



Comparison of linear periodized and non-periodized combined training in health markers and physical fitness of adults with obesity: Clinical trial protocol

Anne Ribeiro Streb*, Robert Passos da Silva, Larissa dos Santos Leonel, Willen Remon Tozetto, Aline Mendes Gerage, Jucemar Benedet, Rodrigo Sudatti Delevatti, Tiago Turnes, Giovani Firpo Del Duca

Federal University of Santa Catarina, Graduate Program in Physical Education, School of Sports, Federal University of Santa Catarina, Florianópolis, Brazil

ARTICLE INFO

Keywords:
Obesity
Exercise therapy
Physical fitness
Adults
Clinical trial

ABSTRACT

The literature discusses that combined training, aerobic more resistance exercises in the same session, is a suitable strategy for people with obesity and that exercise periodization leads to positive health outcomes; however, the implication of different periodizations of combined training for health outcomes in obese adults requires further investigation. The aim of the study will be to describe the methodology used to compare the effect of linear periodized and non-periodized combined training on health markers and health-related physical fitness in adults with obesity. This is a blinded randomized controlled clinical trial investigating adults with obesity in the age group 20–50 years. The sample will be non-probabilistic, and participants will be allocated randomly into one of three groups: control group (CG), non-periodized group (NG), and periodized group (PG). The intervention will occur in 60-min sessions, 3 days a week for 16 weeks, with 1 week dedicated to familiarization with the training and 15 weeks of combined training (aerobic followed by resistance in the same session). The PG group will perform three mesocycles of 5 weeks each, progressing in intensity throughout the intervention [aerobic: from 40–49% to 60–69% of heart rate reserve (HRR); strength: from 12 to 14 maximum repetitions (MR) to 8 to 10MR]; the NG group will maintain the same relative intensity throughout the study (aerobic: 50–59% of HRR; strength: 2 sets of 10–12 MR). Participants in the CG group will maintain their usual activities without the proposed intervention. Pre- and post-intervention assessments will be performed for biochemical markers, body composition, cardiovascular parameters, cardiorespiratory fitness, maximum upper and lower limb strength, flexibility, and subjective health-related parameters. This project was approved by the Committee of Ethics and Research with Human Beings of the institution of origin (protocol 2,448,674) and registered in the Brazilian Registry of Clinical Trials (RBR-3c7rt3).

1. Introduction

Obesity is a disease derived from an imbalance between caloric consumption and expenditure, originating from and/or influenced by several aspects and involving the excessive accumulation of adipose tissue in different parts of the body [1,2]. Obesity is defined as a low-grade subclinical systemic inflammatory state, leading to various types of harm to health and quality of life [3]. In 2016, the number of overweight adults reached 1.9 billion people worldwide, of which 650 million were obese [4]. The Brazilian Unified Health System spent

nearly half a billion reais (R\$) on obesity-related issues, in 2011 [5], reinforcing the importance of the search for obesity prevention and treatment practices with a low cost.

Changes in lifestyle are effective strategies for the preventive and therapeutic management of obesity, minimizing the deleterious effects of this disease [6]. Among the strategies, combined training exercise, which combines aerobic and resistance training in the same session, has been considered an essential tool in the treatment of obesity [7] because this type of exercise contributes to the improvement of anthropometric and metabolic parameters, as compared with other forms of

* Corresponding author.

E-mail addresses: anne.streb@posgrad.ufsc.br (A.R. Streb), robert.passos@posgrad.ufsc.br (R.P. da Silva), leonellari@gmail.com (L.d.S. Leonel), willen_tozetto@hotmail.com (W.R. Tozetto), alinegerage@yahoo.com.br (A.M. Gerage), jucemarb@hotmail.com (J. Benedet), rsdrodrigo@hotmail.com (R.S. Delevatti), tiagoturnes89@gmail.com (T. Turnes), gfdelduca@gmail.com (G.F. Del Duca).

<https://doi.org/10.1016/j.conctc.2019.100358>

Received 17 December 2018; Received in revised form 22 March 2019; Accepted 5 April 2019

Available online 13 April 2019

2451-8654/ © 2019 Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

exercise alone [8]. Thus, the reduction of body mass and improvement in the metabolic profile obtained with aerobic training, added to the increase in muscle mass and strength provided by resistance training, work together effectively [9,10]. Although the relationships between these two exercise modalities have been previously investigated, it is known that adaptations depend on which characteristics are manipulated during training [11], reinforcing the importance of good planning and training periodization.

Periodization is essential to guaranteeing the efficiency in a training program, as it provides systematic, sequential, and integrative programming of sessions, maximizing physiological adaptation and minimizing the risks of overtraining, monotony, and demotivation [12]. Of several possibilities for periodization, two models stand out for their ease of manipulating the variables. The non-periodized model maintains uniform intensity, volume, and workload throughout the mesocycles [13]. The linear periodization model begins with low initial intensity, subsequently introducing a gradual increase of intensity in the mesocycles. Despite its wide use for improving sports performance, the periodized model seems to yield greater benefits for risk factors of cardiovascular diseases and for improved quality of life [13]. While the benefits of periodization have been previously evidenced, few studies have used a model not periodized in its comparison to understand the difference between the methods employed [14,15]. Therefore, improving the knowledge of responses to linear periodization and non-periodization, with equal total volumes, will contribute to more efficient training models and improved health in obesity.

Thus, the objective of the study will be to describe the methodology used to compare the effect of linear periodized and non-periodized combined training on health markers and health-related physical fitness in adults with obesity.

2. Material and methods

2.1. Design

This study is characterized as a randomized controlled clinical trial, conducted in parallel among three groups of adults with obesity. One participant group will undergo a linear periodized combined training (PG group), another group will participate in a non-periodized combined training (NG group), and a third group will serve as the control group (CG). The intervention period will be 16 weeks and individuals will be instructed to restrict participation in other systematic physical training programs during that period. The present study was designed in accordance with the recommendations of CONSORT (Consolidated Standards of Reporting Trials) and SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) [15]. The study is also registered in the Brazilian Registry of Clinical Trials (code RBR-3c7rt3). All procedures will be carried out at the Federal University of Santa Catarina in southern Brazil and a flowchart of all steps of this clinical trial is presented in Fig. 1.

2.2. Participants

The study will include men and women with obesity, aged between 20 and 50 years, who have a medical recommendation for physical exercise and have not been regularly participating in a physical exercise program (< 2 times a week) for the previous 3 months. Acceptable levels of obesity for inclusion in the study will be grades 1 and 2, equivalent to body mass index (BMI) 30–34.9 kg/m² and 35–39.9 kg/m², respectively [16]. Participants with any of the following will be excluded: smoking, excessive alcohol consumption (≥ 7 and ≥ 14 drinks per week for women and men, respectively), use of medications to control obesity, previous bariatric surgery, unavailable for training from 7:00 p.m. to 9:00 p.m., and the presence of bone, muscle or joint lesions that limit the ability to safely engage in physical exercise.

Participant selection will be via on-probabilistic sampling, with

voluntary participation. After eligibility assessment, individuals will be contacted to schedule a face-to-face interview, to confirm the data.

2.3. Sample calculation

Sample calculation was performed using GPower[®] 3.1.7, adopting a significance level of 0.05, a power of 80%, and an effect size of 0.18 in repeated measures analysis, with a ratio of 1:1:1 among the three study groups. The calculation yielded a minimum of 26 participants in each group. Considering the possibility of sample losses during the intervention, 30 participants will be recruited in each group, totaling 90 individuals.

2.4. Interventions

The two intervention groups will be 16-week combined physical training programs, one of PG group and one of NG group. The structure of the training will be such that the duration of each session is the same and only one group has increases in training intensity. In this way, at the end of the interventions, the volume and total intensity of training performed during the 16 weeks are equal between the groups. As a modality of aerobic training, walking and/or race walking will be adopted, depending on the physical conditioning of the individuals. As a form of resistance training, bodybuilding will be adopted, and dynamic exercises will be performed using fitness equipment. The intensity of the aerobic training will be determined according to percentages of the heart rate reserve (HRR), obtained from direct measurement of the resting heart rate and the maximum heart rate (HRmax), in incremental tests. Strength training intensity will be prescribed by repetition maximum ranges (1MR), and the increase in load (kilograms) will be indicated whenever participants perform the predicted series in the upper repetition range. Both training programs will have a frequency of three sessions weekly (Mondays, Wednesdays, and Fridays), taking place between 7:00 p.m. and 9:00 p.m.

The aerobic training will be carried out on a 400-m outdoor running track with a synthetic surface, or in an indoor gymnasium on rainy days. Resistance training will be held at the gym. Each training session (resistance and aerobic exercises) will be conducted by physical education professionals; these professionals will not be involved in the evaluation of participants. Prior to the start of the interventions, participants assigned to the PG and NG groups undergo 1 week of familiarization with the proposed exercises. In this stage, participants from both groups will perform 15 min of aerobic exercise with intensity between 30% and 39% of (HRR), monitored by portable heart rate monitors, and a series of 10–15 repetitions for the six exercises proposed for the interventions, with 60-second intervals between exercises. After this stage, the complete training programs will be applied for the remaining 15-week period.

2.5. Periodized combined training (PG)

Training sessions will have a total duration of around 60 min throughout the training period, consisting of a warm-up (5 min), the main part of the training (50 min), and a cool down (5 min). The main part will be devoted to combined training, with 30 min of aerobic exercise followed by (around 20 min) strength exercises. The cool down will consist of stretching and relaxation exercises. Aerobic training and strength training will be periodized in an increasing linear fashion, with the relative intensity increased over three mesocycles. The first mesocycle will be of low-level intensity, progressing to moderate intensity in the second mesocycle, and ending with vigorous intensity in the third and final mesocycle (Table 1). These mesocycles will last for 5 weeks, and then the intensity will be increased in weeks 6 and 11 of the 16-week intervention. The aerobic training will be carried out continuously, with intensity progressing from 40% to 49% of HRR to 60%–69% of HRR throughout the intervention. Strength training, in

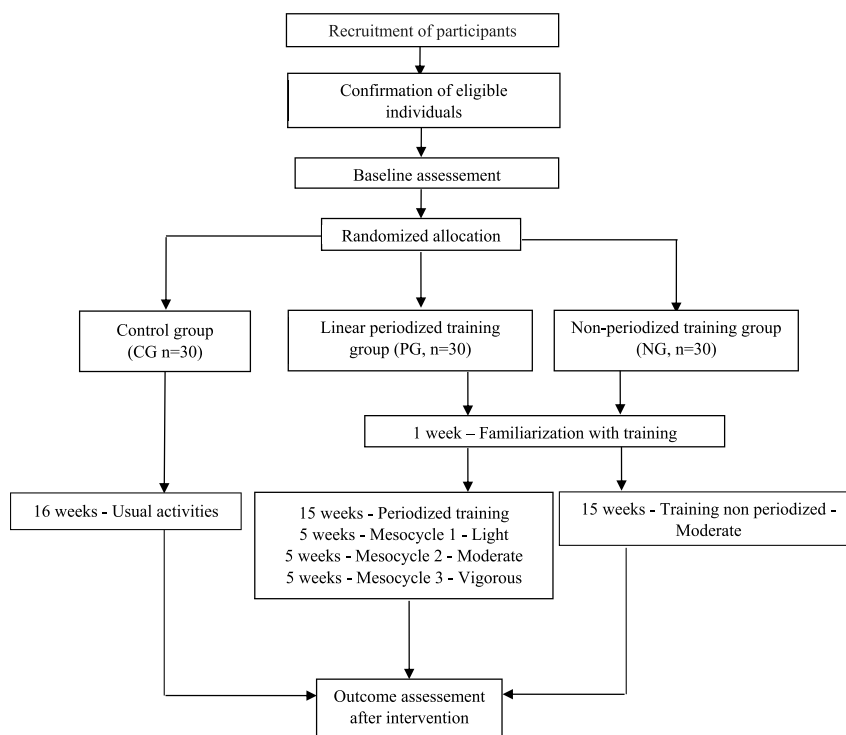


Fig. 1. Study flowchart.

Table 1
Characteristics of combined training.

Groups	Mesocycle I Week 2–6	Mesocycle II Week 7–11	Mesocycle III Week 12–16
Non-periodized			
Aerobic	30 min 50–59% HRR	30 min 50–59% HRR	30 min 50–59% HRR
Strength	2 sets 10–12 MR	2 sets 10–12 MR	2 sets 10–12 MR
Periodized			
Aerobic	30 min 40–49% HRR	30 min 50–59% HRR	30 min 60–69% HRR
Strength	2 sets 14–12 MR	2 sets 10–12 MR	2 sets 8–10 MR

Note: HRR = heart rate reserve; MR = maximum repetition.

turn, will be performed using multiple sets, alternating by segment, starting with 2 sets of 12–14 maximum repetitions (MR) and progressing up to 8 to 10 MR in the last mesocycle, for the bench press, horizontal leg press, low row, peck deck machine, squat smith machine and pull-down, with 60-s intervals between sets and exercises. The volume variables “distance traveled” and “repetitions performed”, as well as the variables “HRR intensity” and “weight” will be recorded during aerobic and strength training, respectively. In addition, in the PG as well as in the NG group, HRR will be reevaluated at weeks 5 and 10, to adjust for possible changes in the HRR during the interventions.

2.6. Non-periodized combined training (NG)

In this group, the duration and organization of each session will be identical to the protocol applied in the PG group. The difference between the groups is restricted to the relative intensity, which will be kept constant in a single mesocycle over 15 weeks (Table 1). As the present study aims to analyze the impact of periodization (progressive vs. constant) of the training dose and not of the dose itself (volume $\times$ intensity), moderate intensity will be prescribed for this group, considering that the PG group will progress in intensity, thus making it possible to compare the training loads when the total 15-week period is analyzed. Thus, the intensity of aerobic training in the NG group will remain between 50% and 59% of HRR, and strength training will

include 2 sets of 10–12 MR per exercise throughout the intervention. The intensity ranges adopted in both groups are in accordance with the intensity ranges recommended by the American College of Sports Medicine [17] for individuals with obesity.

To facilitate communication between researchers and participants, a contact network will be created using an instant messaging application, with the participation of all those involved in the interventions. This network will be used to address research-related issues such as alerts about a change in training location on rainy days, encouraging messages about participation, reminders of evaluation dates, and other issues. Further, a standardized practice will be set such that when a participant misses two consecutive training sessions, a researcher will send them a private message stating the importance of adherence and encouraging the participant to attend training.

2.7. Control group (CG)

The CG will not perform any type of intervention and will be instructed to maintain their usual routine and usual activities. For ethical reasons, after the study period, participants in this group will be provided with combined training for a similar period of time as the intervention.

2.8. Primary outcomes

All outcomes will be assessed before and after 16 weeks of intervention. Pre-intervention evaluation will precede randomization, aiming to control a possible source of bias in the allocation of groups. For analysis of the outcomes, pre- and post-intervention values will be considered. Due to the impossibility of blinding the physical education professionals who will conduct the training sessions and the participants, this trial will be blinded only for the evaluation of outcomes. Regarding participants, there will be blinding of the different doses (volume and intensity) between the training groups.

Health-related physical fitness (HRPF) and the inflammatory profile of participants will be the primary outcomes of this study. The HRPF will be analyzed using the following set of attributes: cardiorespiratory

fitness, neuromuscular fitness, flexibility, and body composition. The inflammatory profile will be assessed via blood collection for quantification of C-reactive protein and interleukin 6 levels. Cardiorespiratory fitness will be evaluated using the maximum oxygen uptake ($\text{VO}_{2\text{peak}}$). Neuromuscular fitness will be determined according to the maximum strength levels of the upper and lower limbs, evaluated by a 1MR bench press and leg press exercises, respectively. Flexibility will be evaluated by the sit-and-reach test, and body composition will be assessed using the two components model (fat mass and lean mass), estimated by bioelectrical impedance analysis.

2.9. Secondary outcomes

As secondary outcomes, biochemical and cardiovascular parameters will be evaluated. The barriers to engaging in physical activity, stages of behavior change, body image, quality of life, and sleep quality will be evaluated through the administration of online questionnaires.

As secondary biochemical endpoints, fasting blood glucose, insulin, total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, interleukin 10, and paraoxonase1 will be evaluated. Furthermore, the value of insulin resistance will be estimated by calculating the homeostatic model assessment – insulin resistance (HOMA-IR).

The cardiovascular parameters analyzed will include systolic blood pressure, diastolic blood pressure, and resting HR, determined using an automatic monitor as well as non-invasive monitoring (photo-plethysmography), which also allows for measurement of systolic volume, cardiac output, and peripheral vascular resistance.

2.10. Control and characterization variables

To quantify the volume of habitual physical activity performed before the intervention and time spent engaged in sedentary behavior, accelerometry measurements will be taken before and after the intervention, to control for a possible intervening effect of these behaviors on the outcomes. Another control variable will be usual dietary consumption, which will take into account the average energy consumption (in kilocalories per day), carbohydrates, lipids, and protein (in grams per kilogram per day).

To characterize the sample and possible sub-analyses, information on the sociodemographic variables of sex, age (in complete years), education level (in years completed), socioeconomic status (six categories), and marital status (with and without a partner) will be collected prior to the intervention.

2.11. Allocation and randomization

Any individual considered eligible for participation will be allocated randomly to one of three experimental groups. To balance the groups in numerical terms as well as with respect to participant characteristics, randomization (stratified by sex, age, and BMI) in a 1:1:1 ratio will be used. The randomization process will be performed using online software (randomizer.org) by a researcher not involved in the other experimental procedures of the study; this researcher will inform the research coordinator to which group each participant is allocated. The allocation list will be hidden from all evaluators of the outcomes.

2.12. Logistics of evaluations

After initial screening, participants will use an online platform (QuestioPro®) to provide personal and sociodemographic data and complete questionnaires regarding barriers to engaging in physical activity [18], stages of behavior change [19], body image scaling [20], quality of life [21], and sleep quality [22,23].

The maximum strength test will be performed according to the 1MR protocol described by Clark et al. [24], with the bench press and 45° leg

press exercises. Each exercise will be preceded by a warm-up (6–10 repetitions), with approximately 50% of the load estimated for the first attempt in the 1MR test. Testing will start 2 min after the warm-up. Participants will be instructed to complete two repetitions. If two repetitions are completed on the first attempt, or even if no repetitions are completed, a second attempt will be performed after a recovery interval of 3–5 min, with a load that is higher (first possibility) or lower (second possibility) to that used in the previous attempt. This procedure will be repeated again in a third and final attempt.

All participants will be tested, in a situation similar to the protocol to be adopted, in at least three different sessions, with intervals of 48 h between sessions, to familiarize participants with the test, in an attempt to reduce the learning effects and establish the reproducibility of the tests, according to the guidelines proposed by Clark et al. [24]. The charge recorded as 1MR will be when the participant can complete only a single maximum repetition. Intraclass coefficients in each exercise will be determined. The form and technique of execution of each exercise will be standardized and continuously monitored, in an attempt to assure the efficiency of the test. The 1MR test is commonly used and traditionally accepted as a standard for dynamic force evaluation, and it is a strong indicator of maximum strength, provided that it is adequately learned and performed [17,25].

Flexibility of the hamstring muscles will be measured by the sit-and-reach test [26], following the Canadian Standardized Test of Fitness (CSTF) [27]. Considered a low-cost alternative with good reproducibility, the sit-and-reach test has acceptable validity for hamstring flexibility [28].

The evaluation of body composition will be done using the bioelectrical impedance method, applied by researchers experienced and trained in use of the device. Participants will wear light clothing and will adhere to the following guidelines: remove any metallic objects they are wearing, such as rings, earrings, piercings, watches, and others; urinate at least 30 min before the test; suspend medications and diuretic drinks 24 h before the test (coffee, tea, mate, and others); avoid consuming food and drink 4 h before the test; do not exercise 24 h before the test; not currently menstruating; do not consume alcoholic beverages 24 h before the test. The test will be performed in a setting with room temperature between 20 °C and 25 °C, with the participant in the orthostatic position on the platform of the scale, holding an electrode in each hand. Stature measurement will be performed with a compact stadiometer with a measuring range of 210 cm and a resolution of 0.1 cm. An anthropometric test without a lock will be used to measure waist circumference (midpoint between the last rib and iliac crest) and the hip (point of greatest gluteal protrusion) [29]. The waist:hip ratio will be calculated based on the waist circumference divided by the perimeter of the hip and the waist: height ratio will be calculated using the waist measurement divided by the measure of height.

Blood sample collection will be done using venipuncture, drawing 20-ml samples into dry vacuum tubes with anticoagulant (EDTA), at the same time for each collection (between 7:00am and 9:00 a.m.). Participants should fast for 12 h prior to sample collection, and should not perform physical exercise in the previous 72 h. The collected samples will be processed and centrifuged to obtain plasma and serum, then stored in a biofreezer at –80 °C for subsequent analysis, which will be done by a technician experienced in the analysis needed and in a suitable environment, such as a laboratory. Serum insulin concentration values will be measured by the chemiluminescent immunoassay method using the ADVIA Centaur XP™ Automated Chemiluminescence System. It will also be quantified PCr dates by the immunoturbidimetry method, measured with the automated Dimension® RxL Max® clinical chemistry system from Siemens Healthcare Diagnostics, Ltda, using the Flex reagent cartridge.

Triglycerides and total cholesterol (enzyme-trinder method), HDL (selective accelerator-detergent method) and LDL (Friedewald method) will all be dosed, all in the BSA20 Mindray apparatus. Insulin resistance will be estimated using the homeostasis model of insulin resistance

(HOMA-IR). The formula used for this calculation was: $\text{HOMA-IR} = [\text{fasting glucose (mmol/L)} * \text{fasting insulin (uU/mL)}] / 22.5$. In addition, IL-6 will be dosed by the bound immunoabsorbance method to the enzyme (ELISA), following the manufacturer's information (BD Biosciences Pharmingen, San Diego - CA), with a detection limit of 2.2 pg/mL. Paraoxonase 1 (PON1) activity will be assayed in 12 h fasting blood serum according to the method already described [30] adding serum to Tris-HCL buffer (100 mmol/L, pH 8.0) containing 2 mmol/L CaCl_2 and 1.1 mmol/L paraoxon (0,0-diethyl-0-p-nitrophenylphosphate; Sigma). The rate of generation of *p*-nitrophenol was determined at 37 °C, and read at 405 nm.

The cardiorespiratory fitness test will be carried out on a treadmill (Millennium Super ATL; Inbramed, Brazil) with a constant incline of 1% [31]. Briefly, after 2 min of warm-up at 4 km/h, the speed will be increased in increments of 0.3 km/h every 30 s, until the participant reaches voluntary exhaustion. Cardiorespiratory variables will be measured breath-by-breath during the entire test using a Quark PFT Ergo gas analyzer (COSMED, Rome, Italy) for posterior analysis of $\dot{V}O_{2\text{peak}}$. HR will be constantly recorded by means of a heart frequency meter (Polar, Kempele, Finland) synchronized to the gas analyzer, for HRmax analysis and subsequent use in the prescription of aerobic training. Studies among participants with obesity have used this protocol to evaluate cardiorespiratory fitness [32,33]. The purpose of this protocol is to find the $\dot{V}O_{2\text{peak}}$ between 8 and 12 min of testing [34].

Before measuring cardiovascular parameters, participants will be instructed to avoid strenuous physical activity for at least 24 h prior to laboratory visits, to avoid alcohol and caffeine intake for at least 12 h, and to eat a light meal before arriving at the laboratory. All measurements will be taken in the supine position in a quiet environment. Blood pressure and HR will be measured on the left arm using an automatic oscillometric device (Omron HEM 742-E, Bannockburn, IL, USA). Three measurements will be taken at 1-min intervals; the average of these three measures will be adopted as the reference value. In addition, non-invasive photoplethysmography blood pressure monitoring will be performed using the Finometer (Finapres Medical Systems, BV, Enschede, The Netherlands). For this, an inflatable cuff is attached to the middle finger of the participant's left hand. Prior to use, the equipment will be calibrated according to the procedures described by the manufacturer. From the measurements obtained by the Finometer, pressure-volume, pressure-compliance, and pressure-impedance relationships will be established, which allows estimation of brachial arterial pressure, peripheral vascular resistance, cardiac output, and systolic volume.

The level of physical activity will be objectively measured by accelerometry. For this, each participant will be instructed in the use of an ActiGraph GT3X+, to be worn on the right hip for 7 consecutive days and removed only for sleeping, bathing, or water-related activities. For purposes of analysis, to be performed using ActiLife software, data will be considered valid with a minimum of 10 h of daily use of the device, for at least 4 days, including at least one weekend day. The data will be recorded at a frequency of 100 Hz and analyzed using epochs of 60 s. Periods with consecutive zeros for 60 min or longer (with 2 min of tolerance) will be interpreted as non-use time and will be excluded from the analysis [35]. The time spent engaged in sedentary behavior and in mild, moderate, and vigorous physical activity will be calculated from the cut-off points proposed and validated by Freedson et al. [36] and Sasaki et al. [37], adjusting the values according to the number of valid days and hours of use.

To obtain data of usual food consumption, three 24-h reminders will be used, which are based on obtaining verbal information about food consumption on the previous day including foods and beverages consumed, quantities, portions in home measures, method of preparation, and ingredients [38]. These data will be collected for 3 non-consecutive days, 2 weekdays and 1 weekend day. This option will be performed in an attempt to avoid reporting typical days only. The first 24-h reminder should be applied at the time of data collection and the subsequent

reminders will be sent in the weeks following telephone data collection. In addition, to reduce possible biases in the data collection regarding dietary consumption, a 24-h dietary recall will be used, with the "USDA Automated Multiple-Pass Method", which prompts the respondent to recall in detail the foods and beverages consumed the previous day, by following five steps [39]. Energy and nutrient intake will be estimated by the Nutrition Data System for Research® (NDSR) Grad-Pack 2017 (NCC Food and Nutrient Database, University of Minnesota, Minneapolis, MN, USA). Data entry is to be performed according to the "Manual of Evaluation of Food Consumption in Population Studies" [40]. An adjustment of the inter- and intra-personal variability of nutrients is made based on estimation of the habitual consumption distribution, according to the Iowa State Method, to reduce the probability of information bias (day of the week, sex, age, education level, and BMI) [41], as well as food consumption by total energy value. In addition, after entering the data, a consistency analysis of the dietary data will be performed, to check for possible typing errors, outliers of energy or grams, and other items, to avoid sub- or overestimation. The following food consumption variables will be considered: average energy consumption (in kilocalories per day), carbohydrate, lipids, and protein (in grams per kilogram per day).

2.13. Safety monitoring plan

Although combined training is quite safe and well tolerated by this target population, any adverse events that may occur during the intervention, such as nausea, pain or bone, muscle and joint injuries, weakness, and falls, among others, will be reported in a spreadsheet by one of the researchers present during the exercise session.

2.14. Ethical considerations

This project was approved by the Human Research Ethics Committee of the Federal University of Santa Catarina, under opinion n. 2,448,674. All participants will be duly informed about all procedures of the study and, after agreeing to participate, participants will sign an informed consent form.

2.15. Analysis plan

Primary and secondary outcomes will be treated per protocol analysis and intention to treat analysis. For this, all randomized participants who withdraw from the study will be invited for post-intervention reevaluation. In the case of missing data, the quasi-likelihood technique will be used to impute missing data. The distribution of the data will be verified using the Shapiro-Wilk test, and the Levene test will be adopted to verify the homogeneity of the variances. Continuous variables will be expressed as mean and standard deviation, and categorical variables will be expressed as relative frequency and percentage. Differences between the groups at pre-intervention will be tested through analysis of variance for independent samples. To compare the results within and between groups, analysis using generalized estimating equations will be performed, adopting the Bonferroni post-hoc test. The significance level will be set to 0.05; however for group-time interactions, $p < 0.10$ will be considered marginally significant. All these analyses will be carried out using IBM SPSS version 21.0 (IBM Corp., Armonk, NY, USA). Additionally, we intend to perform subgroup analysis according to frequency of intervention ($\geq 75\%$ and $< 75\%$).

3. Discussion

The benefits of regular physical exercise to reduce body weight, increase physical fitness indicators (cardiorespiratory and neuromuscular), and adaptations of the biochemical profile and physiological health markers are well propagated in the literature [29,33]. However, few studies have been carried out among individuals with obesity;

therefore, questions remaining this population with respect to periodization, mainly regarding the distribution of the assigned variables, particularly the intensity during the initial periods of training.

Commonly, studies among people with obesity have focused on the different effects between exercise models [8,10,32], with little consideration or complete disregard of periodization, which may provide health benefits for untrained individuals with impaired health conditions [13]. However, one recurrent doubt regarding the organization of training is whether protocols with similar duration and exercises, but with a distinct intensity progression, can generate divergent effects on important health outcomes. Based on this premise, the present study on physical exercise in special populations aims to compare the effect of combined training and non-periodized and linear periodization on markers of health and physical fitness related to the health of adults with obesity. In addition, the study also proposes total volume equivalence between the protocols and assessment of adherence to the physical training program.

Our expectation is to add to the knowledge regarding exercise prescribed for individuals with obesity, and to reveal new possibilities for management of the intervention variables, which can be aligned with and can complement the current recommendations for physical activity to reduce and maintain body weight [42]. Collectively, our major focus is on the possibility that intensity progression, regardless of training volume, may potentiate the positive effects of physical training regarding not only anthropometric, biochemical, and physical fitness variables, but also adherence to training programs. Low adherence to exercise programs is a clinical problem that can be extrapolated to the universe of the population with obesity, and better understanding of how to improve this situation is lacking [43]. Our proposal of more dynamic structuring can promote positive perspectives, which can in turn affect the permanence of participants, a fact of great relevance considering that the time of exposure to exercise is crucial for obtaining and stabilizing the results.

In addition, our results may contribute to instrumentalizing professionals who work directly with prescribed exercises in clinics, fitness studios, and gyms. Although the amount of research on this topic and in this population is emerging, most of the models tested present results that are not applicable in everyday practice, where there is still a tendency to use conservative protocols when it comes to exercise management in people with obesity. Thus, through our hypotheses, we envisage that periodic exercise programs can become more individualized and attractive to people who wish to reduce body weight, maintain the effectiveness of physical training, and promote overall health benefits.

Funding

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.conctc.2019.100358>.

References

- [1] A.F. Godoy-Matos, Síndrome Metabólica. 1ª, Editora Atheneu, São Paulo, 2005.
- [2] G.H. Goossens, The role of adipose tissue dysfunction in the pathogenesis of obesity-related insulin resistance, *Physiol. Behav.* 94 (2008) 206–218.
- [3] A. Zago, A. Jokura, Efeitos do exercício físico no estado inflamatório crônico de baixo grau induzido pela obesidade, *Rev. Odontológica Araçatuba* 24 (2013) 27–32.
- [4] WHO. World Health Organization, Obesity and Overweight, (2018) <http://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight>, Accessed date: 13 November 2018.
- [5] M.L. Oliveira, Estimativa dos custos da obesidade para o Sistema Único de Saúde do Brasil 95 f Tese (Doutorado em Nutrição Humana) - Universidade de Brasília, Brasília, 2013 2013.
- [6] T.A. Wadden, V.L. Webb, C.H. Moran, B.A. Bailer, Lifestyle modification for obesity, *Circulation* 125 (2012) 1157–1170, <https://doi.org/10.1161/CIRCULATIONAHA.111.039453>.
- [7] C.E. Garber, B. Blissmer, M.R. Deschenes, B.A. Franklin, M.J. Lamonte, I.-M. Lee, et al., American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise, *Med. Sci. Sports Exerc.* 43 (2011) 1334–1359, <https://doi.org/10.1249/MSS.0b013e318213f6fb>.
- [8] L. Schwingshackl, S. Dias, B. Strasser, G. Hoffmann, Impact of different training modalities on anthropometric and metabolic characteristics in overweight/obese subjects: a systematic review and network meta-analysis, *PLoS One* 8 (2013), <https://doi.org/10.1371/journal.pone.0082853> e82853.
- [9] A.R. Dâmaso, R.M.S. Campos, D.A. Caranti, A. Piano, M. Fisberg, D. Foschini, et al., Aerobic plus resistance training was more effective in improving the visceral adiposity, metabolic profile and inflammatory markers than aerobic training in obese adolescents, *J. Sport. Sci.* 32 (2014) 1435–1445, <https://doi.org/10.1080/02640414.2014.900692>.
- [10] L.H. Willis, C.A. Slentz, L.A. Bateman, A.T. Shields, L.W. Piner, C.W. Bales, et al., Effects of aerobic and/or resistance training on body mass and fat mass in overweight or obese adults, *J. Appl. Physiol.* 113 (2012) 1831–1837, <https://doi.org/10.1152/jappphysiol.01370.2011>.
- [11] S.J. Fleck, W.J. Kraemer, Fundamentos do treinamento de força muscular, Artmed Editora, 2017.
- [12] J. Grigic, P. Mikulic, H. Podnar, Z. Pedisic, Effects of linear and daily undulating periodized resistance training programs on measures of muscle hypertrophy: a systematic review and meta-analysis, *PeerJ* 5 (2017), <https://doi.org/10.7717/peerj.3695>.
- [13] K. Strohacker, D. Fazzino, W.L. Breslin, X. Xu, The use of periodization in exercise prescriptions for inactive adults: a systematic review, *Prev. Med. Rep.* 2 (2015) 385–396, <https://doi.org/10.1016/j.pmedr.2015.04.023>.
- [14] R.M. Macedo, J.R. Faria Neto, C.O. Costantini, M. Olandoski, D. Casali, A.C.B. de Macedo, et al., A periodized model for exercise improves the intra-hospital evolution of patients after myocardial revascularization: a pilot randomized controlled trial, *Clin. Rehabil.* 26 (2012) 982–989, <https://doi.org/10.1177/0269215512439727>.
- [15] A.-W. Chan, J.M. Tetzlaff, D.G. Altman, A. Laupacis, P.C. Göttsche, K. Krle A-Jerčić, et al., SPIRIT 2013 Statement: defining standard protocol items for clinical trials, *Rev. Panam Salud Publica Pan. Am. J. Public Health* 38 (2015) 506–514.
- [16] A.B.E.S.O. Associação, Brasileira para o Estudo da Obesidade e da Síndrome Metabólica, Diretrizes Brasileiras de obesidade, 2016.
- [17] ACSM. American College of Sports Medicine, Diretrizes do ACSM para os testes de esforço e sua prescrição, ninth ed., Guanabara Koogan, Rio de Janeiro, RJ, 2013.
- [18] C.R. Martins, E.L. Petroski, Insatisfação com a imagem corporal em adolescentes do sexo feminino de uma cidade de pequeno porte: prevalência e correlações, *Motricidade* 11 (2015) 94–106, <https://doi.org/10.6063/motricidade.3670>.
- [19] J.O. Prochaska, B.H. Marcus, The Transtheoretical Model: Applications to Exercise, (1994).
- [20] A.J. Stunkard, The Salmon lecture. Some perspectives on human obesity: its causes, *Bull. N. Y. Acad. Med.* 64 (1988) 902–923.
- [21] R. Ciconelli, M. Ferraz, W. Santos, I. Meinão, M. Quaresma, Tradução para a língua portuguesa e validação do questionário genérico de avaliação da qualidade de vida SF-36 (Brasil SF-36), *Rev. Bras. Reumatol.* 39 (1999) 143–150.
- [22] A.N. Bertolazi, S.C. Fagundes, L.S. Hoff, E.G. Dartora, I.C. da S. Miozzo, M.E.F. de Barba, et al., Validation of the Brazilian Portuguese version of the pittsburgh sleep quality index, *Sleep Med.* 12 (2011) 70–75, <https://doi.org/10.1016/j.sleep.2010.04.020>.
- [23] D.J. Buysse, C.F. Reynolds, T.H. Monk, S.R. Berman, D.J. Kupfer, The Pittsburgh sleep quality index: a new instrument for psychiatric practice and research, *Psychiatr. Res.* 28 (1989) 193–213, [https://doi.org/10.1016/0165-1781\(89\)90047-4](https://doi.org/10.1016/0165-1781(89)90047-4).
- [24] D.H. Clarke, Adaptations in strength and muscular endurance resulting from exercise, *Exerc. Sport Sci. Rev.* 1 (1973) 73.
- [25] I. Levinger, C. Goodman, D.L. Hare, G. Jerums, D. Toia, S. Selig, The reliability of the 1RM strength test for untrained middle-aged individuals, *J. Sci. Med. Sport* 12 (2009) 310–316, <https://doi.org/10.1016/j.jsams.2007.10.007>.
- [26] K.F. Wells, E.K. Dillon, The sit and reach—a test of back and leg flexibility, *Res. Q. Am. Assoc. Health Phys. Educ. Recreat.* 23 (1952) 115–118.
- [27] Fitness Canada, Canadian Standardized Test of Fitness (CSTF) Operations Manual, WRMS, 1992.
- [28] D. Mayorga-Vega, R. Merino-Marban, J. Viciano, Criterion-related validity of sit-and-reach tests for estimating hamstring and lumbar extensibility: a meta-analysis, *J. Sport. Sci. Med.* 13 (2014) 1–14.
- [29] M. Nikseresht, M.R. Hafezi Ahmadi, M. Hedayati, Detraining-induced alterations in adipokines and cardiometabolic risk factors after nonlinear periodized resistance and aerobic interval training in obese men, *Appl. Physiol. Nutr. Metabol.* 41 (2016) 1018–1025, <https://doi.org/10.1139/apnm-2015-0693>.
- [30] M.I. Mackness, P.N. Durrington, B. Mackness, The role of paraoxonase 1 activity in cardiovascular disease: potential for therapeutic intervention, *Am. J. Cardiovasc. Drugs Dev. Interv.* 4 (2004) 211–217, <https://doi.org/10.2165/00129784-200404040-00002>.
- [31] A.M. Jones, J.H. Doust, A 1% treadmill grade most accurately reflects the energetic cost of outdoor running, *J. Sport. Sci.* 14 (1996) 321–327.
- [32] I.L.P. Bonfante, M.P.T. Chacon-Mikahil, D.T. Brunelli, A.F. Gáspari, R.G. Duft, W.A. Lopes, et al., Combined training, FND5/irisin levels and metabolic markers

- in obese men: a randomised controlled trial, *Eur. J. Sport Sci.* 17 (2017) 629–637, <https://doi.org/10.1080/17461391.2017.1296025>.
- [33] D.T. Brunelli, M.P.T. Chacon-Mikahil, A.F. Gáspari, W.A. Lopes, V. Bonganha, I.L.P. Bonfante, et al., Combined training reduces subclinical inflammation in obese middle-age men, *Med. Sci. Sports Exerc.* 47 (2015) 2207–2215, <https://doi.org/10.1249/MSS.0000000000000658>.
- [34] G.J. Balady, R. Arena, K. Sietsema, J. Myers, L. Coke, G.F. Fletcher, et al., Clinician's guide to cardiopulmonary exercise testing in adults: a scientific statement from the American Heart Association, *Circulation* 122 (2010) 191–225.
- [35] L. Choi, Z. Liu, C.E. Matthews, M.S. Buchowski, Validation of accelerometer wear and nonwear time classification algorithm, *Med. Sci. Sports Exerc.* 43 (2011) 357–364, <https://doi.org/10.1249/MSS.0b013e3181ed61a3>.
- [36] P.S. Freedson, E. Melanson, J. Sirard, Calibration of the computer science and applications, Inc. accelerometer, *Med. Sci. Sports Exerc.* 30 (1998) 777–781.
- [37] J. Sasaki, A. Coutinho, C. Santos, C. Bertuol, G. Minatto, J. Berria, et al., Orientações para utilização de acelerômetros no Brasil, *Rev. Bras. Atividade Física Saúde* 22 (2017) 110–126.
- [38] B.S. Burke, The dietary history as a tool in research, *J. Am. Diet. Assoc.* 23 (1947) 1041–1046.
- [39] J.M. Conway, L.A. Ingwersen, A.J. Moshfegh, Accuracy of dietary recall using the USDA five-step multiple-pass method in men: an observational validation study, *J. Am. Diet. Assoc.* 104 (2004) 595–603.
- [40] R.M. Fisberg, B.S. Villar, Manual de receitas e medidas caseiras para cálculo de inquéritos alimentares: manual elaborado para auxiliar o processamento de dados de inquéritos alimentares, (2002).
- [41] J.M. Dodd, A.R. Deussen, J. Louise, Optimising gestational weight gain and improving maternal and infant health outcomes through antenatal dietary, lifestyle and physical activity advice: the OPTIMISE randomised controlled trial protocol, *BMJ Open* 8 (2018), <https://doi.org/10.1136/bmjopen-2017-019583> e019583.
- [42] ACSM. American College of Sports Medicine, Guidelines for exercise testing and prescription 9th ed. 2014, *J. Can. Chiropr. Assoc.* 58 (2014) 328.
- [43] G.A. Bray, G. Frühbeck, D.H. Ryan, J.P.H. Wilding, Management of obesity, *Lancet* 387 (2016) 1947–1956, [https://doi.org/10.1016/S0140-6736\(16\)00271-3](https://doi.org/10.1016/S0140-6736(16)00271-3).