CHOICE Study Protocol with Statistical Analysis Plan

NCT Number: NCT03576924

Document Date: March 3, 2025

Participants

Potentially eligible participants for this trial were referred by their family physician to partake in a community-based DPP (*Small Steps for Big Changes*) if they had a hemoglobin A1c (HbA1c) test within the American Diabetes Association's (ADA) prediabetes range of 5.7%-6.4% in the last 6 months. Potential participants who did not have a recent HbA1c test result but scored a 5 or higher on the ADA diabetes risk assessment were also invited to participate. Advertisements for recruitment included pamphlets in healthcare offices, website adverts, social media posts, and word of mouth. Potential participants were screened by a member of the research team via phone to ascertain if they met the following inclusion criteria: between 18 and 75 years of age, engaged in two or fewer bouts of purposeful physical activity per week in the last 6 months, had a recent HbA1c test result between 5.7%-6.4% or an ADA risk assessment score $\geq$5, and were cleared to engage in physical activity as determined by the Get Active Questionnaire. Participants were excluded from this trial if they had a previous diagnosis of T2D, were taking glucose-lowering medications or beta-blockers, had a history of cardiovascular disease, were diagnosed with uncontrolled hypertension (resting blood pressure >160/90), or had explicit contraindications to exercise. All participants provided written informed consent prior to enrollment.

Predicted Maximal Exercise Testing

Participants who met the eligibility criteria and provided consent subsequently completed a 12-lead electrocardiogram stress test at a local cardiac rehabilitation clinic supervised by a certified exercise physiologist prior to beginning the intervention. Depending on each participant's baseline physical ability and/or comfort level with treadmills, the exercise physiologist employed a Bruce or Modified Bruce protocol for the stress test. Protocol stages

were performed on a treadmill and incremented sequentially every 3 minutes until participants reached volitional exhaustion or the test was stopped by the exercise physiologist according to safety cut-offs (blood pressure >250/120, oxygen saturation <82%, physical concerns). Participants' heart rate, blood pressure, oxygen saturation, and perceived rating of exertion (RPE) were monitored at each stage of the protocol. Stress test results were reviewed by a cardiologist to determine whether exercise was safe for the individual or whether any underlying cardiac issues were present that needed further attention. Additionally, results from the stress test were used to measure each participant's resting heart rate and maximum heart rate (HR_{max}) to calculate individualized exercise intensity zones for the intervention. This test also served to estimate cardiorespiratory fitness based on the total test duration (details found in supplemental material). The 12-lead electrocardiogram test was repeated with each participant 6 months post-intervention to assess changes in cardiorespiratory fitness.

Small Steps for Big Changes

Participants that were cleared to exercise by a cardiologist were enrolled in *Small Steps for Big Changes* (SSBC), a 4-week community-based DPP. The full details of SSBC, including its efficacy and effectiveness in laboratory and community settings have been published previously. Briefly, SSBC consists of six one-on-one sessions with a trained community coach (i.e., fitness professionals working at a recreation facility) over a 4-week period, delivered either virtually or in-person at one of three community recreation facilities. Each session entails a brief behavioral counselling component during which trained coaches use motivational interviewing-informed techniques to foster participants' self-efficacy and determination for changing and maintaining healthy nutritional and physical activity behaviors. Information pertaining to specific content delivered during sessions and fidelity of program delivery by community

coaches has been previously published. Community coaches subsequently follow up with participants 1, 6, and 12 months after the 4-week supervised intervention.

In addition to behavioral counselling, SSBC participants also complete supervised progressive exercise during each of the six sessions. For this trial, SSBC participants provided additional consent for a sub-study for which they were randomly allocated to one of three conditions: HIIT was introduced and performed for all 6 sessions (HIIT-only); MICT was introduced and performed for all 6 sessions (MICT-only); and HIIT and MICT were introduced during sessions 1 and 2 in a randomized counterbalanced order, and participants were provided the choice of which exercise to perform during sessions 3-6 (CHOICE). In all three conditions, participants were able to choose whether to exercise on a treadmill, exercise bicycle, or elliptical. Exercise duration for each session was designed to elicit matching work volumes based on prescribed intensities for both HIIT and MICT during the progressive nature of the intervention. The use of progressive exercise was intended to help familiarize participants with exercise modalities they may not have been familiar with and/or ease the introduction of exercise to those who were previously insufficiently active. Exercise was individualized for each participant by prescribing exercise intensities based on their measured resting heart rate and HR_{max} from the stress test using the Karvonen formula. Exercise intensity compliance was measured during each exercise session via heart rate monitors and participants' RPE. Exercise intensity was recorded by the supervising community coach at the beginning and at 25%, 50%, and 100% of exercise completion, and coaches encouraged participants to adjust speed, resistance, or incline if target heart rate was not achieved. Following the 4-week supervised intervention, participants in all three conditions were encouraged to continue performing MVPA on their own according to Canada's physical activity recommendations for adults but were not told to exclusively perform

either HIIT or MICT due to the pragmatic nature of the SSBC program and this trial. Apart from condition allocation, all other aspects of the DPP were identical for all three conditions.

High-Intensity Interval Training. Participants who were randomized to the HIIT-only condition began each exercise session with a 3-minute warmup at a comfortable self-selected pace. During sessions 1 and 2, participants completed five 30-second intervals >80% HR_{max} interspersed by four 60-second periods of light recovery at a self-selected pace. For sessions 3 and 4, duration of high-intensity intervals increased from 30 seconds to 45 seconds, and for sessions 5 and 6, duration was increased again to 60 seconds, so that by the end of the supervised intervention, participants were completing five 60-second intervals interspersed by four 60-second recovery periods. All sessions concluded with a 2-minute cooldown. Including warmup and cooldown, the total duration of sessions ranged between 11.5 to 14 minutes for sessions 1 to 6, respectively.

Moderate-Intensity Continuous Training. Participants who were randomized to the MICT-only condition exercised continuously for 20 minutes at an intensity between 60%-80% HR_{max} during sessions 1 and 2. Duration of exercise was increased to 25 minutes for sessions 3 and 4, and to 30 minutes for sessions 5 and 6. There were no warmup or cooldown periods, resulting in total session durations ranging from 20 to 30 minutes for sessions 1 to 6, respectively.

Choice. Participants who were randomized to the CHOICE condition were introduced to either HIIT or MICT during session 1 and introduced to the other exercise modality during session 2. The introduction order of HIIT or MICT was randomized in a counterbalanced fashion to diminish potential anchoring bias. HIIT and MICT protocols were the same as in the other two conditions, and progression of exercise followed the same convention.

Outcomes

For full details regarding outcome measures of this trial, please refer to the trial registry details. Briefly, individuals' perceived autonomy support was measured post-intervention to discern any differences between conditions. Within-condition changes in motivation regulation from pre-intervention were assessed post-intervention and 6-months post-intervention. Within-condition changes in free-living physical activity and cardiorespiratory fitness were assessed from pre-intervention to 6-months post-intervention. Between-condition differences were also assessed at each timepoint for motivation regulation, physical activity, and cardiorespiratory fitness. A manipulation check was conducted with a sub-set of participants to determine the modality of exercise that participants engaged in during the 6-month follow-up period.

Changes Consequent to COVID-19

Recruitment for this trial commenced in February 2019 using a monthly rolling recruitment strategy (~6-10 participants/month). Originally, follow-up appointments were planned to discern changes in the outcome variables 12 months post-intervention. However, at the beginning of the 12-month follow-up phase (February 2020), the COVID-19 pandemic resulted in the curtailment of all research activities at the host institution. A total of 75 participants were not able to complete follow-up assessments, and data were therefore lost for this first cohort. Recruitment for this trial could not be resumed until October 2021. To complete data collection in a timely manner given these unanticipated resource constraints, follow-up assessments were conducted 6 months post-intervention for this second cohort as opposed to the original 12-month timepoint. The complete loss of data on the first 75 participants to enroll in the trial and subsequent curtailment of research for more than 1.5 years therefore significantly limited the final study sample size.

Sample Size

Limited studies have been conducted that assess perceived autonomy support after adults are provided a choice between different types of exercise in an intervention. A study by Lonsdale and colleagues assessed the change in perceived autonomy support among adolescents enrolled in physical education programs. Comparisons between the control group (treatment as usual) and a group that was provided choice in what exercises were performed during class demonstrated a small-to-medium effect favoring the choice group (d = 0.39). Based on these results, we anticipated a crude small-to-medium effect size in favor of the choice condition in the present study (d = ~0.40). At an alpha level of .05 and 80% power, we estimated that 60 participants per condition (n = 180) were required to detect significant between-condition differences at this magnitude. Based on pilot findings by Locke and colleagues, this sample size was then increased by 20% to account for participant attrition, resulting in a total sample size of 216. The severe COVID-19 pandemic limitations impacted the ability to achieve the estimated sample size and data are thus reported for N = 77.

Randomization

SSBC participants were randomly allocated into one of the three arms of this study in a 1:1:1 allocation ratio by using a computer random-number generator that produced variable permuted block sizes. Conditions were stratified for biological sex (male and female) and age (18-45 and 46-75 years). Allocation sequencing was performed by a member of the research team not involved in any other aspect of this trial and allocation was concealed from participants until they began the intervention.

Blinding

Given the pragmatic nature of this trial and the fact that participants and community coaches needed to know which exercise modality to engage in during the exercise sessions, blinding of participants and those delivering the intervention was not possible. Data collected for each participant were blinded during data analysis by replacing the name of the allocated condition with a numerical digit known only to a member of the research team not involved in the data analysis phase so that data analysts would not be biased by condition allocation.

Statistical Methods

Statistical analyses were performed using R (version 4.3.0) or SPSS (version 28). Anthropometric and demographic information were summarized as means (standard deviations) for continuous data and N (%) for categorical data, unless otherwise stated. Medians and ranges are reported for 6-month exercise modality frequency to represent the central tendency and dispersion more accurately.

Blinded data analysis was completed on an intention-to-treat (ITT) basis as all randomized participants were included in the analyses irrespective of their program compliance. No missing data were imputed as per contemporary guidelines. A linear model with restricted maximum likelihood estimation (REML) was used to detect a between-condition difference in perceived autonomy support post-intervention. The model included treatment condition (i.e., HIIT, MICT, or CHOICE) as a fixed factor, and stratified allocation factors (i.e., age and biological sex) as covariates. Similarly, linear mixed models were used to analyze changes in motivation regulation, physical activity behavior, and cardiorespiratory fitness between conditions. Linear mixed models included fixed effects for timepoint (pre-intervention, post-intervention, 6 months post-intervention), treatment condition, as well as the interaction thereof, stratified allocation factors, and a random effect for participants to address non-independence of

measurements arising due to the repeated-measures design of this study. Model assumptions were assessed visually using normal probability plots and residuals vs. fitted values plots (i.e., homoscedasticity). Bonferroni-adjusted preplanned pairwise comparisons of estimated marginal means were conducted to derive effect estimates and accompanying 95% confidence intervals (CIs) after adjusting for included covariates. A two-sided alpha of .05 was used for all statistical analyses.