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Title

Effects of a short health education intervention on physical activity, arterial stiffness and cardiac autonomic function in individuals with moderate-to-high cardiovascular risk

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Highlights

- A short health education program in primary care did not change physical activity
- A short health education program in primary care did not change sedentary time
- Longer lifestyle interventions must be tested to improve cardiovascular health

Abstract

Objective: This study evaluated the effects of a short health education and counseling intervention program, in a primary healthcare setting, on daily physical activity (PA), arterial stiffness, and cardiac autonomic function in individuals with moderate-to-high risk of cardiovascular disease.

Methods: This was a parallel-group study with a 4-month-long intervention, plus 8 months of follow-up. 164 individuals with moderate-to-high cardiovascular risk were allocated to either an intervention (n=87) or a control group (n=77). The intervention consisted of 3 walking and face-to-face group sessions plus text messages. Primary outcome was daily PA (sedentary time, light and moderate-to-vigorous PA, all in min/day); secondary outcomes were arterial stiffness [i.e., carotid-femoral pulse wave velocity (cfPWV, m/s)] and cardiac autonomic function [(i.e., standard deviation of all N-N intervals (SDNN, ms) and absolute high frequency (HF, ms²)].

Results: There were not significant group*time interactions for sedentary time [-7.4 (7.6); p=0.331], light PA [4.4 (6.4); p=0.491] or moderate-to-vigorous PA [0.1 (2.6); p=0.938]. Considering secondary outcomes, there were not significant group*time interactions for cfPWV [0.09 (0.18); p=0.592], Ln_SDNN [0.09 (0.06); p=0.148], or Ln_HF [0.16 (0.14); p=0.263].

Conclusion: The program did not improve daily PA, arterial stiffness, or the autonomic cardiac function.

Practice Implications: Primary care staff should consider longer or other types of intervention to improve daily PA.

Keywords: education, counseling, primary care, cardiovascular risk, daily physical activity, arterial stiffness, cardiac autonomic function

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1. Introduction

Physical activity (PA) confers health benefits [1-4], with evidence indicating that any amount of PA is healthy [5]. Compliance with 150 minutes per week of moderate to vigorous PA is recommended in primary and secondary prevention of cardiovascular disease (CVD) [2, 6]. Despite the recommendations, 31.1% of the adults worldwide fail to meet the PA guidelines [7].

Given that the incidence of CVD remains high [6], the early detection of patients at risk is an important strategy to prevent the onset of CVD [8]. In developed countries, 70-80% of adults visit their general practitioner at least once a year [9], which makes the primary care health services the best setting to assess cardiovascular risk, to manage risk factors, and to promote a healthy lifestyle, including PA [8].

Studies aiming the improvement of PA in primary care [10-15] have produced divergent results, suggesting the necessity of further research [15-17]. The large variation in the intervention designs (i.e., provider, mode, frequency, duration of the intervention, and follow-up) is a barrier to the determination of the best approach [16]. Furthermore, methodological constraints (i.e., trials generally enroll people with inadequate levels of PA [10-12]; and subjective assessment of PA through questionnaires [10-14, 18, 19]) limit the generalization of the results and represent potential source of bias.

Primary care health education and counseling interventions to promote PA can have secondary positive effects in other outcomes such as CVD risk factors [2, 11-13] but long-term health benefits have not been consistently reported [16]. Arterial stiffness and cardiac autonomic function are associated with increased risk of CVD [20, 21]. Furthermore, arterial stiffness and impaired cardiac autonomic function are both negatively associated with daily PA [22, 23]. Hence, the aim of this study was to evaluate the short and long-term effects of a short health education and counseling intervention in primary care on daily PA (primary outcome) and on arterial stiffness and cardiac autonomic function (secondary outcomes) in adults with moderate-to-high cardiovascular risk.

2. Methods

Study design, and participant's allocation

This is a parallel-group study with a non-probabilistic sample, conducted at a primary health care center. The study lasted one year, and the participants were assessed at baseline, after 4 and 12 months (Figure 1). The primary outcome was daily PA, and the secondary outcomes were arterial stiffness and cardiac autonomic function. The outcome evaluators were not blind to the intervention assignment. Two general practitioners and a PA specialist delivered the health educational and counseling program.

One-hundred and sixty-four adults (from a total of 425 assessed for eligibility) registered at the primary health care center, age between 18 and 65 years old, and moderate or high cardiovascular risk according to Systematic Coronary Risk Evaluation (SCORE) charts [24] participated in this study. Exclusion criteria included established diagnosis of cognitive, pulmonary, renal, neurological or thyroid disorders, orthopedic impairments, arrhythmias, severe hypertension, history of acute coronary syndrome, peripheral arterial disease, and cancer.

Participants were randomly selected from the registries of the primary health center and invited by phone calls to perform the initial eligibility assessment. In the first visit, the purposes and procedures were explained, and the participants signed the free and informed consent form; then, the assessments were conducted gathering sociodemographic data, previous and current medical issues, medication, anthropometrics, blood pressure, cardiac autonomic function and arterial stiffness; participants also received an accelerometers to measure daily PA during seven consecutive days. In the second visit (at least eight days after the first one), blood samples were collected, the participants returned the accelerometers, and those eligible were allocated to the intervention group (IG) or the control group (CG) according to their preference and availability. Participants who did not want to join the IG were allocated to the CG. After 4 and 12 months, they returned to the primary health care center to repeat the assessments.

All participants provided written informed consent. The study was approved by the Ethics Committee of the North Regional Health Authority (I.P. 25/2010) and all procedures were conducted according to the Helsinki declaration.

Outcome Measures

Daily physical activity levels

Daily PA was assessed using accelerometers (Actigraph GT1M, Actigraph LLC, Pensacola, FL) over the right hip, for 7 consecutive days, during the waking hours, except while bathing and water-based activities. ActiLife software (Actigraph, Florida, USA, version 6.9) was used to reduce raw activity data into daily PA. The accelerometer measures the intensity of movement, which was averaged for 1-min sampling intervals (counts/min). For data analysis, non-wear periods were defined as ≥ 10 consecutive one-minute sampling intervals with “zero” counts. To be considered as valid data, individuals must have had a minimum of 4 days recorded with at least 8 wear-time hours per day. The average minutes/day spent at different categories of PA intensity was determined according to cut points that relate PA to counts/min: sedentary time (≤ 99 counts/min), light PA (100 - 2019 counts/min) and moderate-to-vigorous MVPA (MVPA) (≥ 2020 counts/min) [25].

Cardiac autonomic function and arterial stiffness

Participants were instructed to refrain from strenuous exercise and to avoid consuming caffeine-containing products or alcohol for at least 24 hours before evaluation. The evaluation room was kept quiet, semi-dark, at an average temperature of 21°C.

Cardiac autonomic function was measured as heart rate variability (HRV). Recording of R-R interval data was performed using the Polar RS800CX (Polar Electro OY, Kempele, Finland) with a temporal resolution of 1ms [26]. The HRV assessment methodology was described in detail elsewhere [27]. In brief, assessments were performed in the supine position, controlling the breathing rate by matching it to a metronome-paced frequency of 12 breaths/min. Following 20 min of recording, R-R interval data were downloaded into Polar Precision Performance software SW

(Polar Electro OY, Kempele, Finland). Using Kubious software 2.0 for Windows (the Biomedical Signal Analysis Group, University of Kuopio, Finland) ectopic beats or arrhythmias were excluded and R-R data were de-trended [28] and resampled at 4Hz. Finally, the last five minutes of each recording were selected and used for calculating HRV indices. The time domain selected index was standard deviation of all N-N intervals (SDNN, ms). Frequency domain indices were determined using the non-parametric method (Fast Fourier transform) and encompassed very low frequency (VLF, 0.0033-0.04 Hz), low frequency (LF, 0.04-0.15 Hz), high frequency (HF, 0.15-0.4 Hz). Absolute HF (ms^2) was used as frequency domain variable. When performed for a short-term interval under controlled laboratory conditions, SDNN and HF predominantly reflect the cardiac vagal modulation [19].

Arterial stiffness was measured as carotid-femoral pulse wave velocity (cfPWV) using the applanation tonometry (SphygmoCor, AtCor Medical, Australia) according to international guidelines [29]. In brief, sequential and consecutive carotid (i.e., right) and femoral (i.e., right) pressure waves were registered with parallel electrocardiogram recording. The electrocardiogram served as a reference to calculate the wave transit time between the two recordings sites (i.e., foot-to-foot method). The distance travelled by the pressure wave was the direct distance between the recording points at the femoral and carotid arteries, corrected by the factor 0.8 [29]. The value of cfPWV was calculated as the direct distance (in meters) divided by the transit time (in seconds). All measurements were performed in duplicate by the same trained researcher. Measurements were considered acceptable if difference between attempts was equal or lower than 1.5 m/s. [29] If the difference was superior to 1.5 m/s, a third measurement was gathered. If this case, the extreme result was excluded, and the mean between the two closest ones was used as the final score.

Intervention: health education and counseling program

The health education and counseling program consisted of three sessions, lasting approximately 90 minutes each, once a week for 3 weeks, followed by 12 text messages over the course of 4 months. A maximum of 10 participants were included in each session group. Sessions were composed of a 30-minute group walk followed by 60 minutes of face-to-face intervention.

In the first session, a general practitioner presented information about the CVD risk, risk factors, and about the deleterious effects of a moderate and high CVD risk on health and quality of life. A general practitioner conducted the second session, and the subject was the positive impact of a healthy lifestyle adoption (i.e., diet; tobacco cessation; salt intake; adherence and compliance with medication; stress management; and PA) on CVD risk. The third session was conducted by a PA specialist. Participants were encouraged to become physically active based on the development of personal goals. Furthermore, PA barriers and overcome strategies were discussed. At the end, participants received a booklet containing sessions' information and a PA plan for each week of the four-month period. After the sessions, participants in the IG received 12 mobile text messages to encourage and reinforce PA adherence. The texts messages were delivered once a week during the first two months, and twice a month in the last 2 months. During the follow-up IG and CG only received the usual care. The intervention program followed the recommendations and standards of the American College of Sports Medicine [30].

The CG received usual medical care and follow-up (i.e., regular medical appointments and optimized medication) during the entire study period.

Statistical analysis

Statistical analysis was performed using IBM SPSS software version 21 (SPSS, Chicago, USA). Heart rate variability indices (SDNN and HF) were transformed in its natural logarithm due to its skewed distribution.

Two data analysis were performed: first, with the inclusion of all participants assessed and allocated into groups at baseline; second, including only the participants who fully accomplished the health education and counseling intervention and who undertook all the evaluations over the three assessment periods. For comparisons between groups at baseline (CG vs. IG), the chi-squared test (categorical variables), *t*-test and Mann Whitney (U) test (quantitative variables) were used as appropriate. Changes in groups over time (group*time interaction) were modeled using a linear mixed-model regression with random-effects statements [unstructured option (completely general covariance matrix)] on the slope and intercept of each participant.

Other covariance types (e.g. first order autoregressive) were also used but presented less accurate results (higher Akaike's Information Criterion values). Normality of residuals was visually verified. Data were expressed as mean $\pm$ SD. Values of P less than 0.05 were considered significant and tests were two-sided.

Power calculation was computed a priori using the software G*Power version 3.1. Considering a repeated measures design, for the within-between interaction, the sample size revealed that 148 subjects (74 per group) were required to detect a small effect size ($f=0.10$). The other parameters considered were a power of 80%, an error type I of 0.05, three measurements (baseline, after 4 and 12 months), two groups (IG and CG), and assuming a correlation equal to 0.55 and a nonsphericity correction of 1. To accommodate an expected, maximal, dropout rate of 10%, the study should enrol a total of 163 subjects.

3. Results

A total of 425 adults were assessed for eligibility. From those, 109 did not meet the inclusion criteria, 39 declined to participate and 113 gave other reasons (Figure 1). A total of 164 participants were allocated to the IG ($n=87$) and the CG ($n=77$). Two participants in the IG did not participate in the sessions (one dropped out because of failure to attend sessions and the other due to employment limitations) and were excluded from procedures.

Intervention and control groups characteristics at baseline are summarized in Table 1. There were significant differences between groups for dyslipidemia ($p = 0.020$), antihypertensive medication ($p = 0.042$), and antidepressants or anxiolytics ($p = 0.036$) (Table 1). The IG showed significantly higher sedentary time ($U=2456.5$; $P=0.040$) and lower light PA ($U=2220.5$; $P=0.004$) than the CG at baseline.

Table 2 presents anthropometrics, hemodynamics, daily PA, arterial stiffness and heart rate variability indexes at baseline, after 4 months and follow up (12 months) for intention-to-treat analysis without adjustments. The linear mixed model presented significant results for group*time interaction for waist circumference, with the IG reducing 1.34 ± 0.38 cm ($P = 0.01$) compared to CG. Significant differences along time for blood pressure variables, resting heart

rate and BMI were observed, but no differences were found between groups and for group*time interaction.

Regarding PA, no significant changes for time and group*time interaction were observed in sedentary time, light PA or MVPA (Table 3, Figure 2). After adjustments for age, gender, BMI, and variables that were different between groups at baseline, the results remained similar (Table 3, Models= 1, 2 and 3).

No statistical changes were observed for group, time and group*time interaction in arterial stiffness parameters during the study. There was no significant group*time interaction for cfPWV, even after adjustments for variables that were different between groups at baseline, mean blood pressure, resting heart rate, and daily PA intensities (Table 4, model 1).

Regarding heart rate variability, for unadjusted models, there was a significant time*group interaction, showing that the IG increased Ln_SDNN in 0.13 ± 0.06 ($p=0.040$) compared to the CG (Table 4, unadjusted model). However, after adjustments for age, gender, BMI, dyslipidemia, antihypertensive and antidepressants/anxiolytic medications, resting heart rate, mean blood pressure, and daily PA, the group*time interaction lost statistical significance (0.09 ± 0.06 ; $p=0.148$) (Table 4, model 2). For the frequency domain index HF, no significant statistical results for group, time and group*time interaction were observed along the intervention and follow-up periods (Table 4; model 3).

Sub-analysis including 100 participants (IG: 58 and GC: 42), showed similar to those for to all participants assessed and allocated into groups at baseline (data non-shown).

4. Discussion and Conclusion

4.1. Discussion

The main findings of this study were that a short health education and counseling program conducted in a primary care setting does not seem to be able to modify PA habits, arterial stiffness and autonomic function in patients with moderate-to-high CVD risk, both after the intervention and at the end of the follow-up period. In the IG group, minimal benefits were observed on

reduction of sedentary time and increase in light and MVPA after four months, but this was reversed during the follow-up (Table 3 and Figure 2).

It is important to note that at baseline this group had significantly higher levels of sedentary time, and lower light PA than the CG. Furthermore, the observed mean values for MVPA indicate that both groups were minimally active at baseline, in light of the current recommendations, suggesting that 30 min/day of MVPA should be performed [31]. Therefore, it is possible that the minimal improvements observed in the IG were influenced by the aforementioned observations because they started the intervention with a poorer PA profile compared to controls; on the other hand, participants were not too inactive, which could have influenced the rate of improvement (diminished returns from the intervention). In addition, it is also possible that the length of the four-month intervention was insufficient to enlarge the improvements in the IG beyond the observed mean values at four months in a way that allowed them to achieve significant differences over the CG. Considering this, primary care staff should consider longer or other types of intervention (or means to deliver) to improve PA levels.

Despite the minimal improvements in daily PA in the IG, the observed trend for the reversion at the end of follow-up indicates that the intervention was insufficient to change the beliefs in the value of PA as a lifestyle risk factor influencing health and well-being, or the readiness and/or self-motivation for PA [32]. Future studies should evaluate the motives and self-regulatory skills associated with adherence to health-related PA.

Intervention studies such as the Hoorn Prevention Study [33] and the IMPALA study [14] aimed to promote lifestyle modifications through health education and counseling programs, including daily PA levels, but these studies also reported no changes in PA. However, comparability between studies is difficult for a number of reasons: the differences in the health education and counseling programs; differences in the strategies of communication to deliver the interventions; length of intervention and duration of follow-up periods; the skills of caregivers or lifestyle facilitators who deliver the program (physicians, nurses, physiotherapists, or PA specialists); and the participant characteristics in intervention and control groups [18, 34]. A recent systematic review assessing the effectiveness of primary care health education

interventions designed to promote healthy lifestyles on PA and cardiovascular risk showed that 7 out of 15 studies failed to improve PA after the intervention [17].

The present study did not find any significant change in the arterial stiffness or cardiac autonomic function variables. It was previously reported that daily PA might directly impact cardiac autonomic function (i.e., down and up-regulation of parasympathetic and sympathetic, respectively [23]) and indirectly on arterial stiffness [22], probably due to its effects on arterial nitric oxide bioavailability. Given that PA did not change significantly, the lack of changes in secondary outcomes in this study should be expected, in light of the hypothesis that daily PA has a role as a modulator or moderator of arterial stiffness and cardiac autonomic function.

Waist circumference is an indicator of central obesity and a strong predictor of CVD [24]. In this study, it was observed a small but significant reduction in waist circumference favouring the IG compared to the CG, which represents a positive outcome of the intervention. This is in line with a recent systematic review that reported that exercise significantly improved waist circumference [35].

Strengths

First, this study used objective measurement for PA, which likely improved the accuracy of assessments over time. Indeed, the use of self-report measures of PA is the most common method in previously published trials, which might inflate estimates of interventions effects [18], once respondents tend to report less sedentary behaviors and more MVPA [18, 34], especially after interventions designed to promote PA.

Second, arterial stiffness and cardiac autonomic function were simultaneously assessed as secondary outcomes, making it the first time this has been done.

Third, this study performed baseline, four-month and 12-month assessments at the same period of the year in both groups, avoiding the between group seasonality effect on daily PA levels.

Limitations

Several limitations of this study should be noted. First, the allocation of patients into groups was made by convenience according to the will and availability to participate in educational and counseling group sessions and to receive text messages on their mobile phones. Those who agreed to participate in the evaluations but were not available to participate in the health education and counseling IG were allocated to the control group (CG). Second, this study did not assess self-regulation for PA and compared this between the groups. Given that allocation was made by convenience, it is possible that those included in the IG were those who were more conscious of and motivated about the importance of lifestyle changes. Third, the sample size, and the participant's retention at one year, was small. Four, those participants willing to take part in the IG could have higher levels of motivation and health consciousness compared to the CG; to control for this variable, future studies should consider assessing motivation for physical activity and exercise.

4.2. Conclusion

In conclusion, this study did not provide evidence for the efficacy of a short health education and counseling program in a primary care setting to improve daily PA levels and modification of arterial stiffness and cardiac autonomic function in individuals with moderate to high cardiovascular risk. These conclusions should not be generalized to other health settings and sample characteristics.

4.3. Practice implication

A short health education-counseling program by general practitioner and PA specialist was not enough to significantly change daily PA, arterial stiffness and cardiac autonomic function in patients with moderate-to-high CVD risk. Primary care staff should consider longer and/or other types of intervention to improve PA levels.

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Conflict of Interest

Authors have no conflict of interest with companies or manufactures.

Results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

Credit Author Statment

Conceived and designed the experiments: José Oliveira, Lucimére Bohn, Ana Ramoa Castro, Fernando Ribeiro. Performed the experiments: Lucimére Bohn, Ana Ramoa Castro. Analysed the data: Pedro Sa-Couto, Lucimére Bohn. Fernando Ribeiro. Wrote the paper: Lucimére Bohn, Fernando Ribeiro, Pedro Sa-Couto, José Oliveira.

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Figure Captions

Caption Figure 1. Flow-chart of the study

Caption Figure 2. Intervention and control groups' daily physical activity over time

Table 1. Overall sample characteristics and between groups comparisons at baseline

	Total	IG	CG	P value
	(n = 162)	(n = 85)	(n =77)	
Age (years)	56.3 ± 7.0	57.2 ± 6.6	55.4 ± 7.3	0.310
Sociodemographic, n (%)				
Gender (Female)	89 (54.9)	46 (54.1)	43 (55.8)	0.825
Cardiovascular risk, n (%)				
Moderate	86 (53.1)	46 (54.1)	40 (51.9)	0.782
High	76 (46.9)	39 (45.9)	37 (48.1)	
Cardiovascular risk factors, n (%)				
Familial history	58 (36.3)	34 (40.0)	24 (32.0)	0.294
Smoking	36 (22.2)	16 (18.8)	20 (26.0)	0.274
Dyslipidemia	146 (90.1)	81 (95.3)	65 (84.4)	0.020
Hypertension	148 (91.4)	76 (89.4)	72 (93.5)	0.354
Diabetes	42 (25.9)	23 (27.1)	19 (24.7)	0.730
Medication, n (%)				
Anti-hypertensive	123 (75.9)	59 (69.4)	64 (83.1)	0.042
Lipid lowering	81 (50.0)	44 (51.8)	37 (48.1)	0.673
Antiplatelet agents	12 (7.4)	8 (9.4)	4 (5.2)	0.306
Anti-diabetic	38 (23.5)	21 (24.7)	17 (22.1)	0.693
Antidepressant or anxiolytics	37 (22.8)	25 (29.4)	12 (15.6)	0.036

Legend: IG, intervention group; CG, control group.

Table 2. Parameters [mean (standard deviation)] at baseline, after 4 months and follow-up (all participants assessed and allocated into groups at baseline).

		Baseline (T1)		4 months (T2)		Follow up (T3)		Statistics results	Changes between T1 and T2	Changes between T2 and T3
Anthropometrics		N		N		N				
Body mass index, kg/m ²	IG	85	29.27 (3.91)	76	28.87 (3.91)	58	28.92 (3.79)	F _{group} (1; 157.72) = 0.696; P = 0.405	0.32 (0.79)	-0.02 (1.10)
	CG	77	29.89 (4.32)	65	30.19 (4.08)	42	28.96 (3.64)	F _{time} (1; 125.89) = 4.402; P = 0.038 F _{group*time} (1; 125.89) = 1.844; P = 0.177	-0.03 (0.74)	0.16 (0.89)
Waist Circumference, cm	IG	85	98.13 (9.81)	76	96.51 (10.07)	58	96.32 (10.24)	F _{group} (1; 154.95) = 0.016; P = 0.900	1.22 (0.34)	-0.07 (2.21)
	CG	77	99.35 (10.19)	65	101.42 (10.40)	42	98.56 (8.71)	F _{time} (1; 122.35) = 0.217; P = 0.642 F _{group*time} (1; 122.35) = 11.935; P = 0.01	-1.29 (3.85)	-0.01 (3.01)
Hemodynamics										
Systolic blood pressure, mmHg	IG	85	134.69 (15.47)	74	126.18 (14.27)	55	130.00 (14.85)	F _{group} (1; 157.99) = 0.941; P = 0.333 F _{time} (1; 126.01) = 17.143; P < 0.001	7.77 (11.88)	-4.59 (15.04)
	CG	77	136.02 (17.31)	63	130.74 (14.87)	41	128.39 (18.10)	F _{group*time} (1; 126.01) = 0.386; P = 0.535	5.61 (14.72)	1.05 (13.79)
Diastolic blood pressure, mmHg	IG	85	79.14 (10.61)	74	75.64 (10.05)	55	76.74 (8.09)	F _{group} (1; 159.31) = 0.013; P = 0.910	2.95 (7.69)	-1.59 (9.71)
	CG	77	78.51 (9.71)	63	75.65 (10.07)	41	75.34 (9.20)	F _{time} (1; 137.48) = 9.821; P = 0.002 F _{group*time} (1; 137.48) = 0.428; P = 0.514	2.70 (8.74)	0.85 (9.08)
Mean blood pressure, mmHg	IG	85	101.11 (12.17)	74	94.93 (11.06)	55	97.20 (10.40)	F _{group} (1; 157.28) = 0.149; P = 0.700	6.20 (8.07)	-3.61 (11.07)
	CG	77	101.31 (12.69)	63	96.87 (11.55)	41	96.78 (13.64)	F _{time} (1; 130.11) = 15.884; P < 0.001 F _{group*time} (1; 130.11) = 0.041; P = 0.839	4.20 (11.25)	1.97 (10.23)

Pulse pressure, mmHg	IG	85	55.54 (9.07)	74	50.54 (8.96)	55	53.34 (10.69)	$F_{\text{group}} (1; 150.27) = 2.032; P = 0.156$	4.50 (8.54)	-2.20 (10.11)
	CG	77	57.51 (11.93)	63	55.11 (9.77)	41	53.02 (12.54)	$F_{\text{time}} (1; 117.03) = 10.808; P = 0.001$	2.94 (8.84)	0.52 (8.79)
								$F_{\text{group*time}} (1; 117.03) = 0.089; P = 0.766$		
Resting heart rate, bpm	IG	84	65.82 (10.43)	69	64.53 (10.13)	55	63.07 (10.76)	$F_{\text{group}} (1; 153.35) = 2.166; P = 0.143$	1.38 (6.24)	1.55 (7.62)
	CG	76	64.32 (8.67)	59	63.03 (10.17)	37	63.91 (9.43)	$F_{\text{time}} (1; 119.62) = 4.609; P = 0.034$	0.40 (7.45)	-1.11 (7.02)
								$F_{\text{group*time}} (1; 119.62) = 2.280; P = 0.134$		
Daily physical activity										
Sedentary time, min/day*	IG	82	472.2 (85.6)	71	452.2 (89.3)	54	454.4 (102.2)	$F_{\text{group}} (1; 167.7) = 5.415; P = 0.021$	13.9 (59.1)	-9.1 (69.2)
	CG	74	435.4 (100.2)	63	426.2 (109.2)	37	441.3 (101.8)	$F_{\text{time}} (1; 237.3) = 0.093; P = 0.761$	6.6 (93.7)	-13.8 (74.3)
								$F_{\text{group*time}} (1; 237.3) = 0.617; P = 0.433$		
Light PA, min/day*	IG	82	289.8 (92.4)	71	299.1 (94.4)	54	294.4 (92.5)	$F_{\text{group}} (1; 154.9) = 7.033; P = 0.009$	-2.3 (52.9)	13.4 (55.9)
	CG	74	337.0 (103.7)	63	331.2 (102.1)	37	320.1 (86.1)	$F_{\text{time}} (1; 108.4) = 1.363; P = 0.246$	8.8 (72.0)	1.9 (57.2)
								$F_{\text{group*time}} (1; 108.4) = 0.530; P = 0.468$		
Moderate-to-vigorous PA, min/day	IG	82	32.9 (25.8)	71	41.0 (29.9)	54	34.3 (27.4)	$F_{\text{group}} (1; 153.9) = 0.219; P = 0.640$	-5.2 (26.0)	6.6 (19.0)
	CG	74	38.3 (31.4)	63	41.0 (30.5)	37	42.5 (39.3)	$F_{\text{time}} (1; 117.4) = 0.367; P = 0.546$	-0.9 (21.7)	-1.8 (36.7)
								$F_{\text{group*time}} (1; 117.4) = 0.023; P = 0.878$		
Arterial Stiffness										
cfPWV, m/s	IG	84	10.3 (2.1)	65	10.0 (2.3)	54	10.1 (2.4)	$F_{\text{group}} (1; 136.1) = 0.476; P = 0.491$	0.3 (1.5)	-0.5 (1.8)
	CG	74	9.9 (1.9)	58	9.9 (2.3)	34	9.7 (2.1)	$F_{\text{time}} (1; 91.2) = 0.318; P = 0.574$	0.5 (1.5)	-0.2 (1.1)
								$F_{\text{group*time}} (1; 91.2) = 0.057; P = 0.812$		
Heart Rate Variability indexes										
Ln_SDNN	IG	84	3.2 (0.6)	67	3.3 (0.7)	54	3.3 (0.6)	$F_{\text{group}} (1; 234.5) = 2.736; P = 0.099$	-0.16 (0.75)	0.06 (0.62)
	CG	75	3.3 (0.6)	58	3.3 (0.6)	36	3.1 (0.6)	$F_{\text{time}} (1; 263.9) = 0.198; P = 0.657$	-0.004 (0.66)	0.25 (0.63)

								$F_{\text{group*time}}(1; 263.9) = 4.261; P = 0.040$		
Ln_HF, ms ²	IG	84	5.5 (1.3)	67	5.6 (1.4)	54	5.7 (1.4)	$F_{\text{group}}(1; 155.2) = 2.061; P = 0.153$	0.03 (1.39)	0.53 (1.43)
	CG	75	5.7 (1.4)	58	5.6 (1.5)	36	5.4 (1.4)	$F_{\text{time}}(1; 123.8) = 1.586; P = 0.210$	-0.18 (1.49)	0.53 (1.43)
								$F_{\text{group*time}}(1; 123.8) = 2.541; P = 0.114$		

IG: intervention group; CG: control group; PA: physical activity cfPWV: carotid femoral pulse wave velocity; Ln_SDNN: natural logarithm of the standard deviation of N-N interval; Ln_HF: natural logarithm of high frequency. * Groups were significantly different at baseline $P < 0.05$.

Table 3. Linear mixed model regression for sedentary time, light and moderate-to- vigorous physical activity

		Slope (SE); statistical inference
Sedentary time, min/day		
Unadjusted model	Group	41.4 (17.9); p= 0.021
	Time	1.83 (5.8); p=0.752
	Group * Time	-5.99 (7.6); p=0.433
Model 1	Group	42.4 (18.2); p=0.021
	Time	2.10 (5.7); p=0.715
	Group * Time	-7.4 (7.6); p=0.331
Light PA, min/day		
Unadjusted model	Group	-50.0 (18.9); p=0.009
	Time	-6.1 (4.9); p=0.213
	Group * Time	4.7 (6.5); p=0.468
Model 2	Group	-50.5 (19.0); p=0.009
	Time	-6.6 (4.8); p=0.168
	Group * Time	4.4 (6.4); p=0.491

MVPA, min/day

Unadjusted model	Group	-2.8 (5.9); p=0.640
	Time	1.0 (1.9); p=0.617
	Group * Time	-0.4 (2.5); p=0.878
Model 3	Group	-2.7 (5.9); p=0.651
	Time	1.2 (1.9); p=0.553
	Group * Time	0.1 (2.6); p=0.938

Model 1: adjusted for age, gender, body mass index, dyslipidemia, antihypertensive and antidepressants/ anxiolytic medication, and light physical activity. Model 2: adjusted for age, gender, body mass index, dyslipidemia, antihypertensive and antidepressants/ anxiolytic medication, and sedentary time. Model 3: adjusted for age, gender, body mass index, dyslipidemia, antihypertensive and antidepressants/ anxiolytic medication, sedentary time, and light physical activity.

Table 4. Linear mixed model regression for arterial stiffness and heart rate variability

		Slope (SE); statistical inference
Arterial stiffness		
cfPWV, m/s		
Unadjusted model	Group	0.23 (0.34); p= 0.491

Model 1	Time	0.02 (0.12); p=0.833
	Group * Time	0.03 (0.16); p=0.812
	Group	0.12 (0.33); p=0.704
	Time	0.00 (0.14); p=0.985
	Group * Time	0.09 (0.18); p=0.592
Heart rate variability		
Ln_SDNN, ms		
Model 2	Unadjusted model	
	Group	-0.21 (0.13); p= 0.099
	Time	-0.08 (0.04); p=0.100
	Group * Time	0.13 (0.06); p=0.040
	Group	-0.15 (0.13); p=0.258
	Time	-0.06 (0.05); p=0.217
	Group * Time	0.09 (0.06); p=0.148
Ln_HF, ms ²		
Unadjusted model	Group	-0.43 (0.30); p= 0.153
	Time	-0.20 (0.11); p=0.063

Model 3	Group * Time	0.23 (0.14); p=0.114
	Group	-0.32 (0.31); p=0.304
	Time	-0.15 (0.11); p=0.178
	Group * Time	0.16 (0.14); p=0.263

Model 1, 2 and 3: Adjustments for age, gender, body mass index, dyslipidemia, antihypertensive and antidepressants/ anxiolytic medication, mean blood pressure, resting heart rate, sedentary time, light PA and moderate-to-vigorous PA