Received: 25 August 2020 | Revised: 15 January 2021 | Accepted: 11 February 2021

DOI: 10.1111/cen.14452

ORIGINAL ARTICLE

WILEY

Exercise training and reproductive outcomes in women with polycystic ovary syndrome: A pilot randomized controlled trial

Jamie L. Benham[1,2] | Jane E. Booth[2] | Bernard Corenblum[1] | Steve Doucette[3] | Christine M. Friedenreich[2,4,5,6,7] | Doreen M. Rabi[1,2,7,8,9] | Ronald J. Sigal[1,2,5,7,8,9]

[1]Department of Medicine, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

[2]Department of Community Health Sciences, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

[3]Department of Community Health & Epidemiology, Dalhousie University, Halifax, NS, Canada

[4]Department of Cancer Epidemiology and Prevention Research, Cancer Care Alberta, Alberta Health Services, Holy Cross Centre, Calgary, AB, Canada

[5]Faculty of Kinesiology, University of Calgary, Calgary, AB, Canada

[6]Department of Oncology, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

[7]O'Brien Institute of Public Health, University of Calgary, Calgary, AB, Canada

[8]Department of Cardiac Sciences, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

[9]Libin Cardiovascular Institute, University of Calgary, Calgary, AB, Canada

Correspondence
Ronald J. Sigal, Division of Endocrinology and Metabolism, Department of Medicine, University of Calgary, 1820 Richmond Road SW, Calgary, AB, T2T 5C7 Canada.
Email: rsigal@ucalgary.ca

Funding information
This trial was supported by a Cumming School of Medicine, University of Calgary/Alberta Health Services Clinical Research Fund grant and a grant from the Libin Cardiovascular Institute, University of Calgary.

Abstract

Objective: Exercise is recommended for polycystic ovary syndrome (PCOS), but the most effective exercise prescription is unclear. This trial compared effects of high-intensity interval training (HIIT), continuous aerobic exercise training (CAET) and no-exercise control on reproductive, anthropometric and cardiometabolic outcomes in PCOS.

Design: Pilot randomized controlled trial.

Participants: Previously inactive women aged 18–40 years with PCOS.

Measurements: Feasibility outcomes included recruitment, retention, adherence to exercise and daily ovulation prediction kit (OPK) testing. Preliminary efficacy outcomes included reproductive, anthropometric and cardiometabolic health markers.

Results: Forty-seven women were randomized to no-exercise control (n = 17), HIIT (n = 16), or CAET (n = 14). Forty (85%) participants completed the trial. Median exercise adherence was 68% (IQR 53%, 86%). Median daily OPK-testing adherence in the first half of the intervention was 87% (IQR 61%, 97%) compared with 65% (IQR 0%, 96%) in the second half. Body mass index decreased significantly in CAET compared with control (−1.0 kg/m^2, p = .01) and HIIT (−0.9 kg/m^2, p = .04). Mean waist circumference decreased in all groups (−7.3 cm, −6.9 cm, −4.5 cm in HIIT, CAET and control) with no significant between-group differences. Mean LDL-C was significantly reduced for HIIT compared to CAET (−0.33 mmol/L, p = .03). HDL-C increased in HIIT compared with control (0.18 mmol/L, p = .04).

Conclusions: There were feasibility challenges with adherence to daily ovulation assessment limiting the ability to analyse the effect of the exercise interventions on ovulation. CAET and HIIT were both effective at improving anthropometrics and some cardiometabolic health markers. Further studies need to determine optimal and acceptable exercise prescriptions for this population.

KEYWORDS
exercise, high-intensity interval training, ovulation, ovulation prediction, polycystic ovary syndrome, randomized controlled trial, women's health

1 | INTRODUCTION

Polycystic ovary syndrome (PCOS) affects about 15% of reproductive-aged women[1] and causes significant morbidity. PCOS is characterized by irregular menses, androgen excess and/or polycystic ovaries[2] and is associated with infertility,[3] reduced health-related quality-of-life,[4] and cardiometabolic abnormalities.[5]

Roles of aerobic exercise including continuous aerobic exercise training (CAET)[6,7] and high-intensity interval training (HIIT)[8,9] in PCOS management have been explored. Preliminary evidence suggests aerobic exercise training may improve cardiometabolic and reproductive health in women with PCOS with overweight or obesity,[6-8] but data on reproductive outcomes are inconsistent.[10] Based on these data, clinical practice guidelines recommend diet and exercise for weight loss to treat PCOS in the context of overweight, but the type and dose of exercise are not specified. No previous studies directly compared effects of HIIT versus CAET in women with PCOS. In a non-PCOS trial, HIIT resulted in improved cardiovascular fitness and greater fat loss compared with CAET.[11] HIIT requires less time than CAET.[12,13] Since time is a major barrier to exercise in women with PCOS,[14,15] comparing effects of CAET and HIIT on reproductive sequelae of PCOS is relevant.

This pilot trial was designed to assess feasibility of conducting a full-scale randomized controlled trial (RCT) evaluating effects of HIIT and CAET compared with no-exercise control on ovulatory rate in women with PCOS. To inform planning of future trials, an evaluation of feasibility regarding recruitment, attrition and protocol adherence was required. In particular, the feasibility of daily at-home ovulation assessments in ambulatory reproductive-aged women needed testing. Our other objective was to evaluate the effects of HIIT and CAET compared with no exercise on reproductive, anthropometric and cardiometabolic health markers in women with PCOS.

2 | MATERIALS AND METHODS

2.1 | Study design

We conducted a 6-month, single-centre RCT in Calgary, Canada, between December 2017 and September 2019. The protocol was registered prospectively (NCT03362918). The trial had a parallel-group design with three phases: (1) 3-month run-in-phase; (2) 6-month intervention after randomization to HIIT, CAET or a no-exercise control group; and (3) 6-month post-intervention follow-up. Trial outcomes were assessed objectively by health professionals and laboratory technologists, blinded to participant group assignment. The protocol was approved by the University of Calgary Conjoint Health Research Ethics Board (REB17-1574). All participants provided written informed consent.

2.2 | Participants

Untrained women aged 18–40 years with PCOS defined by Rotterdam criteria[16] were recruited by advertisements, media, physician referrals and word of mouth. Exclusion criteria included medical conditions restricting exercise, participation in >40 min of exercise training weekly and medications potentially affecting ovulation (glucocorticoids, metformin, gonadotropins, clomiphene, letrozole, oestrogens, progestins). Potential participants were screened for inclusion and exclusion criteria by telephone. If eligible, they were mailed requisitions for the following screening investigations: (1) electrocardiogram and (2) blood tests (serum beta-HCG, 17-hydroxyprogesterone, prolactin, thyroid-stimulating hormone, fasting plasma glucose and haemoglobin A_{1C} (HbA_{1c})). Potential participants meeting trial participation criteria were invited for in-person assessment where a baseline history and physical examination were completed.

2.3 | Run-in phase

Prior to randomization, participants entered a 3-month run-in-phase to assess baseline reproductive function including ovulation rate and menstrual cycle length and frequency. Participants did not exercise during this phase. Participants were asked to track menstrual cycles and check for ovulation using an at-home ovulation prediction kit (OPK) (Verify Diagnostics) daily which measured luteinizing hormone (LH) in urine. As LH surge duration is typically just 24–48 h,[17] adherence to daily testing was important. Participants sent photographs of completed test strips to the research team for verification through a secure messaging application (WhatsApp Inc.). If positive, ovulation was confirmed with a serum progesterone level 1 week after positive OPK results.

2.4 | Randomization

Participants completing >75% of daily OPKs during run-in were randomized to control, HIIT or CAET. Groups were stratified by body mass index (BMI, kg/m^2) (< or ≥28 kg/m^2). Central randomization was done using a secure web application (Research Electronic Data Capture (REDCap)). Block sizes varied among two, four or six. Allocation concealment was used prior to randomization.

2.5 | Intervention phase

Throughout the intervention period, participants were asked to continue tracking menstrual cycles and completing OPK-testing daily. Physical activity was tracked for all participants using Polar A370 (Polar Electro Oy). Control group participants were asked to maintain their usual level of physical activity throughout the intervention and were offered three sessions with a personal trainer upon completion.

Exercise group participants completed three exercise sessions/week using the aerobic exercise equipment of their choice. Gym memberships and parking were provided free of charge. All

exercise sessions included a five-minute warm-up and five-minute cool-down. HIIT participants completed 10 cycles of 30 s at high-intensity (90% of heart rate reserve (HRR), or 9/10 on a modified Borg scale[18]) alternating with 90 s of low-intensity aerobic exercise. CAET participants completed 40 min of moderate-intensity aerobic exercise (50%–60% HRR, or 4-6/10 on a modified Borg scale). For better precision, a Polar H10 heart rate sensor was synced to the Polar A370 watches.

2.6 | Outcomes and measurements

Four feasibility outcomes were determined a priori: (1) randomization of ≥36 participants in 15 months; (2) <25% attrition; (3) adherence to >90% of daily OPK-testing; and (4) adherence to >70% of prescribed exercise. OPK-testing adherence was calculated as the number of OPK digital photographs completed divided by the total number of days of requested OPK tests. Prescribed exercise session completion was assessed as the attendance at the twice-weekly supervised sessions and the number of unsupervised sessions recorded using the Polar Flow App and verified using the Polar Coach platform.[19] Exercise adherence was calculated as the number of exercise sessions completed divided by the number of prescribed sessions.

We evaluated menstrual cycle length, luteal phase length and numbers of ovulation events, pregnancies, abortions and live births. Menstrual cycle length was calculated from the first day of menses to the first day of the subsequent menses. Luteal phase length was calculated from the day of ovulation to the first day of the subsequent menses. An ovulation event was documented if a positive OPK result was confirmed (serum progesterone level ≥5.0 nmol/L). Pregnancy was confirmed by foetal cardiac activity on a first-trimester ultrasound. Ferriman-Gallwey score[20] was assessed pre-intervention and end of intervention.

Height and weight were assessed using a stadiometer (SECA-220, Seca GmbH & Co.) and weigh scale (SECA-703, Seca GmbH & Co.). Waist circumference was measured midway between the lowest rib and iliac crest in the horizontal plane using a tape measure to the nearest 0.5 cm. Blood pressure was measured using an automated device (Omron HEM-907, Omron Healthcare Inc.).

Blood work was drawn after fasting for eight hours. Glucose, total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglycerides, alanine transferase (ALT) and gamma-glutamyl transferase (GGT) were measured using enzymatic methods on a Cobas c701 analyser (Roche Diagnostics). Insulin was measured using a chemiluminescent microparticle immunoassay on an Architect i2000SR analyser (Abbott). HbA_{1c} was measured using a Tina-quant Hemoglobin A1cDx Gen.3 assay and a Cobas c513 analyser (Roche Diagnostics). Low-density lipoprotein cholesterol (LDL-C)[21] and homeostasis model assessment index of insulin resistance (HOMA2-IR)[22] were calculated.

Exercise testing was completed pre-intervention and end of intervention by Certified Exercise Physiologists. Maximal oxygen uptake (VO_{2max}) was determined using a V_{max} Encore 29 metabolic cart (SensorMedics Corporation). Breath-by-breath ventilatory volumes and expiratory gases were measured during a ramp exercise test (Balke-Ware protocol[23]) on a programmable treadmill (Trackmaster, Full Vision Inc.). Ventilatory thresholds were determined and verified by two independent investigators according to the V-slope method.[24]

2.7 | Adverse events

A standard form was created to document adverse events. Participants were asked to report adverse events to the research team at the mid- and end-of-intervention assessments.

2.8 | Sample size

In addition to assessing pre-specified feasibility outcomes, our goal for this feasibility trial was to enrol sufficient participants to evaluate the preliminary effectiveness of HIIT and CAET on ovulatory rate. Previous studies reported improvements of up to 65% in ovulation rate with exercise training.[7,25] We estimated that 36 randomized participants (12 per group) would allow for 81% power to detect a difference of 0.6 in the proportion of women with improvement in ovulation rate between the control group and each exercise group with an $\alpha = 0.05$. We estimated 40% attrition during run-in because of the daily OPK protocol and therefore enrolled sufficient participants to result in ≥36 randomized.

2.9 | Statistical analysis

For baseline characteristics, means were compared with one-way analysis of variance (ANOVA) and proportions were compared with Fisher's exact test. The reproductive analysis was conducted on an intention-to-treat basis and all randomized participants were included. We also performed per-protocol analyses including only participants completing end-of-study measures and ≥75% of daily menstrual cycle and OPK data collection. Tests of proportion were used to compare within- and between-group differences pre- and post-intervention. Mean menstrual cycle and luteal phase lengths were compared within-group pre- and post-intervention using paired t tests and between-groups using ANOVA.

For anthropometric and cardiometabolic outcomes, repeated measures mixed models were used with effects for time, group and time by group interaction, with age as a covariate and an unstructured covariance matrix. Within the mixed models, we estimated 95% confidence intervals (CI) and *p*-values for intergroup contrasts and for change in each variable over time. Only participants who had ≥1 postbaseline assessment were included.

Analyses were conducted using SAS version 9.4 (SAS Institute) and STATA version 15.1 (StataCorp.). Statistical significance was set as $p < .05$.

3 | RESULTS

Between December 2017 and November 2018, 200 women were screened for eligibility (Figure 1) and sixty were enrolled. Forty-seven participants completed run-in and were randomized to control (n = 17), HIIT (n = 16) or CAET (n = 14). Post-randomization attritions were 1 (6%), 3 (19%) and 3 (21%) among those randomized to control, HIIT and CAET, respectively.

3.1 | Participant characteristics

The groups were similar at baseline (Table 1). Twenty-eight participants were PCOS phenotype A (hyperandrogenism, ovulatory dysfunction, polycystic ovaries), 13 were phenotype B (hyperandrogenism, ovulatory dysfunction), two were phenotype C (hyperandrogenism, polycystic ovaries), and four were phenotype D (polycystic ovaries, ovulatory dysfunction). Twelve (26%) participants had previous pregnancies, with six (13%) having live births. The most common PCOS treatments attempted before trial enrolment were mechanical hair removal (89%), oral contraceptive (81%) and lifestyle intervention (53%).

3.2 | Adherence to prescribed exercise

Participants assigned to exercise groups were prescribed 78 exercise sessions over 26 weeks. For those who completed the intervention, median overall adherence to exercise for both exercise groups was 68% (IQR 53%, 86%). There was no statistically significant difference in adherence to exercise between CAET (81%; IQR 56%, 85%) and HIIT (65%; IQR 51%, 85%; p = .91; Figure 2). In the first 3 months of the intervention, median adherence to prescribed exercise was 78% (IQR 55%, 97%) for HIIT and 88% (IQR 56%, 100%) for CAET. Median exercise adherences during the last 3 months of the intervention were 44% (IQR 41%, 69%) for HIIT and 64% (IQR 10%, 77%) for CAET.

3.3 | Ovulation prediction kit testing adherence

During run-in, all 47 randomized participants completed ≥75% of the prescribed daily OPK tests, with 35/47 (74.5%) completing ≥90%; OPK-testing adherence was 97% (IQR 88%, 99%). During the first 3 months of the 6-month intervention, median adherence was 87%

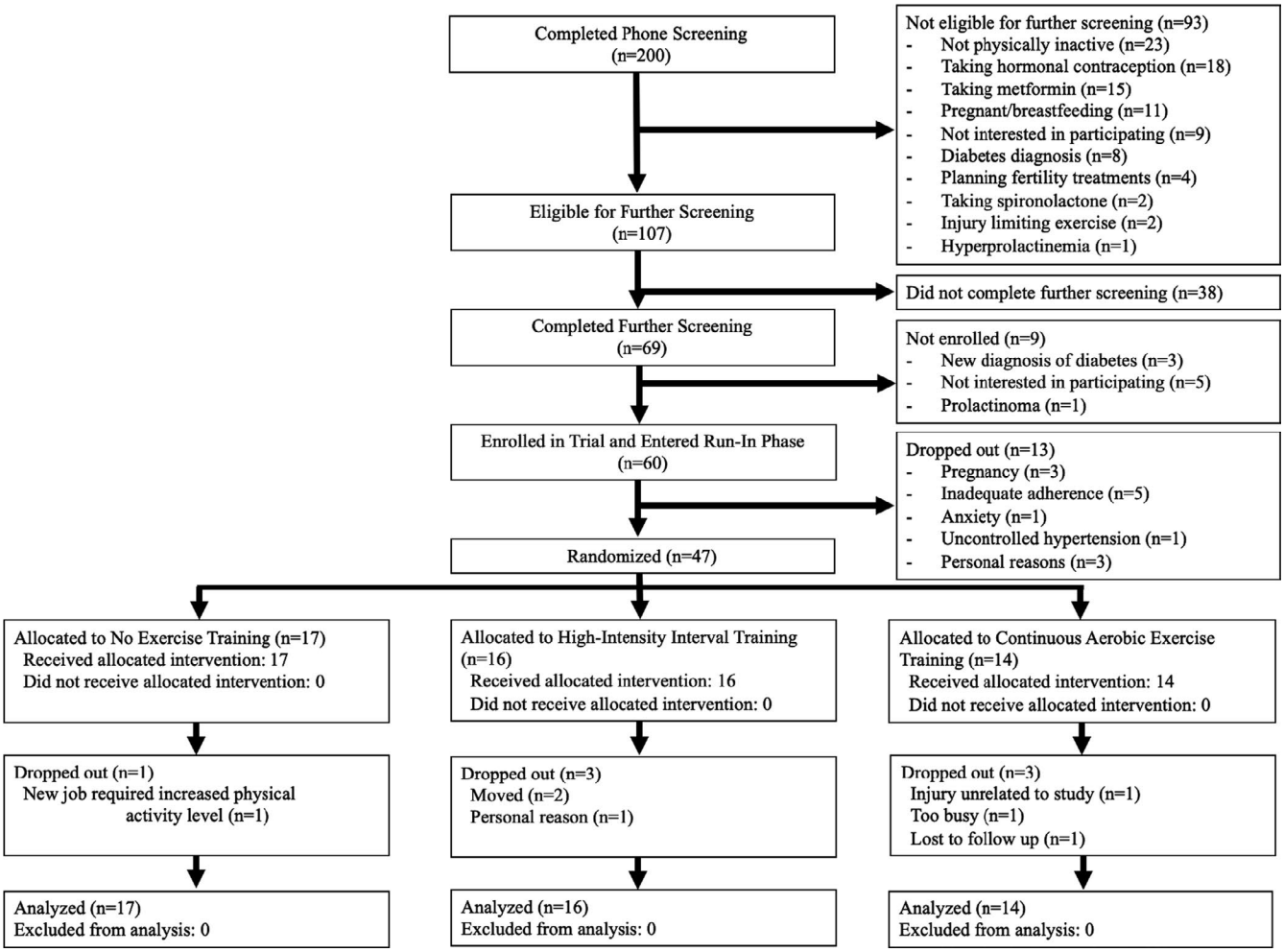

FIGURE 1 Study flow chart

TABLE 1 Baseline characteristics of study participants

Characteristic	Randomized (*n* = 47)	No exercise (*n* = 17)	HIIT (*n* = 16)	CAET (*n* = 14)
Age (y) (SD)	29.2 (4.7)	29.1 (5.4)	29.1 (4.1)	29.5 (4.6)
Weight (kg) (SD)	84.2 (22.5)	86.1 (21.8)	83.4 (22.2)	83.2 (25.1)
Body mass index (kg/m^2) (SD)	31.4 (8.4)	31.6 (8.2)	31.4 (8.6)	31.3 (9.0)
Phenotype				
A (hyperandrogenism, ovulatory dysfunction, PCO)	28 (60%)	10 (59%)	6 (38%)	12 (86%)
B (hyperandrogenism, ovulatory dysfunction)	13 (28%)	5 (29%)	6 (38%)	2 (14%)
C (hyperandrogenism, PCO)	2 (4%)	1 (6%)	1 (6%)	0 (0%)
D (ovulatory dysfunction, PCO)	4 (8%)	1 (6%)	3 (18%)	0 (0%)
Age at menarche (y) (SD)	12.0 (1.9)	11.6 (2.4)	12.4 (1.7)	12.1 (1.3)
Baseline reported menstrual length (days) (SD)	64.7 (45.9)	64.0 (40.8)	51.1 (32.0)	82.9 (62.0)
History of 1 or more pregnancies (*N*)	12 (26%)	4 (24%)	4 (25%)	4 (29%)
History of 1 or more live births (*N*)	6 (13%)	2 (12%)	1 (6%)	3 (21%)
Current smoker (*N*)	2 (4%)	1 (6%)	0 (0%)	1 (7%)
Former smoker (*N*)	10 (21%)	5 (29%)	3 (19%)	2 (14%)
Has a partner (*N*)	30 (64%)	13 (76%)	8 (50%)	9 (64%)
Employed (*N*)	43 (91%)	17 (100%)	13 (81%)	13 (93%)
Previous treatments for PCOS				
Lifestyle (diet and/or exercise) (*N*)	25 (53%)	8 (47%)	8 (50%)	9 (64%)
Oral contraceptive pill (*N*)	38 (81%)	13 (76%)	13 (81%)	12 (86%)
Spironolactone (*N*)	8 (17%)	2 (12%)	3 (19%)	3 (21%)
Metformin (*N*)	18 (38%)	6 (35%)	4 (25%)	8 (57%)
Progesterone (*N*)	18 (38%)	5 (29%)	5 (31%)	8 (57%)
Ovulation induction (clomiphene citrate/letrozole) (*N*)	5 (11%)	3 (18%)	0 (0%)	2 (14%)
Hair removal (*N*)	45 (96%)	17 (100%)	14 (88%)	14 (100%)
Isotretinoin (*N*)	4 (9%)	1 (6%)	2 (13%)	1 (7%)
Medical conditions				
Obstructive sleep apnoea (*N*)	4 (15%)	1 (6%)	2 (13%)	1 (7%)
Depression (*N*)	17 (36%)	10 (59%)	4 (25%)	3 (21%)
Anxiety (*N*)	19 (40%)	7 (41%)	6 (38%)	6 (43%)
Family history				
PCOS (*N*)	20 (43%)	8 (47%)	6 (38%)	6 (43%)
Infertility (*N*)	11 (23%)	6 (35%)	3 (19%)	2 (14%)
Gestational diabetes (*N*)	8 (17%)	3 (18%)	3 (19%)	2 (14%)
Diabetes (*N*)	30 (64%)	9 (52%)	11 (69%)	10 (71%)
Hypertension (*N*)	30 (64%)	12 (71%)	8 (50%)	10 (71%)
Heart disease (*N*)	24 (51%)	10 (59%)	8 (50%)	6 (43%)
Stroke (*N*)	19 (40%)	8 (47%)	6 (38%)	5 (36%)

(IQR 61%, 97%) with 30/47 (63.8%) completing ≥75% of the OPK tests and 19/47 (40.4%) completing ≥90%. During the final 3 months of the intervention, 17/47 (36.2%) participants completed ≥90% of prescribed OPK tests, and median adherence was 65% (IQR 0%, 96%). There was no difference in OPK-testing adherence between-groups at any assessment interval (Figure 3).

3.4 | Reproductive outcomes

Given sub-optimal adherence to OPK-testing throughout the intervention, we were unable to analyse effects of the exercise interventions on ovulation using an intention-to-treat analysis. During the 3-month run-in-phase, 28/47 (59.6%) participants ovulated ≥once. In

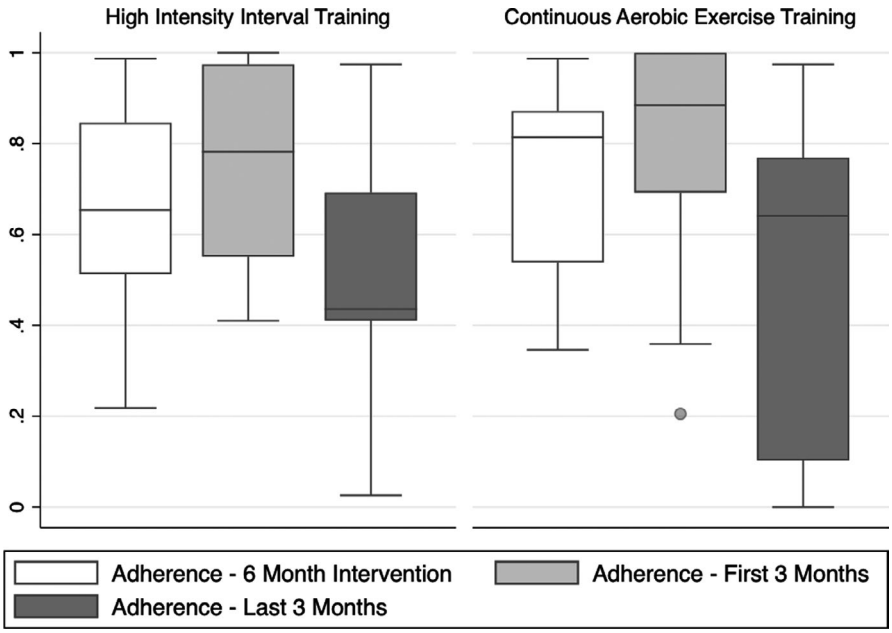

FIGURE 2 Adherence to prescribed exercise

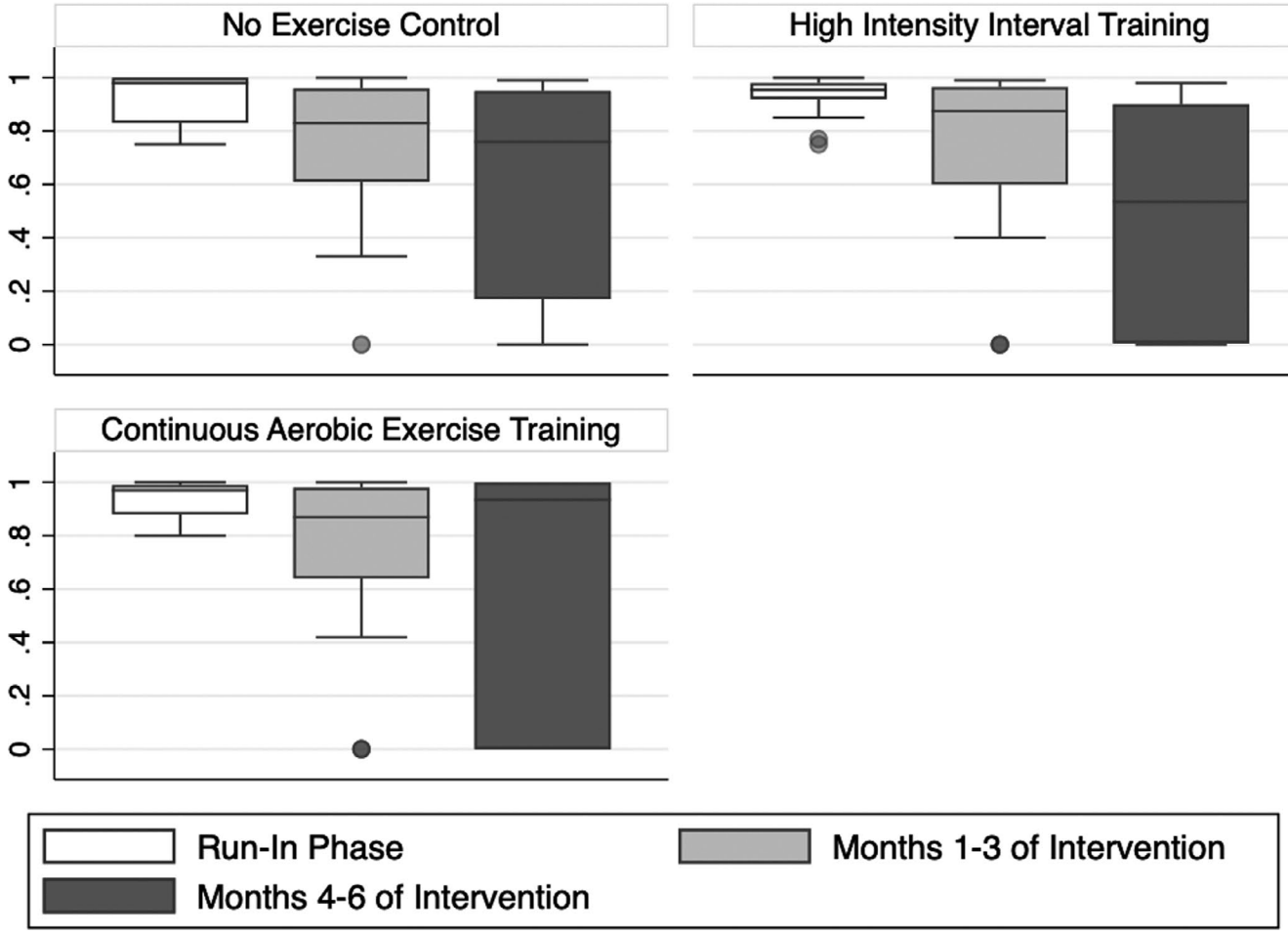

FIGURE 3 Adherence to ovulation prediction kit testing

a per-protocol analysis of 33 participants completing ≥75% prescribed OPKs during the intervention, 22 (67%) had ≥1 documented ovulation. Further, there was no significant between-group difference in ovulation events during the intervention: 8/12 (67%) in control, 8/11 (73%) in HIIT and 6/10 (60%) in CAET.

Forty-two participants tracked menstrual cycles during run-in and intervention phases. Proportions of participants by group with regular menses (21–35 days) pre-intervention compared with the last three months of the intervention were 29% vs 47% (p = .31) in control, 50% vs 53% (p = .85) in HIIT and 29% vs 42% (p = .48) in CAET. There were

TABLE 2 Anthropometric and fitness outcomes

Outcome	Mean (SD)			Change from baseline to 6 months (95% CI)	Difference in change from baseline to 6 months (95% CI)	*p* Value
	Baseline	3 months	6 months			
Body Weight (kg) (SE) [*n*]						
Control group	85.5 (6) [16]	85.7 (6) [16]	86.0 (6.2) [15]	0.5 (−0.9, 1.9)		.45
HIIT group	85.2 (6.2) [15]	85.2 (6.2) [15]	85.3 (6.4) [11]	0.1 (−1.4, 1.6)		.87
CAET group	84.5 (6.9) [12]	83.4 (6.9) [12]	83.3 (7.1) [12]	-1.2 (−2.8, 0.4)		.13
Intergroup comparisons						
CAET vs Control					-1.7 (−3.8, 0.4)	.10
HIIT vs Control					-0.4 (−2.4, 1.6)	.69
HIIT vs CAET					1.3 (−0.9, 3.5)	.22
Body mass index (kg/m^2) (SE) [*n*]						
Control group	31.1 (2.2) [16]	31.1 (2.2) [16]	31.3 (2.2) [15]	0.2 (−0.3, 0.7)		.49
HIIT group	31.8 (2.3) [15]	31.9 (2.3) [15]	31.9 (2.3) [11]	0.1 (−0.5, 0.7)		.82
CAET group	31.4 (2.6) [12]	31 (2.5) [12]	30.6 (2.6) [12]	**-0.8 (−1.4, −0.2)**		.01
Intergroup comparisons						
CAET vs Control					**-1 (−1.8, −0.2)**	<.01
HIIT vs Control					-0.1 (−0.9, 0.7)	.78
HIIT vs CAET					**0.9 (0, 1.7)**	.04
Waist circumference (cm) (SE) [*n*]						
Control group	96.6 (4.7) [16]	94.3 (4.6) [16]	92.1 (4.7) [14]	**-4.5 (−8.6, −0.4)**		.03
HIIT group	98.7 (4.8) [15]	96 (4.7) [15]	91.4 (4.9) [11]	**-7.3 (−11.8, −2.9)**		<.01
CAET group	98.5 (5.4) [12]	94.2 (5.3) [11]	91.6 (5.4) [12]	**-6.9 (−11.5, −2.3)**		<.01
Intergroup comparisons						
CAET vs Control					-2.4 (−8.6, 3.8)	.44
HIIT vs Control					-2.8 (−8.8, 3.3)	.36
HIIT vs CAET					-0.4 (−6.8, 6)	.90
VO_{2max} (mL/kg/min) (SE) [*n*]						
Control group	29.6 (1.8) [15]	-	29.2 (1.7) [13]	-0.4 (−2.1, 1.4)		.69
HIIT group	28.4 (1.9) [14]	-	30 (1.9) [12]	1.5 (−0.2, 3.3)		.09
CAET group	30.1 (2) [12]	-	29.9 (2) [10]	-0.2 (−2.2, 1.7)		.80
Intergroup comparisons						
CAET vs Control					-0.1 (−2.7, 2.5)	.93
HIIT vs Control					1.9 (−0.6, 4.4)	.13
HIIT vs CAET					1.8 (−0.8, 4.4)	.18

Note: HIIT, high-intensity interval training; CAET, continuous aerobic exercise training; VO_{2max}, maximal oxygen uptake; SE, standard error. Bold indicates statistically significant result ($p < .05$).

no significant between-group differences in proportions with regular menstrual cycles pre-intervention ($p = .51$) or in the last three months of the intervention ($p = .87$). Eight participants with amenorrhoea or oligomenorrhoea at baseline had regular cycles during the intervention: four in control, three in HIIT and one in CAET ($p = .32$). These participants all had BMI > 25 kg/m^2 at baseline and were PCOS phenotype A or B, and half lost weight during the intervention. One control participant and one CAET participant had regular menses at baseline that became irregular over the six-month intervention; both had baseline BMI > 40 kg/m^2.

Twenty-nine participants had menstrual cycle lengths recorded during both run-in-phase and intervention. For ten control group participants, mean cycle length pre-intervention was 45.1 (SD 17.9) days compared with 37.7 (SD 13.9) days at the end of intervention ($p = .23$). For 12 HIIT participants, mean menstrual lengths pre-intervention and end of intervention were 35.9 (SD 11.9) days and 32.5 (SD 9.5) days, respectively ($p = .23$), compared with seven CAET group participants who had mean lengths of 46.8 (SD 20.0) days and 34.3 (SD 6.1) days, respectively ($p = .09$). There were no between-group differences pre-intervention ($p = .53$) or end of intervention ($p = .57$).

Twenty-seven participants had documented ovulation events and menstrual periods during the pre-intervention run-in-phase allowing estimation of the luteal phase length: nine in control, 12 in HIIT and

six in CAET compared with 11 participants in the last three months of the intervention (three in control, five in HIIT and three in CAET). The mean luteal phase was 13.6 days (SD 2.5) compared with 14.2 days (SD 1.5) for the 23 participants during the intervention (p = .55). There were no between-group differences in the mean luteal phase length pre-intervention (p = .54) or end of intervention (p = .38).

Three participants achieved pregnancy during run-in and all resulted in live births.

3.5 | Hirsutism

The mean Ferriman-Gallwey hirsutism scores[20] were not significantly different pre-intervention and end of intervention in control (p = .31), HIIT (p = .44), or CAET (p = .86). There were no significant between-group differences: control vs HIIT (p = .91), control vs CAET (p = .58) and HIIT vs CAET (p = .68).

3.6 | Anthropometric and physical fitness outcomes

There was a statistically significant decrease of −0.8 kg/m^2 in BMI in the CAET group (95%CI −1.4–0.2, p < .01; Table 2). Waist circumference decreased significantly within the controls (−4.5 cm, 95%CI −8.6–0.4; p = .03), CAET (−6.9 cm, 95%CI −11.5–2.3; p < .01) and HIIT groups (−7.3 cm, 95%CI −11.8–2.9; p < .01), with no statistically significant between-group difference. No within- or between-group differences were observed in VO_{2max} (Table 2).

3.7 | Cardiometabolic outcomes

Mean fasting glucose increased in HIIT (0.3 mmol/L, 95% CI 0.1–0.6; p =. 02), which was significantly different from controls (p = .04) (Table 3). Mean fasting insulin levels increased significantly in controls by 19.5 mIU/L (95% CI 0.9–38.2; p = .04) with no changes within the CAET (p = .19) or HIIT group (p = .90), nor were between-group differences observed. LDL-C was reduced in the HIIT group compared with CAET (−0.3 mmol/L, 95%CI −0.6–0.1; p = .03). HDL-C increased in the HIIT group compared with control (0.2 mmol/L, 95%CI 0.0–0.4; p = .04), with no difference between CAET and control (p = .47). No within- or between-group differences were observed in blood pressure, HbA_{1c}, HOMA2-IR, total cholesterol, triglycerides, ALT or GGT (Table 3).

3.8 | Adverse events

No trial-related adverse events were reported. One participant in the CAET group sustained a musculoskeletal injury unrelated to exercise training and withdrew from the trial.

4 | DISCUSSION

We evaluated feasibility of a randomized trial evaluating HIIT and CAET versus control on reproductive outcomes. Recruitment and retention were adequate to conduct such a trial, but adherence to exercise and especially to OPK-testing, failed to meet pre-specified success criteria.

Exercise adherence has not been widely reported in PCOS exercise trials.[10] One trial[26] reported 60% adherence. Another[27] only included the 14/16 (87.5%) participants who completed ≥75% of prescribed exercise sessions in their analysis, but did not specifically report exercise adherence. In our trial, we found median adherence of 68% (IQR 53%, 86%), slightly below our pre-defined feasibility criterion of >70%. In both exercise groups, exercise adherence trended down over time, similar to other exercise intervention studies in women.[28,29] Exercise adherence is influenced by many participant factors including perceptions about exercise, perceived supportive behaviour and autonomous motivation.[30] Low exercise adherence in our trial could be secondary to barriers including lack of time, fear of injury, physical limitations or lack of confidence with respect to exercise as noted in other studies.[14,15] This study illustrates the importance of a feasibility study. Proposed lifestyle interventions for women with PCOS must be appropriate and easily integrated into their lives to encourage adherence.

HIIT and CAET were compared in a previous 8-week trial involving participants without PCOS with overweight or obesity; no differences were reported between training groups in adherence or exercise enjoyment.[31] In our study, we noted a negatively skewed distribution of adherence for participants randomized to CAET where half the participants completed >80% of the prescribed sessions, perhaps suggesting a subgroup of participants were adopters of CAET. Conversely, positive skew was observed for the HIIT group, especially during the final three months of the intervention. While exploratory, these different patterns suggest there may be differences between the training regimens affecting adherence, and may also reflect differences in participant characteristics within and between groups.

Reported attrition in previous PCOS exercise trials was 6%-54%, with most having attrition ≥25%.[15] This pilot trial's relatively low attrition demonstrates interest among women with PCOS in exercise research participation.[32] Unfortunately, low OPK-testing adherence caused inadequate sensitivity; ovulations could have been missed as the LH surge typically would not be detectable by the OPK test for longer than 24–48 h. OPKs have been used in research protocols involving women not actively trying to conceive[33,34]; however, OPK adherence was not reported. While OPKs are practical, easy to use and non-invasive in ovulation monitoring for family planning,[35] this trial suggests prolonged daily OPK use may not be sustainable in individuals not seeking conception. To capture ovulation accurately in a research setting, other techniques such as twice-monthly serum progesterone levels may be necessary.

TABLE 3 Cardiometabolic outcomes

Outcome	Mean (SD)			Change from baseline to 6 months (95% CI)	Difference in change from baseline to 6 months (95% CI)	*p* valve
	baseline	3 months	6 months			
Systolic blood pressure (mmHg) (SE) [*n*]						
Control group	117.7 (3.4) [16]	117.5 (3.0) [16]	116.0 (3.5) [15]	-1.7 (−7.6, 4.2)		.56
HIIT group	114.9 (3.5) [15]	115.8 (3.1) [15]	118.0 (3.9) [11]	3.1 (−3.6, 9.9)		.35
CAET group	113.8 (3.9) [12]	114.1 (3.5) [12]	114.0 (4.0) [12]	0.2 (−6.4, 6.8)		.96
Intergroup comparisons						
CAET vs Control					1.9 (−7.0, 10.7)	.47
HIIT vs Control					4.9 (−4.1, 13.8)	.28
HIIT vs CAET					3.0 (−6.5, 12.4)	.53
Diastolic blood pressure (mmHg) (SE) [*n*]						
Control group	73.7 (2.2) [16]	72.0 (1.7) [16]	72.7 (2.4) [15]	-1.0 (−5.1, 3.2)		.64
HIIT group	72.5 (2.3) [15]	73.7 (1.7) [15]	72.9 (2.7) [11]	0.4 (−4.4, 5.1)		.88
CAET group	72.8 (2.6) [12]	68.6 (1.9) [12]	72.9 (2.7) [12]	0.2 (−4.5, 4.8)		.94
Intergroup comparisons						
CAET vs Control					1.1 (−5.1, 7.4)	.72
HIIT vs Control					1.3 (−5.0, 7.6)	.67
HIIT vs CAET					0.2 (−6.5, 6.9)	.95
Haemoglobin A1c (%) (SE) [*n*]						
Control group	5.3 (0.1) [16]	5.3 (0.1) [15]	5.4 (0.1) [15]	0.1 (0.0, 0.1)		.14
HIIT group	5.4 (0.1) [15]	5.5 (0.1) [15]	5.4 (0.1) [11]	0.0 (−0.1, 0.1)		
CAET group	5.3 (0.1) [12]	5.3 (0.1) [12]	5.4 (0.1) [12]	0.1 (0.0, 0.2)		
Intergroup comparisons						
CAET vs Control					0.0 (−0.1, 0.1)	.60
HIIT vs Control					-0.1 (−0.2, 0.1)	.30
HIIT vs CAET					-0.1 (−0.2, 0.0)	.15
Fasting insulin (mIU/L) (SE) [*n*]						
Control group	99.5 (15.4) [16]	114.0 (17.6) [14]	119.1 (19.0) [15]	**19.5 (0.9, 38.2)**		.04
HIIT group	90.1 (15.9) [15]	84.4 (17.9) [14]	88.8 (20.2) [11]	-1.4 (−23.1, 20.4)		.90
CAET group	83.4 (17.8) [12]	86.4 (19.8) [12]	97.2 (21.7) [12]	13.8 (−7.0, 34.6)		.19
Intergroup comparisons						
CAET vs Control					-5.8 (−33.7, 22.2)	.68
HIIT vs Control					-20.9 (−49.5, 7.7)	.15
HIIT vs CAET					-15.1 (−45.2, 15.0)	.31
Fasting Glucose (mmol/L) (SE) [*n*]						
Control group	5.0 (0.1) [16]	5 (0.1) [15]	4.9 (0.1) [15]	-0.0 (−0.3, 0.2)		.75
HIIT group	5.0 (0.1) [15]	5.1 (0.1) [14]	5.3 (0.1) [11]	**0.3 (0.1, 0.6)**		.02
CAET group	4.9 (0.1) [12]	5 (0.2) [12]	5.0 (0.1) [12]	0.2 (−0.1, 0.5)		.15
Intergroup comparisons						
CAET vs Control					0.2 (−0.1, 0.6)	.19
HIIT vs Control					**0.4 (0.0, 0.7)**	.04
HIIT vs CAET					0.1 (−0.2, 0.5)	.47
HOMA2-IR (SE) [*n*]						
Control group	1.8 (0.3) [16]	2.1 (0.4) [14]	2.2 (0.3) [15]	0.3 (0.0, 0.7)		.05
HIIT group	1.7 (0.3) [15]	1.7 (0.4) [14]	1.7 (0.4) [11]	0.0 (−0.4, 0.4)		.82
CAET group	1.5 (0.3) [12]	1.6 (0.4) [12]	1.8 (0.4) [12]	0.3 (−0.1, 0.7)		.17

(Continues)

TABLE 3 (Continued)

Outcome	Mean (SD)			Change from baseline to 6 months (95% CI)	Difference in change from baseline to 6 months (95% CI)	*p* valve
	baseline	3 months	6 months			
Intergroup comparisons						
CAET vs Control					-0.1 (−0.6, 0.4)	.78
HIIT vs Control					-0.3 (−0.8, 0.2)	.27
HIIT vs CAET					-0.2 (−0.8, 0.3)	.42
Total Cholesterol (mmol/L) (SE) [*n*]						
Control group	4.5 (0.2) [16]	4.7 (0.2) [15]	4.4 (0.2) [15]	-0.06 (−0.29, 0.17)		.59
HIIT group	4.4 (0.2) [15]	4.2 (0.2) [15]	4.2 (0.2) [11]	-0.20 (−0.46, 0.06)		.12
CAET group	4.1 (0.2) [12]	4.2 (0.2) [12]	4.3 (0.2) [12]	0.11 (−0.15, 0.36)		.41
Intergroup comparisons						
CAET vs Control					0.17 (−0.18, 0.51)	.33
HIIT vs Control					-0.14 (−0.49, 0.20)	.41
HIIT vs CAET					-0.31 (−0.67, 0.06)	.09
LDL-C (mmol/L) (SE) [*n*]						
Control group	2.6 (0.2) [16]	2.9 (0.2) [15]	2.7 (0.2) [15]	0.06 (−0.12, 0.24)		.50
HIIT group	2.6 (0.2) [15]	2.5 (0.2) [15]	2.4 (0.2) [11]	-0.17 (−0.38, 0.04)		.10
CAET group	2.5 (0.2) [12]	2.6 (0.2) [12]	2.7 (0.2) [12]	0.16 (−0.05, 0.36)		.13
Intergroup comparisons						
CAET vs Control					0.09 (−0.18, 0.37)	.49
HIIT vs Control					-0.24 (−0.51, 0.04)	.09
HIIT vs CAET					**-0.33 (−0.62, −0.04)**	.03
HDL-C (mmol/L) (SE) [*n*]						
Control group	1.3 (0.1) [16]	1.2 (0.1) [15]	1.2 (0.1) [15]	-0.11 (−0.22, 0)		.05
HIIT group	1.2 (0.1) [15]	1.1 (0.1) [15]	1.2 (0.1) [11]	0.07 (−0.06, 0.20)		.30
CAET group	1.1 (0.1) [12]	1.1 (0.1) [12]	1.1 (0.1) [12]	-0.05 (−0.18, 0.07)		.41
Intergroup comparisons						
CAET vs Control					0.06 (−0.11, 0.23)	.47
HIIT vs Control					**0.18 (0.01, 0.35)**	.04
HIIT vs CAET					0.12 (−0.06, 0.30)	.19
Triglycerides (mmol/L) (SE) [*n*]						
Control group	1.3 (0.2) [16]	1.3 (0.2) [15]	1.2 (0.1) [15]	-0.10 (−0.31, 0.12)		.36
HIIT group	1.3 (0.2) [15]	1.2 (0.2) [15]	1.2 (0.2) [11]	-0.16 (−0.40, 0.09)		.20
CAET group	1.1 (0.2) [12]	1 (0.2) [12]	1.1 (0.2) [12]	0 (−0.24, 0.24)		.99
Intergroup comparisons						
CAET vs Control					0.10 (−0.23, 0.43)	.54
HIIT vs Control					-0.06 (−0.38, 0.27)	.73
HIIT vs CAET					-0.16 (−0.50, 0.19)	.36

(Continues)

TABLE 3 (Continued)

Outcome	Mean (SD) baseline	3 months	6 months	Change from baseline to 6 months (95% CI)	Difference in change from baseline to 6 months (95% CI)	*p* valve
ALT (mmol/L) (SE) [*n*]						
Control group	19.7 (3) [16]	22 (2.6) [15]	25.4 (4) [15]	5.73 (−0.41, 11.86)		.07
HIIT group	15.9 (3.1) [15]	14.6 (2.6) [15]	16 (4.3) [11]	0.11 (−6.84, 7.05)		.98
CAET group	16.5 (3.5) [12]	15.5 (2.9) [12]	16.1 (4.5) [12]	-0.42 (−7.34, 6.50)		.90
Intergroup comparisons						
CAET vs Control					-6.14 (−15.39, 3.10)	.19
HIIT vs Control					-5.62 (−14.89, 3.65)	.23
HIIT vs CAET					0.52 (−9.28, 10.33)	.91
GGT (mmol/L) (SE) [*n*]						
Control group	25.1 (4.5) [16]	29.4 (5.2) [15]	27.9 (4.5) [15]	2.80 (−2.08, 7.68)		.25
HIIT group	22.3 (4.7) [15]	20.3 (5.3) [15]	19.7 (4.7) [11]	-2.61 (−7.83, 2.62)		.32
CAET group	19.3 (5.2) [12]	19.8 (6) [12]	21.3 (5.2) [12]	2 (−3.58, 7.58)		.47
Intergroup comparisons						
CAET vs Control					-0.80 (−8.21, 6.61)	.83
HIIT vs Control					-5.41 (−12.55, 1.74)	.13
HIIT vs CAET					-4.61 (−12.25, 3.04)	.23

Note: HIIT, high-intensity interval training; CAET, continuous aerobic exercise training; SE, standard error, LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; ALT, alanine aminotransferase; GGT, gamma-glutamyl transferase; VO_{2max}, maximal oxygen uptake; bold indicates statistically significant result ($p < .05$).

It is unclear how menstrual regularity is affected by exercise in women with PCOS; some trials demonstrated improvements while others found no change.[10] One exercise trial[7] found participants with reproductive function improvements had significantly more weight loss than those who did not. We found participants from each group experienced improvements in menstrual cycle regularity, with no significant intergroup differences. The participants with increased menstrual cycle regularity had hyperandrogenism (PCOS phenotype A/B), and overweight or obesity; 50% lost weight during the intervention. This finding raises two questions that require further investigation: (1) is the response to exercise related to PCOS phenotype (are phenotypes with hyperandrogenism more responsive to exercise); and (2) does the reproductive response to exercise vary by baseline BMI and/or weight loss?

This study has several strengths including being the first randomized trial to compare effects of HIIT and CAET on reproductive outcomes. It included a three-month run-in-phase to determine baseline reproductive function including ovulations and menstrual cycle lengths in women with PCOS. We included normal-weight women as well as women with elevated BMIs making our study findings more generalizable than previous exercise trials in PCOS[7,27] that only included participants with elevated BMIs. We also included rigorous and direct measurements for the anthropometric, metabolic and hormonal outcomes.

Since this study was a pilot trial to evaluate feasibility and inform planning of future trials, the sample size was inadequate to evaluate efficacy of HIIT and CAET on reproductive health. In addition, low OPK-testing adherence precluded clear conclusions regarding ovulation rates. Finally, participants may have changed their dietary intake, which we did not assess and could not control for in the analyses that might have influenced these results.

In conclusion, while acceptable participant recruitment and relatively low attrition indicate women with PCOS are interested in exercise research participation, future trials should address barriers to exercise adherence, and a different, more feasible and sustainable ovulation testing method should be used. HIIT and CAET did not result in statistically significant improvements in reproductive health outcomes, specifically menstrual cycle and luteal phase length. HIIT and CAET were both effective at improving anthropometrics, insulin resistance and lipids in women with PCOS. Our findings indicate there may be differential anthropometric and cardiometabolic effects of exercise based on exercise type. Further, larger studies are needed to evaluate impacts of these two exercise interventions on reproductive, anthropometric and cardiometabolic outcomes as well as to explore associations of PCOS phenotype and BMI to exercise response, to inform evidence-based clinical practice guidelines for the management of PCOS in reproductive-aged women.

CONFLICTS OF INTEREST

None disclosed.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Jamie L. Benham https://orcid.org/0000-0002-2233-4613

REFERENCES

1. Ding T, Hardiman PJ, Petersen I, Wang FF, Qu F, Baio G. The prevalence of polycystic ovary syndrome in reproductive-aged women of different ethnicity: a systematic review and meta-analysis. *Oncotarget*. 2017;8(56):96351-96358.
2. Lizneva D, Suturina L, Walker W, Brakta S, Gavrilova-Jordan L, Azziz R. Criteria, prevalence, and phenotypes of polycystic ovary syndrome. *Fertil Steril*. 2016;106(1):6-15.
3. Kousta E, White DM, Cela E, McCarthy MI, Franks S. The prevalence of polycystic ovaries in women with infertility. *Hum Reprod*. 1999;14(11):2720-2723.
4. Barnard L, Ferriday D, Guenther N, Strauss B, Balen AH, Dye L. Quality of life and psychological well being in polycystic ovary syndrome. *Hum Reprod*. 2007;22(8):2279-2286.
5. Delitala AP, Capobianco G, Delitala G, Cherchi PL, Dessole S. Polycystic ovary syndrome, adipose tissue and metabolic syndrome. *Arch Gynecol Obstet*. 2017;296(3):405-419.
6. Jedel E, Labrie F, Oden A, et al. Impact of electro-acupuncture and physical exercise on hyperandrogenism and oligo/amenorrhea in women with polycystic ovary syndrome: a randomized controlled trial. *Am J Physiol Endocrinol Metab*. 2011;300(1):E37-45.
7. Thomson RL, Buckley JD, Noakes M, Clifton PM, Norman RJ, Brinkworth GD. The effect of a hypocaloric diet with and without exercise training on body composition, cardiometabolic risk profile, and reproductive function in overweight and obese women with polycystic ovary syndrome. *J Clin Endocrinol Metab*. 2008;93(9):3373-3380.
8. Samadi Z, Bambaeichi E, Valiani M, Shahshahan Z. Evaluation of changes in levels of hyperandrogenism, hirsutism and menstrual regulation after a period of aquatic high intensity interval training in women with polycystic ovary syndrome. *Int J Prev Med*. 2019;10:187.
9. Almenning I, Rieber-Mohn A, Lundgren KM, Shetelig Lovvik T, Garnaes KK, Moholdt T. Effects of high intensity interval training and strength training on metabolic, cardiovascular and hormonal outcomes in women with polycystic ovary syndrome: a pilot Study. *PLoS One*. 2015;10(9):e0138793.
10. Benham JL, Yamamoto JM, Friedenreich CM, Rabi DM, Sigal RJ. Role of exercise training in polycystic ovary syndrome: a systematic review and meta-analysis. *Clin Obes*. 2018;8(4):275-284.
11. Batacan RB Jr, Duncan MJ, Dalbo VJ, Tucker PS, Fenning AS. Effects of high-intensity interval training on cardiometabolic health: a systematic review and meta-analysis of intervention studies. *Br J Sports Med*. 2017;51(6):494-503.
12. Gibala MJ, Little JP, Macdonald MJ, Hawley JA. Physiological adaptations to low-volume, high-intensity interval training in health and disease. *J Physiol*. 2012;590(5):1077-1084.
13. Wewege M, van den Berg R, Ward RE, Keech A. The effects of high-intensity interval training vs. moderate-intensity continuous training on body composition in overweight and obese adults: a systematic review and meta-analysis. *Obes Rev*. 2017;18(6):635-646.
14. Banting LK, Gibson-Helm M, Polman R, Teede HJ, Stepto NK. Physical activity and mental health in women with polycystic ovary syndrome. *BMC Womens Health*. 2014;14(1):51.
15. Thomson RL, Buckley JD, Brinkworth GD. Perceived exercise barriers are reduced and benefits are improved with lifestyle modification in overweight and obese women with polycystic ovary syndrome: a randomised controlled trial. *BMC Womens Health*. 2016;16(1):14.
16. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. *Fertil Steril*. 2004;81(1):19-25.
17. Scolaro KL, Lloyd KB, Helms KL. Devices for home evaluation of women's health concerns. *Am J Health Syst Pharm*. 2008;65(4):299-314.
18. Wilson RC, Jones PW. A comparison of the visual analogue scale and modified Borg scale for the measurement of dyspnoea during exercise. *Clin Sci (Lond)*. 1989;76(3):277-282.
19. Polar. Polar Flow. 2020; https://flow.polar.com. Accessed May 23, 2020.
20. Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. *J Clin Endocrinol Metab*. 1961;21(11):1440-1447.
21. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*. 1972;18(6):499-502.
22. Diabetes Trials Unit. HOMA2 Calculator. https://www.dtu.ox.ac.uk/homacalculator/. Accessed September 14, 2020.
23. Balke B, Ware RW. An experimental study of physical fitness of Air Force personnel. *U S Armed Forces Med J*. 1959;10(6):675-688.
24. Binder RK, Wonisch M, Corra U, et al. Methodological approach to the first and second lactate threshold in incremental cardiopulmonary exercise testing. *Eur J Cardiovasc Prev Rehabil*. 2008;15(6):726-734.
25. Palomba S, Giallauria F, Falbo A, et al. Structured exercise training programme versus hypocaloric hyperproteic diet in obese polycystic ovary syndrome patients with anovulatory infertility: a 24-week pilot study. *Hum Reprod*. 2008;23(3):642-650.
26. Vizza L, Smith CA, Swaraj S, Agho K, Cheema BS. The feasibility of progressive resistance training in women with polycystic ovary syndrome: a pilot randomized controlled trial. *BMC Sports Sci Med Rehabil*. 2016;8:14.
27. Turan V, Mutlu EK, Solmaz U, et al. Benefits of short-term structured exercise in non-overweight women with polycystic ovary syndrome: a prospective randomized controlled study. *J Phys Ther Sci*. 2015;27(7):2293-2297.
28. Huang HP, Wen FH, Tsai JC, et al. Adherence to prescribed exercise time and intensity declines as the exercise program proceeds: findings from women under treatment for breast cancer. *Support Care Cancer*. 2015;23(7):2061-2071.
29. Arikawa AY, O'Dougherty M, Schmitz KH. Adherence to a strength training intervention in adult women. *J Phys Act Health*. 2011;8(1):111-118.
30. Rodrigues F, Teixeira DS, Neiva HP, Cid L, Monteiro D. Understanding exercise adherence: the predictability of past experience and motivational determinants. *Brain Sci*. 2020;10(2):98.
31. Vella CA, Taylor K, Drummer D. High-intensity interval and moderate-intensity continuous training elicit similar enjoyment and adherence levels in overweight and obese adults. *Eur J Sport Sci*. 2017;17(9):1203-1211.
32. Avery JC, Braunack-Mayer AJ. The information needs of women diagnosed with Polycystic Ovarian Syndrome–implications for treatment and health outcomes. *BMC Womens Health*. 2007;7:9.
33. Leiva R, Burhan U, Kyrillos E, et al. Use of ovulation predictor kits as adjuncts when using fertility awareness methods (FAMs): a pilot study. *J Am Board Fam Med*. 2014;27(3):427-429.
34. Schaumberg MA, Jenkins DG, Janse de Jonge XAK, Emmerton LM, Skinner TL. Three-step method for menstrual and oral contraceptive cycle verification. *J Sci Med Sport*. 2017;20(11):965-969.
35. Severy L. Acceptability of home monitoring as an aid to conception. *J Int Med Res*. 2001;29(1_suppl):28A-34A.

How to cite this article: Benham JL, Booth JE, Corenblum B, et al. Exercise training and reproductive outcomes in women with polycystic ovary syndrome: A pilot randomized controlled trial. *Clin Endocrinol (Oxf)*. 2021;95:332–343. https://doi.org/10.1111/cen.14452