors

1. Introduction

The climacteric is the period that marks the transition from the reproductive to the non-reproductive phase in women and is characterized by endocrine changes associated with the natural decline in ovarian estrogen production [1]. This phase begins with variations in the menstrual cycle, and, as estrogen levels progressively decline, longer periods of amenorrhea occur until the complete absence of menstrual bleeding, which characterizes menopause [2].

Climacteric manifestations can range from asymptomatic to severe and are generally classified into three main groups: vasomotor, psychological, and urogenital symptoms [3,4]. Vasomotor symptoms, such as hot flashes, palpitations, and dyspnea, are among the most commonly reported and are associated with alterations in autonomic regulation and thermoregulation mechanisms [5,6]. Psychological symptoms include nervousness, irritability, fatigue, difficulty concentrating, and depressed mood [7–9]. Urogenital symptoms involve changes in the genital tract, such as vaginal dryness, recurrent infections, urinary incontinence, and sexual dysfunctions, including dyspareunia and reduced sexual desire [10–12]. These symptoms may directly affect women's quality of life, highlighting the need for appropriate management strategies [10,13].

The reduction in estrogen production after menopause is also associated with an increased risk of cardiovascular diseases, as this hormone plays an important role in endothelial function, vascular tone, and cardiac function [2]. In this context, the prevalence of arterial hypertension in postmenopausal women is higher compared with women in the premenopausal stage [14,15]. Additionally, a higher incidence of dyslipidemia has been observed in this population [16]. Other metabolic alterations, such as increased abdominal obesity and insulin resistance, are also frequently observed in postmenopausal women [17,18].

The co-occurrence of two or more chronic medical conditions in the same individual, including both physical and mental health conditions, is defined as multimorbidity [19,20]. With the increase in life expectancy and the global promotion of healthy aging proposed by the World Health Organization (WHO), greater attention has been directed toward non-communicable diseases (NCDs) and their outcomes [19]. NCDs are responsible for approximately 68% of deaths worldwide, and about half of these individuals are affected by multimorbidity, which worsens health status and increases the burden on healthcare systems [19].

Multimorbidity imposes a severe, multidimensional burden on both patients and healthcare systems. Clinically, it is associated with increased premature mortality, prolonged hospitalizations, and a heightened risk of functional decline—estimated at 50% per additional chronic condition [21–23]. This cumulative morbidity significantly deteriorates both the physical and mental domains of quality of life, disproportionately impacting women, individuals with excess weight, and socioeconomically vulnerable populations [24,25]. Beyond these clinical repercussions, multimorbidity drives substantial systemic healthcare costs while simultaneously overwhelming patients and caregivers with out-of-pocket expenses, work disability, and complex treatment adherence [21,26–29].

In this context, physical exercise has been recognized as an effective non-pharmacological strategy for both the prevention and management of chronic diseases and multimorbidity, as well as for reducing climacteric symptoms and improving quality of life [30–32]. A systematic review and meta-analysis [33] demonstrated that exercise is safe, improves physical function, and reduces symptoms of anxiety and depression in individuals with multimorbidity. However, the available intervention studies have predominantly included heterogeneous populations with different combinations of chronic diseases, limiting the extrapolation of these findings to postmenopausal women with cardiometabolic multimorbidity. Moreover, although exercise interventions have demonstrated benefits for climacteric symptoms and cardiometabolic health in postmenopausal women, whether the magnitude of these responses differs according to cardiometabolic disease burden remains unclear.

Women with cardiometabolic multimorbidity may also have a greater potential for exercise-induced adaptations because of their baseline metabolic and cardiovascular risks and symptom severity [29,31]. Aerobic exercise can induce adaptations involving body composition, glucose and lipid metabolism, endothelial function, autonomic regulation, and inflammatory pathways, several of which are commonly impaired in individuals with cardiometabolic diseases [29–32]. Therefore, women with a greater burden of these alterations may exhibit a larger magnitude of change in response to exercise, although evidence specifically addressing this hypothesis in postmenopausal women remains limited.

Given the critical need for evidence-based interventions in complex clinical populations, this study aimed to investigate the effects of a 12-week aerobic training program on climacteric symptoms, quality of life, and cardiometabolic profiles in postmenopausal women, with particular emphasis on whether responses differed according to cardiometabolic disease burden by comparing women with a single cardiometabolic condition and those with multimorbidity. This stratified approach addresses the limited evidence regarding whether multimorbidity influences the magnitude of adaptation to aerobic exercise in postmenopausal women. We hypothesized that while aerobic exercise would yield broad benefits across both groups, women with multimorbidity would demonstrate a more pronounced magnitude of improvement, driven by their higher baseline symptom burden and greater metabolic risk.

2. Materials and Methods

2.1. Participants

This study reports a secondary analysis of a previously conducted quasi-experimental controlled clinical trial designed to investigate the effects of a 12-week aerobic exercise program in postmenopausal women. The present manuscript focuses on outcomes that have not been reported previously, including climacteric symptoms, body composition, and cardiometabolic biomarkers. The outcomes and the stratification of participants according to cardiometabolic multimorbidity status examined in the present secondary analysis were pre-specified as part of the original study. However, these outcomes were reported separately from the previously published outcomes to allow a more focused and comprehensive analysis and interpretation. Therefore, the present analyses were not conducted post hoc based on the findings of the previous publication.

Community-dwelling postmenopausal women aged 50–70 years were invited to participate through advertisements on television, radio, and printed posters between August 2019 and March 2020. Eligibility required at least 12 consecutive months of amenorrhea, the ability to safely perform aerobic exercise, absence of smoking, and no hormone replacement therapy during the study. Women with physical limitations or cardiovascular conditions that contraindicated exercise participation were not eligible.

Participants were excluded if they failed to complete the prescribed exercise program, did not receive medical clearance following maximal exercise testing, or initiated another structured exercise program during the intervention period.

The study protocol received approval from the local ethics committee of the Federal University of Uberlândia on 21 July 2019 (CAAE: 12453719.1.0000.5152). The trial was retrospectively registered at ClinicalTrials.gov (NCT05075902). The present study represents a secondary analysis of a previously conducted clinical trial and addresses outcomes that have not been reported previously. While the primary hemodynamic outcomes of this specific article (ambulatory blood pressure, blood pressure variability, and arterial stiffness) [34] have been previously published, the present manuscript focuses on entirely unreleased data regarding climacteric symptoms, body composition, and cardiometabolic markers. All volunteers signed an informed consent statement before the beginning of the study. This study was conducted in accordance with the principles outlined in the Declaration of Helsinki (1975, revised in 2013).

Initially, 607 women expressed interest in participating. After screening, 512 did not meet the eligibility criteria. Forty-four eligible women underwent baseline assessments and were classified according to the presence of cardiometabolic diseases into two groups: SINGLE (one cardiometabolic condition) and MULTI (two or more cardiometabolic conditions). The cardiometabolic conditions considered were obesity, diabetes mellitus, hypertension and dyslipidemia. These conditions were selected because they represent major, interrelated cardiometabolic disorders that frequently coexist and share common metabolic and vascular pathways, including insulin resistance, adiposity, dysregulated lipid metabolism, and elevated blood pressure (BP). Their clustering is commonly used to characterize cardiometabolic multimorbidity and is associated with an increased risk of cardiovascular disease and adverse health outcomes [23,28,29].

The specific cardiometabolic conditions considered in this study include obesity, defined as BMI greater than 29.9 kg/m^2; diabetes mellitus, diagnosed by glycemia above 126 mg/dL and/or glycated hemoglobin (HbA1c) $\geq$ 6.5%; hypertension or the use of antihypertensive drugs, characterized by resting systolic blood pressure (SBP) above 139 mmHg and diastolic blood pressure (DBP) above 89 mmHg; and dyslipidemia, defined as low-density lipoprotein (LDL) $\geq$ 160 mg/dL and/or triglycerides (TG) $\geq$ 150 mg/dL

and/or total cholesterol ≥ 190 mg/dL. In addition, a history of stroke, cerebrovascular disease, or other heart or kidney diseases was also considered.

Participant flow throughout the study is presented in Figure 1. Following classification according to cardiometabolic multimorbidity status, one participant from the SINGLE group did not start the exercise intervention after relocating, whereas two participants from the MULTI group did not start the intervention because one did not receive medical clearance and one declined to participate. Consequently, 41 participants were included in the intention-to-treat analyses (SINGLE: n = 18; MULTI: n = 23). Participants were instructed to maintain their usual dietary habits throughout the intervention; however, dietary intake was not systematically monitored or controlled.

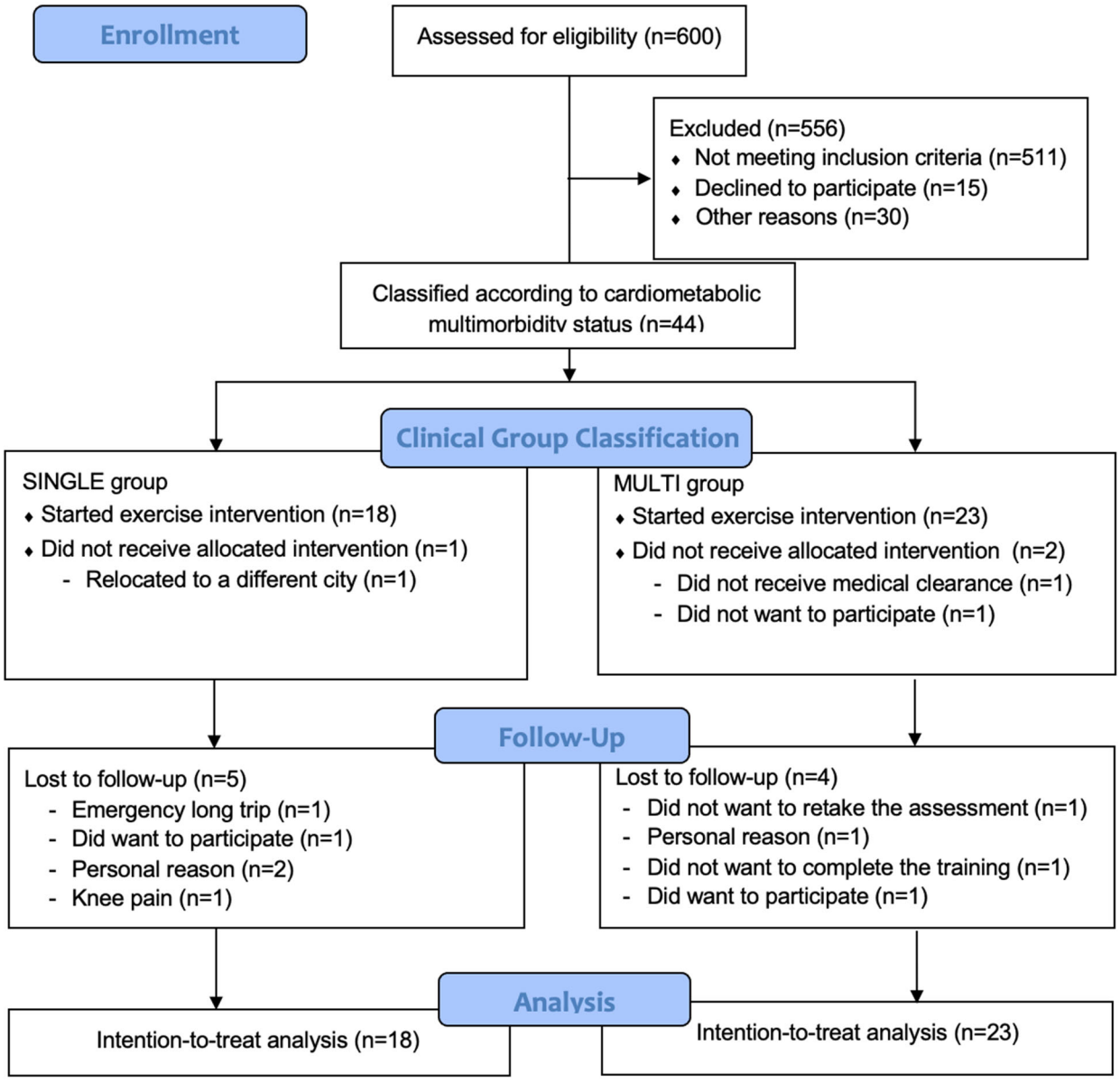


Figure 1. Flowchart.

2.2. Exercise Program

To classify the initial physical activity levels of participants, the International Physical Activity Questionnaire (IPAQ, short version), validated in Portuguese for the Brazilian population, was used [35]. For analysis purposes, classifications were grouped as follows: sedentary + irregularly active, and active + very active.

Participants completed a 12-week supervised aerobic walking/jogging program on an outdoor running track, with three sessions performed on alternate days each week. Exercise intensity was prescribed at 65–75% of heart rate reserve and was monitored throughout each session using heart rate monitors and ratings of perceived exertion (RPE). During the first four weeks, sessions lasted 40 min, whereas from week 5 onward, session duration was increased to 50 min by extending the main aerobic phase, as previously described [34]. Exercise adherence was assessed based on session attendance, calculated as the percentage of completed sessions relative to the total number of scheduled sessions. Compliance with the prescribed exercise intensity was monitored throughout each session using heart rate and RPE.

Before the intervention, all participants underwent a maximal cardiopulmonary exercise test on a treadmill using an adapted Bruce protocol [36], as described in a previous study [34]. Anthropometric measurements were obtained in a private room using a fixed stadiometer (Sanny®, American Medical, São Bernardo do Campo, Brazil) and a non-elastic tape measure (Filizola®, Indústrias Filizola S.A., São Paulo, Brazil). Body composition was assessed after an overnight fast by bioelectrical impedance analysis (InBody® 230, Cheonan-si, Republic of Korea).

2.3. Assessment of Climacteric Symptoms

Climacteric symptoms were evaluated using two validated self-administered questionnaires: the Cervantes Scale (CER) [37] and the Menopause Rating Scale (MRS) [38]. The CER is composed of 31 items organized into four domains (menopause and health, sexuality, couple relationship, and psychological well-being). Each item is scored on a six-point Likert scale (0–5), with reverse scoring applied to positively worded items. Total scores range from 0 to 155, with lower scores indicating better menopause-related quality of life [37].

The MRS consists of 11 items grouped into three domains: somatovegetative (4 items), psychological (4 items), and urogenital symptoms (3 items). Each symptom is rated on a five-point scale according to its severity, generating a total score ranging from 0 to 55. Higher scores indicate greater severity of menopausal symptoms and allow classification of symptom burden as absent or minimal, mild, moderate, or severe [39].

2.4. Lipid and Glycemic Profiles

Fasting blood samples were collected 72 h after the last exercise session to avoid the acute effects of exercise. Plasma concentrations of total cholesterol, TG, high-density lipoprotein (HDL), LDL, glucose, and HbA1c were determined using an automated analyzer (Cobas Mira, Roche Instruments Inc., Bellport, NY, USA) with commercial reagents (Labtest, Minas Gerais, Brazil). Very-low-density lipoprotein (VLDL) was estimated using the Friedewald equation.

2.5. Statistical Analysis

Sample size was estimated using G*Power 3.1 software (Universität Düsseldorf, Germany) based on the expected change in body weight after aerobic training in individuals with cardiometabolic multimorbidity (effect size f = 0.35) [40]. Calculations considered a significance level of 5%, statistical power of 95%, a repeated-measures correlation of 0.5, and a non-sphericity correction of 1.

Continuous variables are presented as mean ± standard deviation. Data normality was assessed using the Shapiro–Wilk test. Baseline differences between groups were evaluated using independent *t*-tests or Mann–Whitney U tests, according to data distribution, whereas categorical variables were compared using the chi-square test.

Intervention effects were analyzed using Generalized Estimating Equations (GEEs), including the factors group, time, and their interaction, with Bonferroni adjustment for multiple comparisons. Analyses followed the intention-to-treat principle, with missing data handled by the last-observation-carried-forward approach. The most appropriate GEE model was selected according to the lowest Quasi-likelihood under the Independence Model Criterion (QIC). Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA), adopting a significance level of $p < 0.05$.

Effect sizes were estimated using Hedges' g. For within-group comparisons, effect sizes were calculated to quantify the magnitude of pre-to-post-intervention changes in each group. The standardized mean change was based on individual change scores, defined as the post-intervention value minus the pre-intervention value, and corrected for small-sample bias using Hedges' adjustment. For the group × time interaction, the effect size was obtained from the standardized difference between the mean change scores of the MULTI and SINGLE groups, using the pooled standard deviation of the change scores as the standardizing factor and applying the corresponding small-sample correction. Effect sizes were reported with their original direction, with negative values indicating a reduction in the outcome from pre- to post-intervention.

3. Results

Exercise adherence was high, with attendance rates exceeding 90% in both groups. Participants were able to perform the exercise sessions within the prescribed intensity range throughout the intervention. No adverse events related to the exercise intervention were reported. The main baseline characteristics of the study participants are presented in Table 1. A comprehensive description of the study, including additional baseline variables, has been previously published by Costa et al. [34], as the present study represents a secondary analysis of the same clinical trial. Participants in the MULTI group were older and had a higher BMI, resting glucose and systolic blood pressure than those in the SINGLE group.

Table 1. Baseline characteristics relevant to the present secondary analysis. The complete baseline characterization of this cohort has been previously reported by Costa et al. [34].

	SINGLE (n = 18) (Mean ± SD)	**MULTI (n = 23) (Mean ± SD)**
Age (years)	56 ± 4	60 ± 4 *
Time After Menopause (years)	8 ± 5	13 ± 6 *
BMI (Body Mass Index) (kg/m^2)	27.4 ± 3.0	31.0 ± 4.3 *
Resting Glucose (mg/dL)	89.9 ± 12.7	112.8 ± 43.6 *
Total Cholesterol (mg/dL)	172.5 ± 32.6	180.0 ± 25.4
Resting Systolic Blood pressure (mmHg)	125 ± 3	136 ± 3 *
Resting Diastolic Blood pressure (mmHg)	80 ± 2	86 ± 2
FSH (mIU/mL)	92.3 ± 23.7	73.8 ± 32.8
Estradiol (pg/mL)	17.1 ± 6.3	17.7 ± 8.2

SINGLE: one cardiometabolic condition; MULTI: two or more cardiometabolic conditions; BMI: body mass index; FSH: Follicle-Stimulating Hormone. * $p < 0.05$.

Table 2 presents the results of the CER before and after the 12-week aerobic training intervention. A significant group-by-time interaction was observed for the total score ($p < 0.01$; interaction Hedges' g −0.100) and the psychological domain ($p < 0.01$; interaction Hedges' g −0.242). For the total score, post hoc analysis revealed a significant reduction in the MULTI group after the intervention (57.5 ± 4.0 vs. 44.6 ± 2.5; mean difference = −12.9, 95% CI: −24.2 to −1.7, $p < 0.05$), whereas no significant change ($p > 0.05$) was observed in the SINGLE group. Although a significant group-by-time interaction was also identified for the psychological domain, post hoc comparisons did not reveal significant within-group

differences between pre- and post-intervention assessments in either the SINGLE or MULTI groups. No significant group-by-time interactions were found for the couple relationship ($p = 0.52$; interaction Hedges' g −0.516), sexuality ($p = 0.25$; interaction Hedges' g −0.073), or menopause and health domains ($p = 0.17$; interaction Hedges' g −0.208). Furthermore, no significant main effects of time or group were observed for these domains (all $p > 0.05$).

Table 2. Scores on the Cervantes Scale obtained before and after 12 weeks of aerobic training in the two groups, separated by domains of climacteric symptoms. Data presented as mean and standard deviation.

Domains	Pre (Mean ± SD)	Post (Mean ± SD)	CI 95%	Effect Size	Time *p*	Group *p*	Group × Time *p*
Total							
SINGLE	50.1 ± 4.6	53.5 ± 3.9	3.4 (−5.7 to 12.5)	−0.283	0.84	0.87	<0.01
MULTI	57.5 ± 4.0	44.6 ± 2.5 *	−12.9 (−24.2 to −1.7)	−0.236			
Psychological							
SINGLE	11.5 ± 2.0	14.8 ± 2.0	3.3 (−0.4 to 7.0)	−0.104	0.26	0.86	<0.01
MULTI	12.6 ± 2.0	8.8 ± 1.3	−3.7 (−8.5 to 1.0)	−0.246			
Couple relationship							
SINGLE	4.2 ± 1.1	3.8 ± 0.6	−0.4 (−3.0 to 2.1)	−0.021	0.19	0.23	0.52
MULTI	5.9 ± 0.9	4.6 ± 0.8	−1.3 (−3.5 to 1.0)	−0.454			
Sexuality							
SINGLE	9.2 ± 1.1	9.5 ± 1.1	0.3 (−3.1 to 3.7)	−0.123	0.44	0.17	0.25
MULTI	11.8 ± 1.0	10.2 ± 1.0	−1.6 (−4.5 to 1.3)	−0.193			
Menopause and health							
SINGLE	25.2 ± 2.7	25.4 ± 1.8	0.3 (−4.8 to 5.3)	−0.418	0.23	0.99	0.17
MULTI	27.3 ± 1.8	23.3 ± 2.0	−3.9 (−10.1 to 2.3)	−0.062			

SINGLE: one cardiometabolic condition; MULTI: two or more cardiometabolic conditions. * $p < 0.05$ compared with pre-intervention. Effect size represents within-group Hedges' g for the pre-to-post change.

Table 3 presents the results of the MRS before and after the 12-week aerobic training intervention. Significant group-by-time interactions were observed for the total score ($p = 0.03$; interaction Hedges' g −0.254) and the psychological domain ($p = 0.04$; interaction Hedges' g −0.257). Post hoc analyses revealed that participants in the MULTI group showed a significant reduction in the total MRS score following the intervention (18.4 ± 1.5 vs. 12.7 ± 1.0, $p < 0.05$), whereas no significant change ($p > 0.05$) was observed in the SINGLE group. Similarly, a significant reduction in the psychological domain score was identified in the MULTI group (7.8 ± 0.8 vs. 5.0 ± 0.5, $p < 0.05$), while no significant change occurred in the SINGLE group. For the somatovegetative domain, a significant main effect of time was detected ($p = 0.01$), indicating an overall reduction in symptom scores from pre- to post-intervention regardless of group allocation. However, neither a group effect ($p = 0.91$) nor a group-by-time interaction ($p = 0.59$; interaction Hedges' g −0.121) was observed. No significant main effects or interactions were found for the urogenital domain (all $p > 0.05$; interaction Hedges' g −0.003).

Table 4 presents the anthropometric and body composition variables before and after the 12-week aerobic training intervention. A significant group-by-time interaction was observed only for body weight ($p = 0.025$). Post hoc analysis revealed a significant, but modest, reduction in body weight in the MULTI group (77.94 ± 10.85 vs. 77.2 ± 10.58 kg), whereas no significant change was observed in the SINGLE group (69.95 ± 9.26 vs. 69.97 ± 9.43 kg).

Table 3. Scores on the Menopause Rating Scale obtained before and after 12 weeks of aerobic training in the two groups, separated by domains of climacteric symptoms. Data presented as mean and standard deviation.

Domains	Pre (Mean ± SD)	Post (Mean ± SD)	Δ CI 95%	Effect Size	Time *p*	Group *p*	Group × Time *p*
Total							
SINGLE	15.9 ± 1.9	14.6 ± 1.2	−1.3 (−5.5 to 2.9)	−0.425	<0.01	0.86	0.03
MULTI	18.4 ± 1.5	12.7 ± 1.0 *	−5.7 (−8.8 to −2.6)	−0.632			
Somatovegetative							
SINGLE	5.5 ± 0.6	4.7 ± 0.5	−0.8 (−2.0 to 0.5)	−0.496	0.01	0.91	0.59
MULTI	5.8 ± 0.6	4.6± 0.4	−1.2 (−2.7 to 0.3)	−0.449			
Urogenital							
SINGLE	3.5 ± 0.6	3.5 ± 0.4	0.3 (−1.6. to 1.7)	−0.232	0.22	0.20	0.20
MULTI	4.9 ± 0.6	3.9 ± 0.6	−1 (−2 to 0)	−0.249			
Psychological							
SINGLE	6.9 ± 1.0	6.3 ± 0.5	−0.6 (−2.7 to 1.5)	−0.397	0.01	0.80	0.04
MULTI	7.8 ± 0.8	5.0 ± 0.5 *	−2.8 (−4.6 to −1.0)	−0.623			

SINGLE: one cardiometabolic condition; MULTI: two or more cardiometabolic conditions. * $p < 0.05$ compared with pre-intervention. Effect size represents within-group Hedges' g for the pre-to-post change.

Table 4. Anthropometric and body composition variables pre- and post-intervention in the SINGLE and MULTI groups. Data presented as mean and standard deviation.

	Pre (Mean ± SD)	Post (Mean ± SD)	Effect Size	Time *p*	Group *p*	Group × Time *p*	Interaction Effect Size
Waist Circumference (cm)							
SINGLE	85.67 ± 7.27	85.53 ± 7.74	−0.038	0.04	<0.01	0.072	−0.573
MULTI	94.73 ± 8.17	92.4 ± 8.68	−0.509				
Hip Circumference (cm)							
SINGLE	104.4 ± 7.68	103.93 ± 8.67	−0.211	0.37	0.03	0.968	−0.037
MULTI	110.46 ± 8.49	109.92 ± 9.42	−0.100				
Abdominal Circumference (cm)							
SINGLE	94.41 ± 6.59	93.54 ± 6.19	−0.295	0.07	<0.01	0.735	−0.152
MULTI	103.84 ± 8.52	102.44 ± 10.26	−0.248				
Waist-Hip Ratio							
SINGLE	0.82 ± 0.05	0.82 ± 0.05	0.214	0.90	0.13	0.153	−0.411
MULTI	0.86 ± 0.08	0.84 ± 0.07	−0.196				
Weight (kg)							
SINGLE	69.95 ± 9.26	69.97 ± 9.43	0.024	0.04	0.02	0.025	−0.727
MULTI	77.94 ± 10.85	77.20 ± 10.58 *	−0.633				
Body Mass Index (kg/m^2)							
SINGLE	27.36 ± 2.97	27.37 ± 2.96	0.021	0.13	<0.01	0.090	−0.600
MULTI	30.99 ± 4.35	30.7 ± 4.26	−0.577				
Muscle Mass (kg)							
SINGLE	22.86 ± 2.65	23.14 ± 2.8	0.372	<0.01	0.44	0.172	0.460
MULTI	23.38 ± 2.93	24.04 ± 3.09	0.583				
Fat Mass (kg)							
SINGLE	28.21 ± 6.69	27.8 ± 6.46	−0.294	0.01	0.01	0.242	−0.424
MULTI	34.78 ± 7.41	33.54 ± 7.2	−0.463				
Fat Percentage (%)							
SINGLE	39.72 ± 5.32	39.16 ± 5.09	−0.327	<0.01	0.02	0.103	−0.617
MULTI	44.36 ± 5.32	42.85 ± 5.26	−0.787				
Fat-Free Mass (kg)							
SINGLE	41.99 ± 4.42	42.43 ± 4.71	0.327	<0.01	0.44	0.132	0.496
MULTI	42.82 ± 4.88	44 ± 5.04	0.593				

SINGLE: one cardiometabolic condition; MULTI: two or more cardiometabolic conditions. * $p < 0.05$ compared with pre-intervention. Effect size represents within-group Hedges' g for the pre-to-post change; Interaction Effect size represents Hedges' g for the standardized difference in change between the MULTI and SINGLE groups.

Significant main effects of time were observed for waist circumference ($p = 0.04$), body weight ($p = 0.04$), muscle mass ($p < 0.01$), fat mass ($p = 0.01$), fat percentage ($p < 0.01$), and

fat-free mass ($p < 0.01$), indicating overall small but significant changes throughout the intervention period regardless of group allocation.

Statistically significant group effects were found for waist circumference ($p < 0.01$), hip circumference ($p = 0.03$), abdominal circumference ($p < 0.01$), body weight ($p = 0.02$), body mass index ($p < 0.01$), fat mass ($p = 0.01$), and fat percentage ($p = 0.02$), indicating overall differences between women with a single cardiometabolic condition and those with two or more cardiometabolic conditions. No significant group-by-time interactions were observed for waist circumference, hip circumference, abdominal circumference, waist-to-hip ratio, BMI, muscle mass, fat mass, fat percentage, or fat-free mass (all $p > 0.05$).

Table 5 presents the biochemical parameters measured before and after the 12-week aerobic training intervention. Significant group-by-time interactions were observed for VLDL cholesterol ($p = 0.001$) and TG ($p = 0.001$). Post hoc analyses demonstrated significant reductions in both VLDL (32.0 ± 15.7 vs. 27.0 ± 14.0 mg/dL) and triglyceride concentrations (159.8 ± 78.4 vs. 134.5 ± 70.8 mg/dL) in the MULTI group, whereas no significant changes were observed in the SINGLE group.

Table 5. Comparison of biochemical parameters between the SINGLE and MULTI groups at pre- and post-intervention. Data presented as mean and standard deviation.

	Pre (Mean ± SD)	Post (Mean ± SD)	Effect Size	Time *p*	Group *p*	Group × Time *p*	Interaction Effect Size
HbA1c (%)							
SINGLE	5.3 ± 0.6	5.1 ± 0.6	−0.246	0.60	0.02	0.222	0.330
MULTI	5.7 ± 1.0	5.8 ± 0.9	0.102				
Glucose (mg/dL)							
SINGLE	89.9 ± 12.7	93.9 ± 13.7	0.447	0.87	0.01	0.156	−0.313
MULTI	112.8 ± 43.6	109.0 ± 28.8	−0.127				
Insulin (µIU/mL)							
SINGLE	12.7 ± 13.6	14.5 ± 13.0	0.473	0.01	0.29	0.961	0.158
MULTI	17.0 ± 6.8	19.3 ± 8.9	0.356				
Total Cholesterol (mg/dL)							
SINGLE	172.5 ± 32.6	173.5 ± 21.7	0.038	1.00	0.46	0.771	−0.089
MULTI	180.0 ± 25.4	179.0 ± 32.8	−0.049				
HDL (mg/dL)							
SINGLE	42.9 ± 9.4	41.74 ± 10.4	−0.186	0.04	0.49	0.422	−0.267
MULTI	41.5 ±10.3	38.87 ± 9.7	−0.377				
VLDL (mg/dL)							
SINGLE	18.2 ± 7.0	22.6 ± 8.8	0.413	0.73	0.01	0.001	−0.992
MULTI	32 ± 15.7	27.0 ± 14.0 *	−0.560				
LDL (mg/dL)							
SINGLE	111.4 ± 30.7	109.2 ± 20.1	−0.098	0.51	0.95	0.196	0.367
MULTI	106.5 ± 23.0	113.1 ± 33.5	0.249				
Non-HDL (mg/dL)							
SINGLE	129.6 ± 28.6	131.8 ± 22.9	0.091	0.59	0.30	0.914	−0.011
MULTI	138.5 ± 23.2	140.1 ± 34.3	0.065				
Triglycerides (mg/dL)							
SINGLE	91.0 ± 35.1	112.6 ± 44.0	0.412	0.74	0.01	0.001	−0.997
MULTI	159.8 ± 78.4	134.5 ± 70.8 *	−0.566				

SINGLE: one cardiometabolic condition; MULTI: two or more cardiometabolic conditions. HbA1c: Hemoglobin A1c; HDL: high-density lipoprotein; VLDL: very-low-density lipoprotein; LDL: low-density lipoprotein; Non-HDL: non-high-density lipoprotein cholesterol; * statistical difference in the MULTI group. * $p < 0.05$ compared with pre-intervention. Effect size represents within-group Hedges' g for the pre-to-post change; interaction effect size represents Hedges' g for the standardized difference in change between the MULTI and SINGLE groups.

Significant main effects of time were identified for insulin ($p = 0.01$) and HDL cholesterol ($p = 0.04$), indicating changes over the intervention period regardless of cardiometabolic condition burden. No significant time effects were observed for HbA1c, glucose, total cholesterol, VLDL, LDL, non-HDL cholesterol, or TG (all $p > 0.05$).

Significant group effects were found for HbA1c ($p = 0.02$), glucose ($p = 0.01$), VLDL cholesterol ($p = 0.01$), and TG ($p = 0.01$), indicating metabolic differences between women with a single cardiometabolic condition and those with two or more cardiometabolic conditions throughout the study period. No significant group-by-time interactions were observed for HbA1c, glucose, insulin, total cholesterol, HDL cholesterol, LDL cholesterol, or non-HDL cholesterol (all $p > 0.05$).

4. Discussion

The present study investigated the effects of a 12-week aerobic training program on climacteric symptoms, quality of life, anthropometric parameters, body composition, and biochemical markers in postmenopausal women with different cardiometabolic morbidity. Overall, the findings partially support our hypothesis, demonstrating that women with multimorbidity derived greater benefits from aerobic exercise than those with a single cardiometabolic condition. Specifically, participants with multimorbidity exhibited significant improvements in menopause-related quality of life, reflected by reductions in total CER, as well as reductions in total and psychological symptom scores on the MRS. In contrast, women with a single cardiometabolic condition showed limited changes in these outcomes. However, the greater reductions observed in the MULTI group should be interpreted with caution, as this group presented greater symptom severity at baseline. Therefore, the larger magnitude of change may partly reflect greater room for improvement and regression toward the mean, rather than greater responsiveness to exercise alone.

Regarding cardiometabolic health, aerobic training promoted favorable modifications in body composition and metabolic parameters, with the most pronounced effects occurring in the multimorbidity group. A significant reduction in body weight was observed exclusively among women with multimorbidity, accompanied by decreases in triglyceride and VLDL concentrations. Although several anthropometric and body composition variables demonstrated significant time effects, indicating overall improvements throughout the intervention period, these changes were generally similar between groups. Likewise, significant temporal effects were observed for insulin, HDL cholesterol, muscle mass, fat mass, fat percentage, and fat-free mass, suggesting beneficial adaptations to aerobic training regardless of cardiometabolic diseases.

An additional finding was that women with multimorbidity consistently presented a less favorable cardiometabolic profile than those with a single cardiometabolic condition, as evidenced by higher values of adiposity-related measures, HbA1c, glucose, TG, and VLDL cholesterol. Nevertheless, these participants also demonstrated greater responsiveness to aerobic exercise, particularly regarding menopause-related symptoms, quality of life, body weight, and lipid metabolism. Collectively, these findings suggest that postmenopausal women with a higher cardiometabolic disease burden may experience greater clinical benefits from aerobic training, reinforcing the role of exercise as an important non-pharmacological strategy for improving both menopausal health and cardiometabolic risk in this population.

Physical exercise is well established as an adjunctive therapy for managing chronic cardiometabolic diseases such as hypertension, diabetes, dyslipidemia, and obesity [41]. These conditions share common pathophysiological mechanisms, including inappropriate activation of the renin–angiotensin–aldosterone system, systemic inflammation, impaired insulin-mediated vasodilation, heightened sympathetic nervous system activity, and oxidative stress from excessive production of reactive oxygen species [42]. Consequently, the efficacy and magnitude of the response to aerobic training may depend on which physiological systems are compromised. This response can occur independently of the specific chronic conditions present, if these conditions contribute to disrupted mechanisms.

Regular aerobic exercise, therefore, may help mitigate health deterioration and prevent the onset of additional comorbidities.

The MULTI group showed higher values of waist, abdominal, and hip circumference, as well as greater body weight, BMI, fat mass, and body fat percentage, when compared with the SINGLE group. Obesity can potentially increase the development of numerous chronic diseases, with a two-percentage-point increase in mean BMI linked to a reduction of approximately one year in life expectancy [43]. Conversely, weight loss has been associated with lower all-cause and cardiovascular mortality, with each kilogram lost reducing the risk of developing diabetes by 16% [44,45].

In our study, although the MULTI group showed a statistically significant reduction in body weight (Δ = −0.74 kg), the small magnitude of this change is unlikely to represent clinically meaningful weight loss when considered in isolation. However, this modest reduction in body weight occurred alongside changes in several body composition parameters. The MULTI group showing notable reductions in waist circumference (Δ = −2.33 [−3 to −0.1] cm), abdominal circumference (Δ = −1.4 cm), BMI (Δ = −0.29 [−1 to −0.1] kg/m^2), fat mass (Δ = −1.24 [−2.5 to −1.2] kg), and body fat percentage (Δ = −1.51 [−3 to −1]%), as well as increases in muscle mass (Δ = 0.66 [0.5 to 1.6] kg) and fat-free mass (Δ = 1.12 kg). In the SINGLE group, reductions were also observed in waist circumference (Δ = −0.14 [−3 to −0.1] cm), abdominal circumference (Δ = −0.87 cm), fat mass (Δ = −0.41 [−2.5 to −1.2] kg), and body fat percentage (Δ = −0.56 [−3 to −1]%), as well as increases in muscle mass (Δ = 0.44 [0.5 to 1.6] kg) and fat-free mass (Δ = 0.46 kg). Taken together, these findings suggest that changes in body weight should be interpreted alongside changes in body composition rather than as evidence of clinically meaningful weight loss alone.

Similar results were observed in the study by Cho et al. [46], which involved a multimorbid population with an average of 2.9 metabolic abnormalities (including hypertension, type 2 diabetes mellitus, and dyslipidemia). Their 12-week intervention yielded reductions in body mass and fat, though no significant improvements were noted in BP, lipid, or glucose profiles. The relatively modest weight loss may account for the lack of metabolic changes, as a reduction exceeding 5% of body weight is often required to observe metabolic benefits [47]. The distribution of body fat, in addition to the overall magnitude of weight loss, appears to be crucial for achieving metabolic benefits and reducing cardiovascular risk and mortality. This distribution can differ significantly between sexes [48]. In a study by Abdelaal and colleagues [49] using a comparable training protocol (12 weeks at 65–75% heart rate reserve) in a sample characterized by obesity, hypertension, and diabetes, reductions in BMI and waist circumference of 7% and 6%, respectively, were reported. These reductions were slightly higher than those observed in our study, which found a 3% reduction in waist circumference. This difference may be attributed to the composition of the sample, which included both men and women, all with obesity. In contrast, our study involved only postmenopausal women, 70% of whom were obese and had a lower average initial body mass.

The significant reductions in TG and VLDL observed in the present study may be partially attributable to the study protocol. Aerobic interventions with peri- and postmenopausal women have demonstrated reductions in TG and VLDL, with durations lasting approximately 12 weeks [50,51]. Although these results have been confirmed as an effect of exercise [50] in climacteric women [51] with overweight and obesity [52,53] in different age groups [52,54], these findings are particularly relevant in light of the scarcity of research focusing on postmenopausal women with multiple chronic conditions [26], and they suggest that physical exercise may attenuate the metabolic decline typically associated with climacteric status in patients with more than one chronic disease. The effects of aerobic

exercise on lipid profile may be explained by two main aspects: aerobic exercise increases whole-body fat oxidation, adipose tissue lipolysis, and fatty acid utilization by skeletal muscle [55], and aerobic exercise regulates intracellular lipid delivery and mitochondrial β-oxidation, stimulating muscle to absorb and use fatty acids and cholesterol [56]. In addition to the better lipid profile, reducing VLDL reduces the progression of atherosclerosis and cardiovascular risk [57], making its monitoring and, when necessary, reduction particularly important in postmenopausal women [57].

Multimorbidity significantly impairs daily functioning and quality of life, particularly among women with higher levels of adiposity [24,25]. Consistent with this evidence, the MULTI group exhibited greater adiposity, poorer metabolic parameters, and more severe climacteric symptoms at baseline compared with women with only one cardiometabolic condition. However, 12 weeks of aerobic training significantly reduced the total MRS score and the psychological domain score exclusively in the MULTI group, whereas no significant changes were detected in the SINGLE group. Similarly, improvements in menopause-related quality of life, assessed by the CER, were observed only among women with multimorbidity. These findings suggest that postmenopausal women with multiple cardiometabolic conditions not only experience a greater burden of climacteric symptoms but may also derive greater benefits from aerobic exercise interventions. A plausible explanation is that individuals with poorer baseline health status have greater potential for physiological and psychological adaptation, resulting in more pronounced improvements following exercise training. Although evidence regarding the beneficial effects of aerobic exercise on menopause-related quality of life is well known [58,59], no studies have analyzed the effects of exercise in climacteric women in association with the number of comorbidities [60–62]. Nevertheless, additional well-designed clinical trials are needed to determine the specific effects of exercise in postmenopausal women. Future studies should move beyond evaluating climacteric symptoms alone and consider the influence of both the number of conditions and distinct multimorbidity patterns [63], thereby enabling the development of more targeted and effective intervention for this population.

The present findings corroborate those reported by Yue (2025) and Liu (2025) [64,65], who reported that exercise can improve quality of life and psychological symptoms characteristic of the climacteric period. However, our study extends the existing literature by demonstrating that the magnitude of these benefits may depend on cardiometabolic disease burden. Specifically, women with multimorbidity exhibited greater improvements in overall menopausal symptoms, psychological symptoms, and menopause-related quality of life than women with a single cardiometabolic condition. The beneficial effects of aerobic exercise on menopause-related quality of life are likely mediated through both physiological and psychological pathways. Physiologically, aerobic exercise enhances cardiorespiratory fitness by increasing cardiac output, stroke volume, and oxygen utilization [66], leading to improved endurance and reduced fatigue during daily activities [67]. It also promotes metabolic adaptations, including glucose regulation, lipid metabolism, and body composition, which are particularly important for women managing coexisting chronic conditions. Psychologically, exercise has been shown to reduce stress, anxiety, and depressive symptoms while promoting emotional well-being, life satisfaction [68] and resilience [69]. In addition, it improves sleep quality [70], which is often disrupted during menopause and can potentiate both physical and psychological symptoms. Collectively, these physical and psychological adaptations may alleviate menopause-related symptoms and enhance overall quality of life in women with multiple chronic conditions and reinforce the potential role of aerobic exercise as a particularly valuable non-pharmacological strategy for this population.

Strengths and Limitations

This study has certain limitations that should be considered when interpreting the findings. First, the relatively small sample size may limit the statistical power and generalizability of the results. In addition, the present study represents a secondary analysis of a previous quasi-experimental trial. Because participants were stratified into naturally occurring clinical groups according to cardiometabolic multimorbidity status, baseline differences between the SINGLE and MULTI groups could not be controlled through randomization and may have contributed to residual confounding. Furthermore, the absence of a non-exercising control group limits the extent to which the observed changes can be attributed exclusively to the exercise intervention. The retrospective registration of the original trial also represents a methodological limitation, as prospective registration is recommended for intervention studies to enhance transparency and reduce the risk of selective reporting. The relatively short intervention period and lack of longer-term follow-up also limit conclusions regarding the maintenance of the observed changes over time. Although 12 weeks is generally sufficient to assess the effects of aerobic training in many studies [33], longer interventions with follow-up assessments and additional repeated measures would provide a more comprehensive evaluation of exercise-induced adaptations. Selection bias may also have occurred because participants interested in the study voluntarily approached the research center, potentially restricting the generalizability of the findings to the broader population of postmenopausal women with multimorbidity. In addition, the use of hormone therapy was an exclusion criterion, reducing the potential influence of exogenous hormone therapy on the assessed outcomes; however, this criterion may limit the generalizability of our findings to postmenopausal women using this type of therapy. Finally, dietary intake was not monitored or controlled during the intervention, and potential changes in dietary habits may have influenced body composition and cardiometabolic outcomes independently of the exercise intervention. However, the participants were instructed to maintain their normal dietary habits during the 12-week intervention period.

Nonetheless, this study has several noteworthy strengths and contributions: (1) it specifically addresses postmenopausal women with cardiometabolic multimorbidity, aligning with recommendations to consider disease patterns when studying this population [71]; (2) it provides a multidimensional assessment encompassing climacteric symptoms, menopause-related quality of life, body composition, and biochemical outcomes; and (3) the supervised exercise intervention and stratification according to cardiometabolic multimorbidity provide relevant evidence regarding potential differences in responses to aerobic exercise according to cardiometabolic health status. From a clinical perspective, supervised aerobic training performed three times per week for 40 min at moderate-to-intense intensity may represent a safe, feasible non-pharmacological approach for this population, helping to prevent the physical decline characteristic of aging, to address psychological symptoms affected by the climacteric period and aggravated by comorbidities, and to reduce the multimorbidity disease burden. Our findings should encourage the prescription of aerobic exercise to promote physical and psychological health in postmenopausal women with diverse cardiometabolic profiles.

However, given the methodological limitations described above, these findings should be interpreted cautiously and confirmed in larger randomized controlled trials with non-exercising control groups and longer-term follow-up. Further research focusing on multimorbidity patterns is warranted to better inform exercise interventions tailored to this population.

5. Conclusions

In conclusion, a 12-week aerobic training program improved climacteric symptoms, menopause-related quality of life, and selected cardiometabolic parameters in postmenopausal women. Although beneficial effects were observed across the study population, women with multimorbidity demonstrated greater responsiveness to the intervention, showing significant improvements in overall and psychological menopausal symptoms, quality of life, body weight, TG, and VLDL cholesterol. These findings suggest that postmenopausal women with a higher cardiometabolic burden may derive greater clinical benefit from aerobic exercise, despite having a less favorable baseline health profile. Therefore, aerobic training represents an effective non-pharmacological strategy for improving both menopausal health and cardiometabolic risk factors, particularly among women with multiple cardiometabolic conditions.

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Data Availability Statement: The data that supports the findings of this study are available from the corresponding author, Puga, G.M., upon reasonable request.

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Abbreviations

The following abbreviations are used in this manuscript:

WHO	World Health Organization
NCDs	Non-communicable diseases
BP	Blood Pressure
BMI	Body Mass Index
kg/m^2	kilogram per square meter
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
HDL	High-Density Lipoprotein
LDL	Low-Density Lipoprotein
TG	Triglycerides
VLDL	Very-Low-Density Lipoprotein
HbA1c	Glycated Hemoglobin
IPAQ	International Physical Activity Questionnaire

RPE	Ratings of Perceived Exertion
CER	Cervantes Scale
MRS	Menopause Rating Scale
QIC	Quasi-Likelihood under Independence Model Criterion
mmHg	Millimeters of Mercury
mg/dL	Milligrams per Deciliter

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