Aerobic Exercise Training Modalities and Prediabetes Risk Reduction

CHIP P. ROWAN[1], MICHAEL C. RIDDELL[1,2], NORMAN GLEDHILL[1], and VERONICA K. JAMNIK[1]

[1]York University, School of Kinesiology and Health Science, Toronto, ON, CANADA; and [2]LMC Diabetes and Endocrinology and Manna Research, Toronto, ON, CANADA

ABSTRACT

ROWAN, C. P., M. C. RIDDELL, N. GLEDHILL, and V. K. JAMNIK. Aerobic Exercise Training Modalities and Prediabetes Risk Reduction. *Med. Sci. Sports Exerc.*, Vol. 49, No. 3, pp. 403–412, 2017. **Purpose**: Prediabetes is linked to several modifiable risk factors, in particular, physical activity participation. The optimal prescription for physical activity remains uncertain. This pilot study aimed to investigate the effectiveness of continuous moderate intensity (CON) versus high-intensity interval training (HIIT) in persons with prediabetes. Outcome measures included glycated hemoglobin (A1C), body composition, musculoskeletal and aerobic fitness. **Methods**: Participants (n = 35) were recruited and screened using a questionnaire plus capillary blood point-of-care A1C analysis. After baseline screening/exclusions, 21 participants were randomly assigned to either HIIT or CON training three times per week for 12 wk. All participants also undertook resistance training two times per week. A1C, an oral glucose tolerance test, select measures of physical and physiological fitness were assessed at baseline and follow-up. **Results**: There were no significant differences in improvements in select metabolic indicators to training between CON and HIT groups. Pooled participant data showed a mean reduction in A1C of 0.5% (95% confidence interval [CI] = 0.3%–0.7%), whereas β-cell function (%β) improved by 28.9% (95% CI = 16.5%–39.2%) and insulin sensitivity (%S) decreased by 34.8 (95% CI = 57.8%–11.8), as assessed by the Homeostatic Model Assessment. Significant reductions in waist circumference of 4.5 cm (P < 0.001) and a 20% (P < 0.001) improvement in aerobic fitness were also observed in both training groups. **Conclusion**: The completion of a 12-wk exercise program involving both resistance training and either HIIT or CON training results in improved glycemic control, visceral adiposity, and aerobic fitness in persons with prediabetes. **Key Words:** A1C, GLYCEMIC CONTROL, PHYSICAL ACTIVITY, FITNESS, HOMA

There is overwhelming evidence to support the importance of both habitual physical activity (PA) participation and structured exercise for the prevention of many chronic conditions, including type 2 diabetes (T2D) and cardiovascular disease (CVD) (23,42,48). In the United States, it is currently estimated that ~9.3% of the general population have diabetes, whereas ~37% of all adults 20 yr or older have the antecedent to T2D, prediabetes (8). The resultant economic effect to the United States is substantial with an estimated cost of $322 billion in 2012 encompassing both direct medical costs ($244 billion) and indirect costs ($78 billion) to these common metabolic conditions (11). In Canada, similar trends have been shown, and the expected number of diagnosed T2D cases will be 3.7 million by the year 2019 resulting in direct and indirect costs of ~$16.9 billion by 2020 (7). These widely published statistics emphasize an overwhelming need to develop effective intervention strategies that are cost-effective and prediabetes-specific. Prediabetes is associated with several modifiable risk factors, most notably all facets of PA participation (both exercise and nonexercise related), diet, and body composition (1). Addressing these factors with the goal of preventing and/or delaying the onset of T2D has been shown to result in significant reductions in diabetes risk in several populations (23,29,42).

Several previous clinical trials have targeted persons with prediabetes with lifestyle modification, all with encouraging results (23,29,42). It is important to note, however, that many of these earlier studies were primarily education-based interventions geared toward both diet and PA participation with limited supervision of the PA component. Relatively less is known regarding the effect of structured exercise-only based interventions on specific markers of glycemic control, such as glycated hemoglobin (A1C), in persons with prediabetes. The acute and chronic effects of supervised exercise training are not fully understood among persons with prediabetes, and further exploration into the physiological and anthropometric adaptations that occur using different training modalities is of interest. There are several well-established mechanisms through which both aerobic and resistance-based exercise can benefit persons with prediabetes via improved insulin sensitivity, including enhanced endothelial function, reductions in

Address for correspondence: Veronica K. Jamnik, Ph.D., School of Kinesiology and Health Science, York University, 4700 Keele St., Toronto, ON M3J 1P3, Canada; E-mail: ronij@yorku.ca.
Submitted for publication August 2016.
Accepted for publication October 2016.

0195-9131/17/4903-0000/0
MEDICINE & SCIENCE IN SPORTS & EXERCISE®

DOI: 10.1249/MSS.0000000000001135

adiposity, increased GLUT4 content and function, increased lean tissue mass, and improved oxidative and nonoxidative glucose metabolism (6). Formulating a focused exercise prescription to take advantage of these mechanisms and improve one's ability to prevent or delay T2D is very attractive and should be a priority.

High-intensity interval or intermittent training (HIIT) is not a novel concept, with roots tracing back at least to the 1970s (14). Recently, however, it has become a popular alternative to the more traditional moderate intensity continuous aerobic (CON) training approach among healthy individuals (16) as well as several clinical human populations such as those with heart failure, coronary artery disease, and postmyocardial infarction (34,44,46). It is important to use caution, however, when interpreting the findings from HIIT interventions given the high degree of variability in approaches, which can all be considered HIIT. All HIIT approaches incorporate an exercise intensity that is ≥80% HR_{max} and can range from very short maximal effort sprint intervals lasting 30–60 s followed by either a brief passive rest or light intensity active recovery period (17,18) or longer lasting 2- to 4-min work bouts followed by either a longer passive rest or light intensity active recovery periods (22). Evidence from studies using comparable HIIT approaches to that used in the present study indicate that HIIT is a safe and effective method for improving cardiorespiratory fitness, improving health-related quality of life, improving exercise capacity, enhancing anaerobic tolerance, reducing blood pressure, improving blood lipid profiles, and improving insulin sensitivity among persons with lifestyle-induced cardiometabolic chronic diseases (34,44,46,47). HIIT also appears effective in improving select metabolic indicators, particularly in those at risk of or with T2D (21), but additional studies are needed to confirm these results, particularly in those who also perform resistance-based training (RT).

The primary aim of this pilot study was to investigate the effectiveness of HIIT versus CON training on glycemic control, as measured by A1C, in persons with prediabetes who also perform RT. A secondary aim was to examine how these two very different modalities of exercise (CON vs HIIT) affect body composition, musculoskeletal and aerobic fitness in this population. It was hypothesized that both training modalities would induce positive changes with the HIIT group showing greater improvement in select metabolic indicators and overall fitness.

METHODS

For this randomized 12-wk exercise intervention only study (i.e., no dietary intervention), participants were recruited from the York University staff population via e-mail distribution of project materials to staff contact lists and through advertisement in the campus daily e-newsletter. Men and women, age 30–65 yr, were eligible to participate if their A1C value fell within the prediabetes range (5.7%–6.4%) as defined by the American Diabetes Association (ADA) (2). Participants were ineligible if they had already been diagnosed with diabetes, if their A1C value exceeded 6.4%, if they were currently involved in a structured exercise regimen, or if they had a musculoskeletal constraint preventing them from fully participating in the exercise intervention. All participants completed the Physical Activity Readiness Questionnaire For Everyone (PAR-Q+) and, if required because of a positive response on the PAR-Q+, the follow-up ePARmed-X+ (www.eparmedx.com) (5,31,45). All protocols were approved by the York University Human Participants Research Subcommittee and Biosafety Officer, and all participants provided written informed consent.

A total of 73 participants responded to the advertisement during the recruitment phase of which 35 had their A1C assessed. From this group, 21 were eligible for participation in the exercise intervention based on having an A1C in the prediabetes range (5.7%–6.4%). These 21 participants were stratified based on sex and then randomly assigned to either the CON or HIIT intervention groups. Randomization was performed using a random number generator in Microsoft Excel. There were no significant adverse events observed during the testing or exercise interventions of this study, other than muscle soreness.

Blood testing protocols. Fingerstick capillary blood was collected using sterile techniques, and A1C was analyzed using the Bio-Rad in2it (Bio-Rad Laboratories, Hercules, CA) point-of-care device, which performs boronate affinity chromatography. A1C was selected as the primary biomarker because it provides a rolling 3-month indicator of glycemic control, it is less variable than fasted blood glucose sampling, and it does not require the participant to be fasted. Previous work from this laboratory has shown that there were no significant biases between values from the in2it device used and those analyzed using the gold standard high-performance liquid chromatography (33).

During the second visit to the laboratory, a 2-h oral glucose tolerance test was performed to confirm the findings regarding glycemic control. After arriving in a fasted state (no food or caloric drinks for a minimum of 8 h prior), fingerstick capillary blood was collected and whole blood glucose was analyzed using the OneTouch UltraMini blood glucose monitoring system (LifeScan Canada Ltd., BC, Canada), and a second sample of approximately 200 μL was collected from the same fingerstick via microvette. The second sample was centrifuged, and plasma was separated and stored −18°C for the analysis of insulin. The insulin samples were analyzed using a Human Insulin ELISA kit (Abcam®, Cambridge, MA). After the fasting samples were collected, participants consumed a 75-g glucose beverage (Trutol™; Thermo Scientific, USA) within a 5-min period and were then asked to remain seated and refrain from activity during the remainder of the protocol. After 2 h, participants provided a second fingerstick blood sample from a different finger, and both the blood glucose and the insulin samples were collected. HOMA-%β and HOMA-%S were calculated by using the Oxford University HOMA Calculator (www.dtu.ox.ac.uk/homacalculator) according to Wallace et al. (43). Upon completion of the 36 exercise sessions, all participants aimed to provide follow-up blood tests within 4 d of completing the final exercise session. The median time between exercise session 36 and follow-up blood test date was 4 d with an interquartile range of 2. The median time between the blood testing follow-up visit and the follow-up fitness visit was 2 d with an interquartile range of 1.

Health-related physical and physiological fitness assessment and body composition. During a third baseline laboratory visit, resting blood pressure (BP) and HR were measured with participants in a seated position using the BpTRU^{TM} electronic monitor (BpTRU^{TM} Medical Devices Ltd., BC, Canada), which performed six cycles of BP and HR measurement, each separated by 1 min allowing for the calculation of an average value for each. Participants then had their height measured using a stadiometer. Body mass and percent body fat were measured using a bioelectrical impedance analysis scale (BF-350; Tanita Corporation of America, Arlington Heights, IL) (41). Waist circumference was measured by the same tester for all participants via anthropometric tape following the National Institutes of Health (NIH) protocol (20). Grip strength was measured using a hand grip dynamometer (Takei T.K.K. 5401, Niigata, Japan), and vertical jump was measured using the Vertec device (JumpUSA, Sunnyvale, CA). Peak leg power was calculated using the Sayers equation (35). Aerobic fitness ($\dot{V}O_2$ peak) was assessed via an incremental to maximum treadmill walking/jogging protocol, and $\dot{V}O_2$ was measured by analysis of expired gas using open-circuit spirometry (S-3A/II oxygen, CD-3A carbon dioxide; AEI Technologies, Pittsburgh, PA). HR was monitored throughout the aerobic fitness test and during all exercise sessions via the Polar monitoring system (Polar Electro Canada, QC, Canada).

The treadmill protocol was adapted from that of Ebbeling et al. (13), in which the participant initially walks for 4 min at 0% grade to determine a walking speed that is safe and comfortable to elicit an HR between 50% and 70% age-predicted HR_{max}. Participants then walked for an additional 4 min at 5% grade at the same walking speed. After the second 4-min workload, participants completed a series of 2-min intervals at the same walking speed while adding 2% grade each interval until the test was terminated. Aerobic fitness test termination was determined by volitional fatigue. Participants were also offered an opportunity to complete an additional workload after a 2- to 3-min active recovery period at the end of their continuous incremental to maximum aerobic fitness test in an attempt to achieve a higher $\dot{V}O_{2peak}$. Participants followed the identical treadmill protocol during their final assessment with additional workloads completed following the same loading sequence if the participant was able to exceed his or her baseline termination point. Upon completion of all 36 exercise sessions, all participants aimed to complete all parts of the baseline fitness assessment within 4 d of completing their final exercise session. The median time between the follow-up fitness assessment and the last exercise session (session 36) was 2 d with and an interquartile range of 1 d.

Exercise intervention. Participants were randomly assigned to one of two different structured and supervised exercise interventions that included both aerobic (CON or HIIT) and RT. The RT portion was identical for both CON and HIIT groups and included full-body movements with and without dumbbells, medicine balls, and kettlebells. The RT portion was designed to act as a secondary exercise component, aimed at engaging more muscle mass, enhancing joint mobility, and improving insulin sensitivity rather than increasing overall muscle mass and strength. The 36 supervised exercise sessions were completed in an average of 16.6 wk.

Aerobic training component. Group 1 performed HIIT on a motor-driven treadmill. Participants were required to complete supervised exercise sessions in the laboratory three times per week for a total of 36 sessions. After a 5-min warm-up on the treadmill, a series of four high-intensity intervals were performed at 90% HR reserve (HRR), each lasting 4 min and separated by 3 min of active recovery at 50%–60% HRR. HRR was selected for the exercise prescription because of the variability in resting HR among the participants. In all cases, the use of %HRR allowed participants to exercise at a slightly higher intensity when compared with their $\%HR_{max}$. The %HRR prescription for each participant was calculated using the resting HR and HR_{max} directly measured during their baseline fitness assessment. The total "active component" of the HIIT protocol lasted 28 min. Upon completion of the four intervals, a 5-min cooldown took place followed by the RT component during two of the three weekly training sessions.

Group 2 performed CON exercise on a motor-driven treadmill. Similar to Group 1, supervised sessions were completed in the laboratory three times per week until 36 sessions were completed (i.e., two or three times per week). After a 5-min warm-up on the treadmill, participants exercised at their designated moderate intensity (60%–70% HRR) for a period of 28 min. This was followed by an active cooldown on the treadmill lasting 5 min and completion of the RT component during two of the three weekly training sessions.

All sessions for both groups were supervised by a qualified exercise professional with HR monitoring taking place every minute. If participants were not meeting their prescribed HR targets, adjustments to the treadmill took place to ensure the prescribed exercise intensity was being attained.

RT component. All participants, regardless of their randomly assigned aerobic exercise training modality, performed RT on two of the three training sessions per week immediately after their aerobic fitness session. Exercises were selected to include large muscle groups and multiple joints. The exercises were arranged in a circuit, and the participants were asked to perform as many repetitions as possible within a given time while maintaining proper breathing technique. One to two sets of the circuit were performed during each RT session. The qualified exercise professionals supervising these sessions progressed the training stimulus on the participants on an individualized basis by adding resistance to the movements or by increasing their time, thereby requiring more repetitions to complete each component of the circuit. The circuit consisted of full-body movement exercises, including marching on the spot with high knees, squats with an overhead kettlebell press, push-ups (or modified wall push-ups), forearm plank, step-ups with a medicine ball shoulder press, quadra-ped (aka Bird-Dog), wall sit with isometric medicine ball front hold, and stair climb. This type of RT regimen was selected over traditional weight machines because of the fully body movement requirements, which engage a larger muscle mass, enhanced joint mobility, and allow participants to self-select their progressive effort for the 36-wk period.

Statistical analyses. An *a priori* sample size calculation was performed (PASS 14, NCSS Statistical Software, UT) using previously reported differences in A1C (36) to detect a 0.65 SD difference between groups, with a resultant total sample of 88 required to detect temporal changes in A1C with 80% statistical power. This calculation was based on the desired comparison between the HIIT and the CON groups using repeated-measures ANOVA. It should be noted that only 21 participants from the initial 73 recruited met the inclusion criteria based on blood test scores falling out of the desired range. Participant characteristics were analyzed using an independent samples *t*-test to assess potential differences between exercise intervention groups at baseline. Blood and fitness data were analyzed using repeated-measures ANOVA to assess within (baseline vs follow-up) and between (CON vs HIIT) mode differences. Bonferroni adjustment was used for comparisons of estimated marginal means. The ANOVA included age and sex as covariates in the model. Assumptions of normality and heterogeneity of variance were tested for all variables. All analyses described in this investigation were performed using IBM SPSS version 22 (IL) and Graphpad Prism 7 (CA) using a two-sided 5% level of significance.

RESULTS

The results of the randomization allocated 11 participants (3 males and 8 females) into the HIIT exercise group and 10 participants (3 males and 7 females) into the CON group. Figure 1 shows the flow of participants from recruitment to study completion.

Blood testing results. Select baseline participant characteristics are summarized in Table 1. No significant differences between the two groups were observed for any measured variables at baseline. A mean total group A1C value of 6.2% was observed while the results of the oral glucose tolerance test revealed mean fasting glucose and mean 2 h glucose values of 6.0 and 8.1 mmol·L^{-1}, respectively.

Postintervention blood testing indicated no between-group differences (HIIT vs CON) for any of the blood variables measured. However, significant within-group pre- versus postimprovements were observed in A1C and fasting glucose. A summary of blood test outcomes is contained in Table 2 and visually displayed in Figure 2. HOMA-%S decreased from baseline to follow-up (−34.8%S, 95% confidence interval [CI] = −57.8 to −11.8, P = 0.006). HOMA-%β showed significant and similar improvements post-CON and HIIT intervention (+28.9%B, 95% CI = 18.1–39.6, P < 0.001), which is indicative of improved β-cell function.

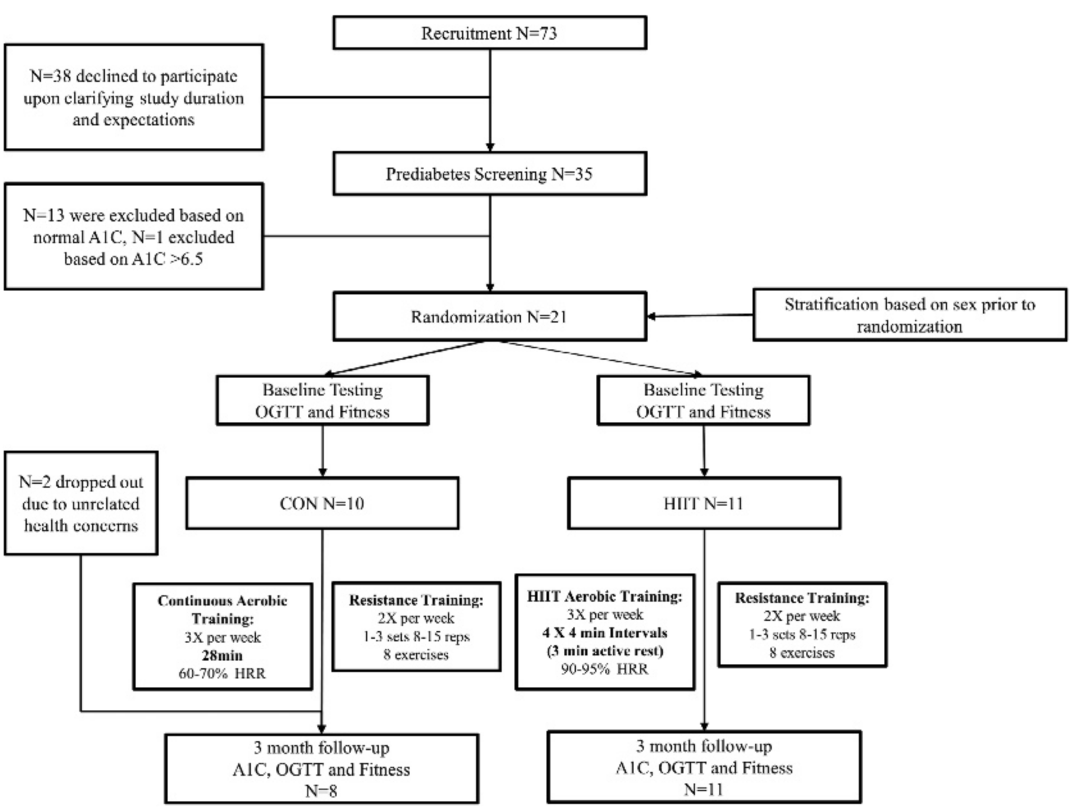

FIGURE 1—Participant flow from recruitment to postassessment, including randomization and descriptions of the two intervention arms.

TABLE 1. Select baseline participant physical characteristics, fitness, and blood test results reported by randomly assigned intervention group.

Variable	Group	N	Mean	SD	P (HIIT vs CON)	95% CI Lower	95% CI Upper
Age (yr)	CON	10	47.7	6.93	0.1	−12.83	1.13
	HIIT	11	53.6	8.21			
	Combined	21	50.8	8.02			
Body mass index (kg·m^{-2})	CON	10	30.8	8.49	0.69	−7.35	4.95
	HIIT	11	32.0	4.61			
	Combined	21	31.4	6.59			
NIH waist circumference (cm)	CON	10	105.4	20.06	0.88	−16.43	14.23
	HIIT	11	106.5	10.72			
	Combined	21	106.0	15.46			
A1C (%)	CON	10	6.1	0.27	0.3	−0.49	0.16
	HIIT	11	6.3	0.42			
	Combined	21	6.2	0.36			
Fasting glucose (mmol·L^{-1})	CON	10	5.8	0.61	0.16	−1.14	0.21
	HIIT	11	6.2	0.85			
	Combined	21	6.0	0.77			
2 h glucose (mmol·L^{-1})	CON	10	7.9	1.27	0.67	−2.41	1.59
	HIIT	11	8.3	2.8			
	Combined	21	8.1	2.17			
HOMA-%β	CON	10	70.6	30.5	10.7	−14.0	35.3
	HIIT	11	59.9	23.3			
	Combined	21	65.0	26.9			
HOMA-%S	CON	10	127.9	62.5	2.3	−67.2	62.6
	HIIT	11	130.2	77.8			
	Combined	21	129.1	69.1			
Resting systolic blood pressure (mm Hg)	CON	10	119.8	15.8	0.2	−25.14	5.65
	HIIT	11	129.6	17.72			
	Combined	21	124.9	17.15			
Resting diastolic blood pressure (mm Hg)	CON	10	76.6	6.75	0.2	−12.78	2.89
	HIIT	11	81.6	9.92			
	Combined	21	79.2	8.73			
Peak HR (bpm)	CON	10	169.9	24.48	0.9	−17.06	19.23
	HIIT	11	168.8	9.92			
	Combined	21	169.3	17.87			
Relative $\dot{V}O_{2peak}$ (mL·kg^{-1}min^{-1})	CON	10	25.1	10.71	0.86	−7.26	8.6
	HIIT	11	24.4	4.29			
	Combined	21	24.8	7.81			

P values represent baseline between-group comparisons.

Health-related physical plus physiological fitness results. Baseline assessments of fitness and body composition, summarized in Table 1, indicate that the participants possessed characteristics typically associated with a high-risk profile for CVD and diabetes. A mean BMI of 31.4 kg·m^{-2} coupled with a mean waist circumference of 106 cm indicates that this group of participants were classified as obese with high-central adiposity. Baseline aerobic fitness results showed

TABLE 2. Blood test results of the repeated-measures ANOVA showing within-group differences before and after the two intervention groups.

Variable	Group	n	Before	n	After	Within-Group Changes	95% CI Lower	95% CI Upper	P
A1C (%)	CON	10	6.1	8	5.7	−0.5*	−0.8	−0.2	0.01
	HIIT	11	6.2	11	5.7	−0.6*	−0.8	−0.3	0.00
	Combined	21	6.2	19	5.7	−0.5*	−0.7	−0.3	<0.001
Fasting glucose (mmol·L^{-1})	CON	10	6.0	8	5.6	−0.3	−0.7	0.2	0.19
	HIIT	11	6.2	11	5.7	−0.5*	−1.0	−0.1	0.03
	Combined	21	6.1	19	5.7	−0.4*	−0.7	−0.1	0.01
Fasting insulin (pmol·L^{-1})	CON	10	15.6	8	15.8	−1.2	−12.1	9.8	0.81
	HIIT	11	9.6	11	10.8	2.2*	0.4	4.0	0.02
	Combined	21	12.6	19	13.3	0.7	−3.6	5.0	0.74
2 h glucose (mmol·L^{-1})	CON	10	8.1	8	7.8	−0.6	−1.9	0.7	0.34
	HIIT	11	8.3	11	8.2	0.2	−1.3	1.6	0.83
	Combined	21	8.2	19	8	−0.2	−1.1	0.8	0.70
2 h insulin (pmol·L^{-1})	CON	10	61.2	8	43.6	−19.4	−45.4	6.6	0.12
	HIIT	11	35.8	11	29.4	−5.1	−22.0	11.8	0.52
	Combined	21	48.5	19	36.5	−12.0	−26.4	2.4	0.10
HOMA-%β	CON	10	70.57	8	109.4	35.0*	13.7	56.3	0.006
	HIIT	11	59.9	11	82.6	22.7*	4.9	40.5	0.02
	Combined	21	65.0	19	93.9	28.9*	18.1	39.6	<0.001
HOMA-%S	CON	10	127.9	8	76.1	−35.5*	−60.2	−10.8	0.01
	HIIT	11	130.2	11	95.1	−35.1*	−70.3	−0.1	0.05
	Combined	21	129.1	19	87.1	−34.8*	−57.8	−11.8	0.006

There were no between-group differences observed for any measured outcomes (CON vs HIIT).
*$P < 0.05$.

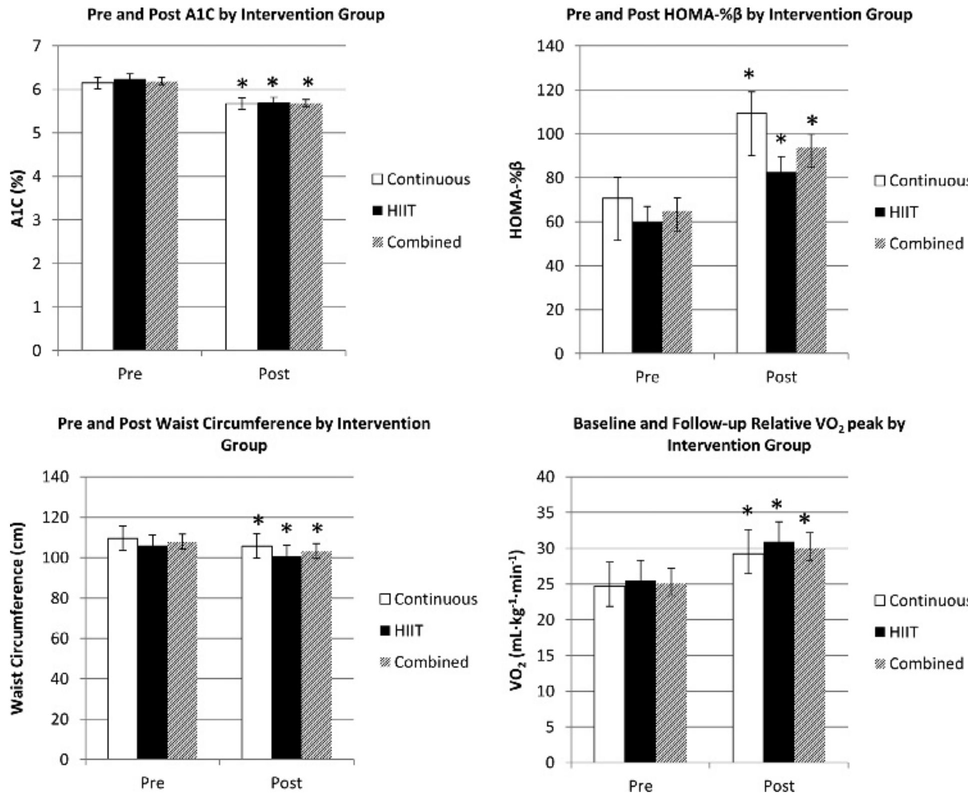

FIGURE 2—Summary of select significant blood and fitness results (mean ± SEM) showing temporal changes in both intervention groups and when the groups were combined (*Improvements from baseline to post, $P < 0.05$).

a mean $\dot{V}O_{2peak}$ of 24.8 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$, which is equivalent to approximately 7 METs. This is in line with previously described populations classified as having a low level of baseline aerobic fitness (4).

Postintervention fitness assessment revealed no significant differences between the HIIT and the CON groups posttraining. When examining the within-group pre- to postchanges, significant improvements were observed for waist circumference (−4.5 cm), vertical jump (+2.6 cm), both absolute and relative $\dot{V}O_{2peak}$ (+0.4 $L{\cdot}min^{-1}$ and +5.0 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$, respectively), and time on treadmill during the aerobic fitness test (+4.8 min). A summary of fitness assessment outcomes is provided in Table 3 and is visually depicted in Figure 2. Figure 3 shows individual participant data for $\dot{V}O_{2peak}$, A1C, HOMA-%β, and HOMA-%S. The participants are ranked based on their change in $\dot{V}O_{2peak}$ postintervention.

Participant adherence. All participants completed 36 supervised exercise sessions for an average of 16.6 wk. It should be noted that this time frame included a 2-wk period for the December holidays during which participants did not undergo their laboratory training sessions. They were encouraged to be active but not to deviate from their typical lifestyle habits (diet and PA participation) throughout this period.

Participants were asked, apart from the supervised exercise intervention, to maintain their typical lifestyle habits for the entire duration of the study. A self-report questionnaire was completed by participants after the conclusion of the intervention to ascertain if they did or did not alter their lifestyle beyond their participation in the study. The questionnaire revealed that for 9 of 15 participants, non–exercise-related activities (activities of daily living, active commuting, etc.) remained the same or decreased during the study. The questionnaire also indicated that 13 of 15 participants noted that their participation in structured exercise sessions outside their participation in the study either stayed the same or decreased. When asked about dietary habits, 7 of 15 participants noted that their diet was only slightly healthier during their participation in the study, whereas the remaining 8 participants noted that their diet remained constant or was less healthy. Finally, 9 of 15 participants perceived their overall lifestyle to be healthier during their participation in the study, whereas the remaining 6 participants reported that their overall lifestyle did not change. None of the participants reported a perception of having a less healthy lifestyle.

DISCUSSION

The primary finding from this study is that, in both intervention groups, there was a significant improvement in A1C but there were no significant differences between the two modalities of aerobic training. The observed exercise-induced improvements in glycemic control, as measured by A1C, were corroborated by a significant reduction in fasting glucose

TABLE 3. Fitness results of the repeated-measures ANOVA showing within-group differences before and after the two intervention groups.

Variable	Group	*n*	Before	*n*	After	Within-Group Changes	95% CI Lower	95% CI Upper	*P*
Weight	CON	10	90.1	8	89.8	−0.7	−2.6	1.2	0.42
	HIIT	11	88.6	11	87.5	−0.8	−2.0	0.4	0.18
	Combined	21	89.3	19	88.6	−0.7	−1.6	0.2	0.13
BMI ($kg{\cdot}m^{-2}$)	CON	10	32.2	8	32	−0.3	−0.9	0.4	0.37
	HIIT	11	31.9	11	31.6	−0.3	−0.7	0.2	0.19
	Combined	21	32.1	19	31.8	−0.3	−0.6	0.1	0.11
Body fat (Tanita) (%)	CON	10	36.8	8	36.3	−0.4	−2.4	1.6	0.67
	HIIT	11	37.8	11	37.7	−0.2	−1.0	0.7	0.72
	Combined	21	37.3	19	37	−0.3	−1.1	0.6	0.52
NIH waist circumference (cm)	CON	10	109.6	8	105.6	−4.3*	−7.7	−1.0	0.02
	HIIT	11	106.0	11	100.9	−4.8*	−8.0	−1.5	0.01
	Combined	21	107.8	19	103.3	−4.5*	−6.8	−2.2	0.00
Resting HR (bpm)	CON	10	77.7	8	74	−4.3	−15.8	7.3	0.41
	HIIT	11	78.3	11	72.3	−5.6	−12.9	1.6	0.11
	Combined	21	78.0	19	73.1	−4.9	−10.8	1.1	0.10
Resting systolic blood pressure (mm Hg)	CON	10	114.4	8	116.8	1.6	−2.2	5.5	0.35
	HIIT	11	129.3	11	128.7	−0.1	−5.3	5.1	0.97
	Combined	21	121.9	19	122.8	0.9	−2.3	4.1	0.57
Resting diastolic blood pressure (mm Hg)	CON	10	75.1	8	76.7	0.9	−3.1	4.9	0.62
	HIIT	11	81.7	11	78.5	−2.6	−8.1	2.8	0.30
	Combined	21	78.4	19	77.6	−0.8	−4.3	2.7	0.64
Combined hand grip (kg)	CON	10	62.4	8	67.4	4.5	−3.2	12.3	0.21
	HIIT	11	68.2	11	69.8	1.9	−2.2	6.0	0.32
	Combined	21	65.3	19	68.6	3.3	−0.6	7.2	0.09
Vertical jump (cm)	CON	10	21.4	8	25.3	1.8	−0.1	3.7	0.06
	HIIT	11	24.5	11	25.8	0.3	−1.1	1.7	0.62
	Combined	21	23.0	19	25.6	2.6*	0.1	5.2	0.05
Sayers peak leg power (W)	CON	10	2399.1	8	2697.9	79.4	−63.2	222.3	0.23
	HIIT	11	2483.4	11	2466.9	−16.5	−102.4	69.4	0.68
	Combined	21	2443.3	19	2564.2	31.3	−32.3	94.8	0.31
Absolute $\dot{V}O_2$ ($L{\cdot}min^{-1}$)	CON	10	2.1	8	2.4	0.3*	0.1	0.6	0.01
	HIIT	11	2.2	11	2.7	0.4*	0.2	0.6	<0.001
	Combined	21	2.2	19	2.5	0.4*	0.2	0.5	<0.001
Relative $\dot{V}O_2$ ($mL{\cdot}kg^{-1}{\cdot}min^{-1}$)	CON	10	24.7	8	29.3	4.9*	0.9	8.9	0.02
	HIIT	11	25.5	11	30.9	5.2*	2.8	7.6	0.00
	Combined	21	25.1	19	30.1	5.0*	2.8	7.1	<0.001
Time on treadmill (s)	CON	10	14.8	8	19.7	5.1*	3.5	6.8	<0.001
	HIIT	11	14.4	11	19.3	4.6*	3.2	5.9	<0.001
	Combined	21	14.6	19	19.4	4.8*	3.9	5.7	<0.001

There were no between-group (CON vs HIIT) differences observed for any measured outcomes.
*$P < 0.05$.

levels and an improvement in beta cell function, as measured by an increase in the HOMA-%β score. Surprisingly, the improvements in A1C and fitness occurred despite a slight but statistically significant reduction in insulin sensitivity as measured by HOMA-%S. The mean reduction in fasting glucose of 0.4 $mmol{\cdot}L^{-1}$ may be clinically modest in the prediabetes

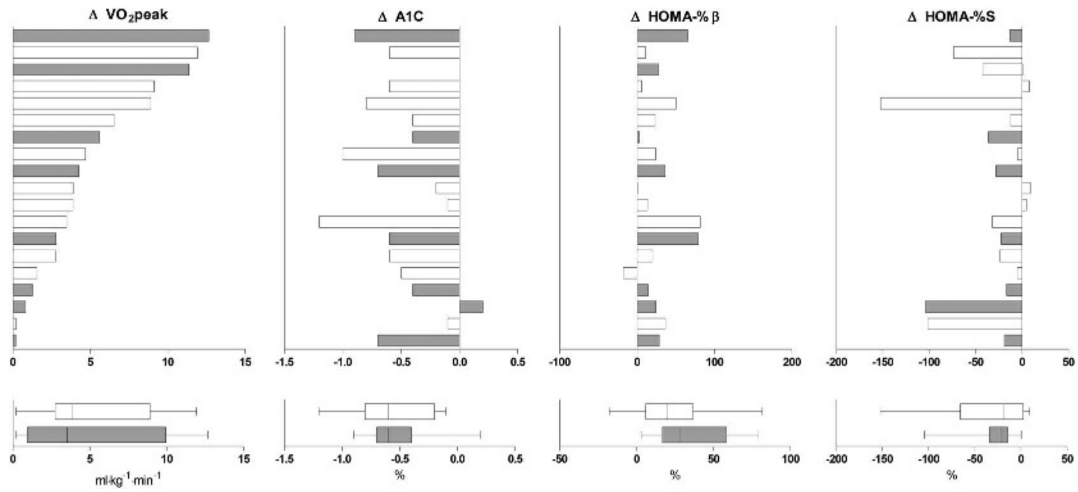

FIGURE 3—Individual participant data for A1C, HOMA-%β, and HOMA-%S ranked based on change in $\dot{V}O_{2peak}$ after 3 months of intervention. Shaded lines represent participants in the CON training group while white bars represent participants in the HIIT group. Wisker box plots show the range, median and interquartile range of each variable.

population, whereas the mean reduction in A1C of 0.5% is typically deemed clinically important from a cadiovascular risk perspective (28).This drop in A1C with a structured and supervised exercise program is similar to what is seen with various pharmacological interventions such as glucagon-like peptide-1 receptor (49) in persons with dysglycemia/diabetes. Reductions in A1C of ~1.0% are associated with a reduction in myocardial infarction risk of 14% and a 37% reduction of microvascular complications among persons with diabetes (38), whereas reduction in A1C of 0.5% is associated with a 20%–30% reduction in developing coronary heart disease risk in apparently healthy men and women without diabetes (28). The 0.5% reduction in A1C observed in this study for persons with prediabetes for such a short period (3 months) may also help to delay or prevent the progression toward T2D, particularly if the participants were to remain physically active. The mean A1C at baseline fell within the ADA diagnostic range (2) for prediabetes, whereas the mean A1C postintervention for all participants was 5.7%, which is identical with the lower boundary of the ADA criteria (5.7%–6.4%). The observed reduction in A1C is in line with that observed in other exercise intervention studies (9,36) involving T2D; however, it is the first that we are aware of to observe such findings among persons with prediabetes. The mean increase in HOMA-%β by ~35% between baseline and postintervention among all study participants provides further support for improvements in glycemic control with both exercise interventions. Enhancement of pancreatic function (i.e., β cell mass or secretory capacity) with regular exercise training has been demonstrated in humans with T2D (12,24) and prediabetes (27). Given that a value of 100% for HOMA-%β is indicative of "normal" beta cell function, it was not surprising that the mean for all participants met, or were below, this threshold at baseline (43). We did not anticipate observing impaired β cell function in our prediabetic cohort at baseline, given that damage to these cells typically occurs as a result of long-term hyperglycemia and glucose toxicity (32). That said, the improvement in HOMA-%β observed with either exercise modality in this study should be regarded positively (43). Although we found a reduction in HOMA-%S in this study (suggestive of a loss in insulin sensitivity), no significant changes were observed when we calculated HOMA-IR using the original HOMA model (43). The failure to observe changes in HOMA-IR with exercise in our study is similar to what others have observed with a resistance training program in persons with prediabetes (15) but counter to what many believe to be the main driver of improved glucose control with regular exercise, at least for type 2 diabetes (10).

Exercise training often improves both aerobic fitness, as measured by $\dot{V}O_{2max}$, and glycemic control, as measured by A1C, in patients with type 2 diabetes (37). However, it has recently been demonstrated that in individuals with type 2 diabetes who exercise but do not achieve a significant increase in $\dot{V}O_{2max}$ (deemed "nonresponders") can also have significant reductions in A1C levels (30). Similarly, we found no clear relationship between improvements in aerobic fitness and improvements in A1C in our subjects with prediabetes, in either of the two exercise treatment arms (Fig. 3). On the basis of this pilot investigation, it does appear, however, that changes in beta cell function are most closely linked to changes in A1C, but not to changes in $\dot{V}O_{2max}$ (Fig. 3). This is somewhat surprising given that a recent cross-sectional observation study demonstrated an association between $\dot{V}O_{2max}$ and insulin sensitivity and improved beta cell function in people with prediabetes (26). Further studies are needed to better understand the interactions between the changes in aerobic fitness, body composition, insulin sensitivity, and beta cell function in individuals with prediabetes who perform either CON or HIIT aerobic and resistance type training.

In addition to the observed improvements in glycemic control, participants in both exercise intervention groups had significant reductions in waist circumference and improvements in aerobic fitness, with no significant differences between the two groups. The mean reduction in waist circumference of 4.5 cm coupled with the finding of no changes in body mass or percent body fat suggests an improvement in visceral or central adiposity. The relationship between central adiposity, diabetes, cardiovascular, and greater long-term cardiometabolic risk has been thoroughly explored in individuals who have a high waist circumference regardless of BMI classification (3,20). Although classified as "obese" at baseline, based on both BMI and WC values, the reduction in WC postintervention drops the participants' mean WC into a lower risk classification for their given BMI (3).

The lack of weight loss/BMI reduction is in line with similar studies involving a combination of aerobic plus RT (9) and may be explained by a maintenance of muscle mass resulting from the RT component as well as the fact that participants were told not to modify their typical diet and lifestyle behaviors. This is corroborated by the participants' self-reported information regarding diet and PA participation outside the supervised intervention sessions. That is, the majority of participants noted that they were equally or less active during the study than they were before their involvement and that their dietary habits were also equally or less healthy. None of the participants indicated significant changes to their PA participation or their diet during the study when compared with their prestudy habits. These points support the contention that exercise-induced improvements to glycemic control can be quite significant, even in the absence of dietary modifications and/or weight loss.

The significant postintervention improvements in aerobic fitness, evidenced by both an increased $\dot{V}O_{2peak}$ and an increased time of the treadmill test, indicate that the participants had significantly improved their functional capacity. The mean gains in $\dot{V}O_{2peak}$ (by ~20%) extend beyond the typical accepted level of error for this measure using indirect calorimetry, which is approximately 2%–4% (19). Previous research has shown that aerobic fitness has a protective effect for CVD mortality as well as diabetes prevalence regardless of BMI classification (4,25). In addition to the cardiometabolic effect of improved aerobic fitness, PA accumulation and the resultant improvements in functional capacity have also been associated with improved quality of life (39).

Study limitations. Although this pilot study yielded interesting and significant findings pertaining to prediabetes and differing exercise interventions, there are limitations that must be acknowledged. First, the limited sample size and lack of control group limits the generalizability regarding the study outcomes. The sample may, in fact, be inadequately powered to fully determine significant differences in fitness or measures of metabolic control, between the two intervention arms. In addition, although the RT component was only a small relative dose, a group which performed no RT would further broaden the scope of conclusions drawn from this study. The study duration may also be considered somewhat limiting. Studies using A1C as a primary outcome have typically taken place for longer time frames, such as 6 months or more (9,36). However, despite the relatively short duration, this exercise intervention still achieved clinically relevant reductions in A1C (i.e., ~0.5%). It would be important to conduct a much longer intervention in a follow-up study to confirm that both training modalities (CON and HIIT) can sustain such positive metabolic and fitness outcomes, particularly because longer duration studies often demonstrate a relapse in various cardiometabolic outcomes with lifestyle intervention, perhaps because of reduced participant compliance (40).

CONCLUSION

The completion of 36 supervised exercise sessions for a 16-wk period involving either HIIT or CON aerobic training, both supplemented by RT, resulted in significantly improved glycemic control, central adiposity, and musculoskeletal and aerobic fitness in a population of individuals with prediabetes. These findings provide support that the goals of the study (detecting temporal changes in glycemic control, body composition, and fitness) were partially met although further investigation with larger samples may help to identify any potential differences between aerobic exercise modalities.

The authors thank PRE-PAID participants, volunteers, and community partners. Funding for this initiative was provided by the Ontario Ministry of Health Promotion and Sport and the Ontario Trillium Foundation.

For this manuscript, C. P. R. was the primary author and was the primary facilitator of data collection and entry, data analysis, and interpretation as well as the primary contributor to the manuscript preparation. C. P. R. was also the point person for developing community partnerships during recruitment. M. C. R., V. K. J., and N. G. all provided guidance regarding project design and were involved in the interpretation of the data analysis as well as revision of the manuscript. M. C. R., V. K. J., and N. G. also helped to facilitate community partnerships during project recruitment. M. C. R., V. K. J., and N. G. provided support with data collection.

The authors have no conflicts of interest to disclose and acknowledge that the results of the present study do not constitute endorsement by the American College of Sports Medicine and are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

REFERENCES

1. Alberti KG, Zimmet P, Shaw J. International Diabetes Federation: a consensus on type 2 diabetes prevention. *Diabet Med*. 2007;24(5):451–63.
2. American Diabetes Association. Standards of medical care in diabetes—2012. *Diabetes Care* 2012;35(1 Suppl):S11–63.
3. Ardern CI, Janssen I, Ross R, Katzmarzyk PT. Development of health-related waist circumference thresholds within BMI categories. *Obes Res*. 2004;12(7):1094–103.
4. Blair SN, Kohl HW, Barlow CE, Paffenbarger RS, Gibbons LW, Macera CA. Changes in physical fitness and all-cause mortality: a prospective study of healthy and unhealthy men. *JAMA*. 1995;273(14): 1093–8.
5. Bredin SSD, Gledhill N, Jamnik VK, Warburton DER. PAR-Q+ and ePARmed-X+: New risk stratification and physical activity clearance strategy for physicians and patients alike. *Can Fam Physician*. 2013;59(3):273–7.
6. Burr JF, Rowan CP, Jamnik VK, Riddell MC. The role of physical activity in type 2 diabetes prevention: physiological and practical perspectives. *Phys Sportsmed*. 2010;38(1):72–82.
7. Canadian Diabetes Association. An Economic Tsunami: The Cost of Diabetes in Canada. Toronto (ON): Canadian Diabetes Association; 2009.
8. Centers for Disease Control and Prevention. National Diabetes Statistics Report: 2014 estimates of diabetes and its burden in the United States. *Natl Diabetes Stat Rep*. 2014;2009–12.
9. Church T, Blair S, Cocreham S, et al. Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: a randomized controlled trial. *JAMA*. 2010;304(20):2253–62.
10. Colberg SR, Sigal RJ, Fernhall B, et al. Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement. *Diabetes Care*. 2010;33(12):e147–67.
11. Dall TM, Yang W, Halder P, et al. The economic burden of elevated blood glucose levels in 2012: Diagnosed and undiagnosed diabetes, gestational diabetes mellitus, and prediabetes. *Diabetes Care*. 2014;37(12):3172–9.
12. Dela F, von Linstow ME, Mikines KJ, Galbo H. Physical training may enhance beta-cell function in type 2 diabetes. *Am J Physiol Endocrinol Metab*. 2004;287(5):E1024–31.
13. Ebbeling C, Ward A, Puleo E, Widrick J, Rippe JM. Development of a single-stage submaximal treadmill walking test. *Med Sci Sports Exerc*. 1991;23(8):966–73.
14. Edwards RH, Ekelund LG, Harris RC, et al. Cardiorespiratory and metabolic costs of continuous and intermittent exercise in man. *J Physiol*. 1973;234(2):481–97.
15. Eikenberg JD, Savla J, Marinik EL, et al. Prediabetes phenotype influences improvements in glucose homeostasis with resistance training. *PLoS One*. 2016;11(2):e0148009.
16. Gibala MJ, Gillen JB, Percival ME. Physiological and health-related adaptations to low-volume interval training: influences of nutrition and sex. *Sports Med*. 2014;44:127–37.
17. Gibala MJ, McGee SL. Metabolic adaptations to short-term high-intensity interval training: a little pain for a lot of gain? *Exerc Sport Sci Rev*. 2008;36(2):58–63.
18. Gillen JB, Gibala MJ. Is high-intensity interval training a time-efficient exercise strategy to improve health and fitness? *Appl Physiol Nutr Metab*. 2014;39:409–12.
19. Gledhill N, Cox D, Jamnik R. Endurance athletes' stroke volume does not plateau: major advantage is diastolic function. *Med Sci Sports Exerc*. 1994;26(9):1116–21.
20. Janssen I, Katzmarzyk PT, Ross R. Body mass index, waist circumference, and health risk: evidence in support of current National Institutes of Health guidelines. *Arch Intern Med*. 2002;162: 2074–9.

21. Jelleyman C, Yates T, O'Donovan G, Gray LJ, et al. The effects of high-intensity interval training on glucose regulation and insulin resistance: a meta-analysis. *Obes Rev*. 2015;16(11):942–61.
22. Kemi OJ, Wisloff U. High-intensity aerobic exercise training improves the heart in health and disease. *J Cardiopulm Rehabil Prev*. 2010;30(1):2–11.
23. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker E, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med*. 2002;346(6):393–403.
24. Krotkiewski M, Lönnroth P, Mandroukas K, et al. The effects of physical training on insulin secretion and effectiveness and on glucose metabolism in obesity and Type 2 (noninsulin-dependent) diabetes mellitus. *Diabetologia*. 1985;28(12):881–90.
25. Lee CD, Blair SN, Jackson AS. Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men. *Am J Clin Nutr*. 1999;69:373–80.
26. Lidegaard LP, Hansen AL, Johansen NB, et al. Physical activity energy expenditure vs cardiorespiratory fitness level in impaired glucose metabolism. *Diabetologia*. 2015;58(12):2709–17.
27. Malin SK, Solomon TP, Blaszczak A, Finnegan S, Filion J, Kirwan JP. Pancreatic β-cell function increases in a linear dose-response manner following exercise training in adults with prediabetes. *Am J Physiol Endocrinol Metab*. 2013;305(10):E1248–54.
28. Pai JK, Cahill LE, Hu FB, Rexrode KM, Manson JE, Rimm EB. Hemoglobin a1c is associated with increased risk of incident coronary heart disease among apparently healthy, nondiabetic men and women. *J Am Heart Assoc*. 2013;2(2):e000077.
29. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. *Diabetes Care*. 1997;20(4):537–44.
30. Pandey A, Swift DL, McGuire D, et al. Metabolic effects of exercise training among fitness-nonresponsive patients with type 2 diabetes: the HART-D study. *Diabetes Care*. 2015;38(8):1494–501.
31. Riddell MC, Burr J. Evidence-based risk assessment and recommendations for physical activity clearance: diabetes mellitus and related comorbidities 1. *Appl Physiol Nutr Metab Physiol*. 2011; 36(1 Suppl):S154–89.
32. Robertson RP, Harmon J, Tran PO, Poitout V. Beta-cell glucose toxicity, lipotoxicity, and chronic oxidative stress in type 2 diabetes. *Diabetes*. 2004;53(1 Suppl):S119–24.
33. Rowan CP, Miadovnik LA, Riddell MC, Rotondi MA, Gledhill N, Jamnik VK. Identifying persons at risk for developing type 2 diabetes in a concentrated population of high risk ethnicities in Canada using a risk assessment questionnaire and point-of-care capillary blood HbA 1c measurement. *BMC Public Health*. 2014;14(929):1–9.
34. Safiyari-Hafizi H, Taunton J, Ignaszewski A, Warburton DE. The health benefits of a 12-week home-based interval training cardiac rehabilitation program in patients with heart failure. *Can J Cardiol*. 2016;32(4):561–7.
35. Sayers SP, Harackiewicz DV, Harman E, Frykman PN, Rosenstein MT. Cross-validation of three jump power equations. *Med Sci Sports Exerc*. 1999;31:572–7.
36. Sigal RJ, Kenny GP, Boulé NG, et al. Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial. *Ann Intern Med*. 2007;147(6):357–69.
37. Snowling N, Hopkins W. Effects of different modes of exercise training on glucose control and risk factors for complications in type 2 diabetic patients: a meta-analysis. *Diabetes Care*. 2006;29(11):2518–27.
38. Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ*. 2000; 321:405–12.
39. Taylor LM, Spence JC, Raine K, Plotnikoff RC, Vallance JK, Sharma AM. Physical activity and health-related quality of life in individuals with prediabetes. *Diabetes Res Clin Pract*. 2010;90(1):15–21.
40. The Look AHEAD Research Group. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med*. 2013;369:155–64.
41. Tsui EY, Gao XJ, Zinman B. Bioelectrical impedance analysis (BIA) using bipolar foot electrodes in the assessment of body composition in type 2 diabetes mellitus. *Diabet Med*. 1998;15(2):125–8.
42. Tuomilehto J, Lindström J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med*. 2001;344(18):1343–50.
43. Wallace T, Levy J, Matthews D. Use and Abuse of HOMA Modeling. *Diabetes Care*. 2004;27(6):1487–95.
44. Warburton DER, McKenzie DC, Haykowsky MJ, et al. Effectiveness of high-intensity interval training for the rehabilitation of patients with coronary artery disease. *Am J Cardiol*. 2005;95(9):1080–4.
45. Warburton D, Jamnik V, Bredin S, Gledhill N. The Physical Activity Readiness Questionnaire for Everyone (PAR-Q+) and Electronic Physical Activity Readiness Medical Examination (ePARmed-X+). *Heal Fit J Canada*. 2011;4(2):3–17.
46. Weston KS, Wisløff U, Coombes JS. High-intensity interval training in patients with lifestyle-induced cardiometabolic disease: a systematic review and meta-analysis. *Br J Sports Med*. 2014;48(16):1227–34.
47. Wisløff U, Ellingsen Ø, Kemi OJ. High-intensity interval training to maximize cardiac benefits of exercise training? *Exerc Sport Sci Rev*. 2009;37(3):139–46.
48. World Health Organization. *Global Atlas on Cardiovascular Disease Prevention and Control* [Internet]. World Health Organization. 2011 [cited 2013 Feb 27]. Available from: http://scholar.google.com/scholar?hl=en&btnG=Search&q=intitle:Global+Atlas+on+cardiovascular+disease+prevention+and+control#3.
49. Zaccardi F, Htike ZZ, Webb DR, Khunti K, Davies MJ. Benefits and harms of once-weekly glucagon-like peptide-1 receptor agonist treatments: a systematic review and network meta-analysis. *Ann Intern Med*. 2015;164(2):1–12.