

Scientific background: When exercise training is adequately supervised and adherence is high, it has a therapeutic effect in individuals with prediabetes or type 2 diabetes mellitus (T2DM) (Little et al., 2011; Johansen et al., 2017). Many of the cardiometabolic risk factors associated with T2DM can be improved or ameliorated with weight control and diet, as well as with regular exercise. Indeed, the beneficial effects of high-intensity interval (HIIT) and resistance (RT) training on insulin resistance have been extensively studied at the level of skeletal muscle and adipose tissue (Zanuso et al., 2017). Notwithstanding the irrefutable clinical benefits of exercise in general, there is known to be individual variability in the response to different exercise interventions (Bouchard et al., 2012b), including CT (Stephens et al., 2015). Whereas some individuals, the so-called ‘responders’ improve their metabolic profile after a training intervention (*e.g.*, a decrease in fasting glucose) others, the ‘non-responders’ show no response or even an opposite response (Boulé et al., 2005). From a statistical viewpoint, a non-response for a given variable is a lack of difference between a control and a treatment condition. The non-responder phenomenon has been shown in a non-negligible proportion of participants in exercise intervention studies, for instance, in 4–9% of adults at risk for T2DM (Phillips et al., 2017) or in 21% of patients with T2DM (Stephens et al., 2015). **Objectives:** To investigate the effects of a 20-week CT intervention on cardiovascular risk factors such as body composition, blood pressure and lipid profile among adult women with hyperglycaemia. A secondary aim was to report prevalence of non-responders for the different study outcomes. **Design:** An experimental, and randomized control clinical study. **Methods:** Physically inactive overweight/obese and hyperglycaemic adult women between 20 and 50 years, will be randomly assigned to a 20-weeks of an exercise intervention group or to a control (non-exercise) group. Comorbidities indices for body composition [body mass, waist circumference (WC), fat and lean mass], blood pressure and metabolic profile (total, LDL- and HDL-cholesterol, triglycerides, and fasting glucose) will be assessed before and after the 20-week intervention. The clinical trials will be taken in the Family Healthcare Center *Tomás Rojas* of the city of Los Lagos, Chile, which is a public healthcare centre of this country. We hope to apply the following eligibility criteria a) age between 30 and 59 years, b) not living in a rural area, c) physical activity levels [as assessed by the International Physical Activity Questionnaire (IPAQ) < 600 metabolic equivalents (MET)·min/week, d) non-involvement in regular exercise during the previous 6 months, e) fasting glucose of 100–125 mg/dL, and f) 1+ values above (or below for HDL-cholesterol) normal cutoffs for: body composition [*i.e.*, WC >

80 cm, which denotes ‘high cardiovascular risk’ in South American individuals (Alberti et al., 2009)]; blood pressure [Systolic (SBP) and diastolic blood pressure (DBP) of 130–139 mmHg and 85–90 mmHg, respectively, denoting ‘high blood pressure’, or SBP and DBP >140 mmHg and 90 mmHg, respectively, denoting ‘hypertension’]; or blood lipid profile (*i.e.*, total cholesterol > 200 mg/dL, LDL-cholesterol > 140 mg/dL, HDL-cholesterol < 50 mg/dL, or triglycerides \geq 150 mg/dL). Exclusion criteria were: a) cardiovascular contraindications to exercise, b) history of stroke, asthma or chronic obstructive pulmonary disease, c) muscle-skeletal disorders, and d) smoking. A compliance rate to the exercise program \geq 70% was required for the participants in the intervention group to be included in the statistical analyses.

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Statistical Analysis Plan (SAP): We will apply 2 main forms of statistical analyses a) to report the pre-post changes in mean terms, and b) to report the results according with the inter-individual responses based on the technical error criteria, where according with the error calculated in the three previous measurements registered by the sample that was voluntary. Thus, for example, we will classify the subjects in responders and non-responders by the technical error of measurement, and additionally, we will classify the subjects according with a responder and non-responder clinical criteria, where we will classify as responders to all subjects who can be able of changing an initial adverse clinical altered profile for a healthy new classification. Thus, the specific statistical methods that we hope to apply for each analysis are; test of normality and homoscedasticity assumptions using Shapiro-Wilk and Levene's tests, the Student's *t* test for the identification of differences at baseline. An ANCOVA will be conducted (for potential confounders outcomes) in those altered baseline differences outcomes. We also hope to apply the repeated measures of two-way (group, time) to assess occurrence of an actual training effect [*i.e.*, $p < 0.05$ for the interaction (group \times time) for the different study outcomes]. Among the specific statistical methods we hope to apply the Bonferroni *post hoc* test we hope to apply when we can be seen test differences among groups. Similarly, we hope to apply the Cohen's *d* test in order to detect effect size, using the threshold values of 0.20, 0.60, 1.2, and 2.0 for small, moderate, large, and very large effects, respectively (Hopkins et al., 2009), with 95% confidence intervals (CI). The alpha level was fixed at $P < 0.05$ for statistical significance.