

A review analysis of exercise training regimes among females with polycystic ovary syndrome

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Abstract

Objective: The current systematic review was planned to provide quality assessment of different exercise regimes and their outcomes on the symptoms of polycystic ovary syndrome, and to see if one exercise regime was better than the rest.

Methods: Search was conducted on PubMed and Google Scholar databases for studies published between 2001 and 2021 whose full text was available. The search yielded 28 studies that were reviewed.

Results: The current evidence suggests that exercise regimes, such as high-intensity interval training, progressive resistance training, aerobic exercises, and yoga may improve polycystic ovary syndrome conditions. This is accomplished through treating associated risk factors, like body morphology, insulin resistance, hyperandrogenism, lipid profile, reproductive hormones, menstrual cycle, and quality of life.

Conclusion: Exercise regimes improves several symptoms of polycystic ovary syndrome. However, selecting a specific exercise regime over others as the standardised treatment protocol remained inconclusive.

Key Words: Polycystic ovarian syndrome, Exercises, High-intensity interval training, Aerobic exercises.

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Introduction

Polycystic ovary syndrome (PCOS) is a complex multifactorial disorder. It is a common endocrinopathy impacting females of reproductive age, globally affecting 20% of the women¹. Different diagnostic criteria define PCOS with the presence of clinical or/and biochemical hyperandrogenism, long-term anovulation, hirsutism, acne, oligomenorrhea and infertility. Rotterdam criterion

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2003 is the standard used for diagnostics, while the Androgen Excess and PCOS Society Criterion 2006 (AE-PCOS) is another common criterion for PCOS^{2,3}.

PCOS is associated with several ailments, such as cardiometabolic, psychological and reproductive disorders⁴. The most common cardiometabolic conditions representing high risk for PCOS women are high blood pressure (BP), altered lipid profile, insulin resistance (IR), insulin-resistant diabetes, non-alcoholic fatty liver, and cardiovascular diseases⁵. PCOS is also associated with psychological distress that indicates a high risk of anxiety, depression, stressfulness and high sensitivity due to low self-esteem and negative body image. These risk factors, in turn, negatively affect the health-related quality of life (HRQOL)⁶.

The recommended first line of management for PCOS is lifestyle modification which can effectively reduce IR, improve metabolism and reproductive functions, promote weight loss which further restores ovulation and menstrual cycle. Being physically active and losing weight are advised for managing PCOS symptoms^{7,8}. Different exercise interventions have been studied, evaluating the effects on improving PCOS features. Moderate exercises, resistance exercise, and aerobic exercise, as treatment of the clinical complication of PCOS, are considered to be beneficial due to their positive impact on other insulin-resistant populations in the absence of weight loss^{9,10}. Several reviews and analyses about the management of PCOS over the years have stated beneficial outcomes of exercise training, but the literature in support of one exercise regime over the other till date remains lacking and inconclusive⁸. Several review and analysis have focussed on one or two outcome measures have never entirely focussed on exercise alone. The current systematic review was planned to summarise the effects of different exercise regimes on body morphology, metabolic, reproductive, cardiovascular and psychological features among females with PCOS in the hope of proving one exercise regime to be superior to other regimes in managing PCOS.

Materials and Methods

The current systematic review was conducted as per the Preferred Reporting Items for Systematic Reviews and

Inclusion criteria	Exclusion criteria
Studies include spanning the last two decades (2001-2021).	Study in any other language than English.
The study had at least one statistically significant outcome measure.	Studies not focused mainly on PCOS.
The targetted population was pre-diagnosed women (reproductive age) with PCOS.	Reviews or analysis the summary of the disease.
Criteria used for the diagnosis of PCOS were Rotterdam Criterion and AE-PCOS Criterion.	Study with prior exercise intervention.
Some studies had a diagnosis of PCOS confirmed by a general practitioner without indicating the use of any of the diagnostic criteria.	Target population: post-menopausal women.
Only randomized control trials/ randomized clinical trials were included.	

Figure-1: Inclusion and exclusion criteria for studies reviewed.

Table-1: Search Booleans

HIIT OR Aerobic OR Physical activity OR PRT OR Yoga OR Exercise OR Physical therapy AND PCOS OR Polycystic Ovary Syndrome AND Reproductive age AND Insulin resistance OR Insulin sensitivity OR Reproductive function OR cardiovascular function OR psychological function OR Health-related quality of life OR Metabolic function.

Meta-Analysis (PRISMA) guidelines¹¹, and was registered with the international Prospective Register of Systematic Reviews (PROSPERO) reg no: CRD42021267721¹².

Sampling method: Literature was selected by thorough search on PubMed and Google Scholar databases for studies published from 2001 to 2021 and whose full text was available. The search strategy included key words, like PCOS, exercise, high-intensity interval training (HIIT), progressive resistance training (PRT), yoga, strength training, aerobic exercise, physical activity, etc. (Table 1). Inclusion and exclusion criteria were outlined in detail (Figure 1) The data extracted from the studies included primary author's name, publication year, study arms, sample sizes, study design, demographic details, like body mass index (BMI), as well as clinical details, like the diagnostic criterion used for PCOS, the type of control group, type of intervention, duration, frequency of exercise, randomisation of subjects, and significant primary and secondary outcome pre- and post-intervention data. If available, p-value and confidence interval (CI) were also extracted.

Primary outcome measures: IR, body weight, BMI, waist circumference (WC), body fat percentage and mass (% or kg), free androgen index (FAI), testosterone, Modified Ferriman-Gallwey score, epiandrosterone/Dehydroepiandrosterone- Sulfate (DHEA/DHEA-S), number of follicles, Luteinizing hormone (LH), follicular stimulating hormone (FSH) and sex hormone-binding globulin (SHBG).

Secondary outcome measure: Lipid profile, high-density lipoprotein (HDL), low-density lipoprotein (LDL), total cholesterol (TC), triglycerides (T), systolic blood pressure (SBP), diastolic blood pressure (DBP), maximal oxygen consumption (VO₂max), HRQOL, Depression, Anxiety,

Stress Scale-21 (DASS-21), Polycystic Ovary Syndrome Questionnaire (PCOSQ-50), Short Form-36 (SF-36), Beck anxiety inventory (BAI) score, and Beck's depression inventory-II (BDI-II) score.

Assessment of RCT quality: The quality and internal validity, along with the risk of bias of all the included RCTs, were evaluated. For this purpose, the 15-point tool for the assessment of study quality and reporting in exercise scale (TESTEX scale) and the Modified Cochrane Collaboration tool were used to assess the risk of bias for RCTs¹³.

Results

Of the 311 RCTs found, 28(9%) were reviewed (14-41) (Figure 2).

Attributes of RCTs in the review: The total number of participants was 1367 (range: 12-94).

Characteristics of interventions: Overall, 21(75%) studies reported a comparison between aerobic exercises with a control group (with/without intervention), 3(10.7%) studies compared HIIT with a control group, 3(10.7%) studies focussed on yoga with a control group (conventional physical therapy), and 1(3.6%) study focussed on PRT with a control group without intervention. The duration of intervention was 10 weeks, 12 weeks, 16 weeks, and 26 weeks (6 months), exercise intensity in most studies was either moderate or high, and aerobic exercises, HIIT, PRT, yoga and physical activity showed significant results post-intervention on a range of parameters (Table 2).

On the basis of the TESTEX scale, it was noted among other things, that the eligibility criteria were described in all the studies, statistical data reported in the RCTs was constant, and the limitation of RCTs was primarily associated with lack of data or lack of blind allocation of groups, failure to evaluate the outcome measures, and failure to either mention or implement the intention-to-treat (ITT) analysis (Table 3).

Risk of bias: All the RCTs reviewed were evaluated for risk of bias. The majority of the RCTs demonstrated a high risk

Table-2: The randomised controlled trials (RCTs) reviewed

Author, Publication year	Design, Sample size, Demographics	Intervention	Significant outcome measures
Hoeger et al, 2004 ¹⁴	RCT - 38 overweight and obese PCOS. Age: 29.4 ± 5.7 (years). BMI: 39.7 ± 7.1 (kg/m ²).	Lifestyle modification: Combined: exercise (150 min/week) for 12 months and diet (500–1000 kcal/day). Placebo: one tablet 2/day	Total Testosterone (<0.05) FAI (<0.05)
Bruner et al, 2006 ¹⁵	RCT - 12 PCOS into exercise group (n=7) and control group (n=5). Exercise group: Age: 32.3 ± 1.0 (years). BM: 36.2 ± 2.0 (kg/m ²). Control group: AGE: 28.4 ± 2.7 (years). BMI: 37.1 ± 3.4 9 (kg/m ²).	12-week endurance training on treadmill (walking) or stationary cycling at moderate level (70%-85% of age-predicted MHR). Resistance exercise included 12 exercises: biceps curl, lat pulldown, leg curl, leg extension, shoulder press, chest press, leg press, hip abduction, hip adduction, hip flexion, hip extension and back extension.	WC (0.001) Vo2max (0.017) Fasting insulin (0.03)
Vigorito et al, 2007 ¹⁶	RCT - 90 equally divided into two groups. PCOS group: Age: 21.7 ± 2.3 (years). BMI: 29.3 ± 2.9 (kg/m ²). Control group: Age: 21.9 ± 1.9 (years). BMI: 29.4 ± 3.5 (kg/m ²).	3-month structured ET program: 30 min on a bicycle ergometer with the target of 60–70% of the maximal oxygen consumption (VO2max). Control group: No intervention.	Vo2max (< 0.001) BMI (< 0.001) WC (< 0.001) Fasting insulin (< 0.001)
Orio et al, 2008 ¹⁷	RCT - 64 (32 per group). PCO-Trained group: BMI: 28.9 ± 3.0 (kg/m ²). PCO-Detrained group: BMI: 28.9 ± 2.3 (kg/m ²).	24-week ET program: 30–40 min on a bicycle ergometer with the target of 60%–70% of the VO2max. Followed by 12-week detraining period.	2th week: BMI (0.017) Fasting insulin (0.001) Lipid profile: HDL-C (< 0.001) LDL-C (0.002) VO2max (< 0.001) 24th week: BMI (0.017) Fasting insulin (0.001) Lipid profile: LDL-C (0.002) HDL-C (< 0.001) VO2max (< 0.001)
Thomson et al, 2008 ¹⁸	RCT - 94 overweight/obese PCOS into diet only group (n=30), diet and aerobic group (n=31) and diet + aerobic and resistance group (n=33). Age: 29.3 ± 0.7 (years). BMI: 36.1 ± 0.5 (kg/m ²).	Aerobic exercise: 20-week walking/jogging program 5 days/week or walking/jogging 3 days/week plus PRT 2 days/week on non-consecutive days. Resistance training: bench press, lat pull down, leg press, knee extension, and sit-ups. Diet: 5000–6000 kJ/day (30% protein, 40% CHO, 30% fat).	BF (< 0.03) SBP (< 0.01) DBP (≤ 0.05) Insulin (< 0.01) HOMA-IR (< 0.01) Lipid profile: TC (< 0.01) LDL (< 0.01) Testosterone (< 0.01) SHBG (< 0.01) FAI (< 0.01)
Moro et al, 2009 ¹⁹	RCT - 15 (8 hyper androgenic obese PCOS and 7 healthy BMI-matched controls). Age: 25 ± 1 (years). BMI: 32.0 ± 1.6 (kg/m ²).	16-week supervised and individualized aerobic exercise; 5 day/week; treadmill at 55% VO2max. Control group: no exercise	VO2 max (0.009)

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Author, Publication year	Design, Sample size, Demographics	Intervention	Significant outcome measures
Stener-Victorin et al, 2009 ²⁰	RCT - 20 PCOS into Exercise (n=5), EA (n=9) and control (n=6). Physical activity group: Age: 30.4 ± 5.5 (years). BMI: 26.8 ± 4.8 (kg/m ²). EA group: Age: 29.9 ± 4.5 (years). BMI: 27.5 ± 8.6 (kg/m ²). Control group: Age: 31.0 ± 3.2 (years). BMI: 28.0 ± 6.2 (kg/m ²).	16-week aerobic exercise at self-selected pace; at least 3 days/week; 30–45 min at faster than normal walking pace. EA: Acupuncture. Control group: no exercise.	BMI (0.05)
Jedel et al, 2011 ²¹	RCT - 84 PCOS into EA (n=29), Exercise (n=30) and control (n=15). Exercise group: Age: 30.2 ± 4.7 (years). BMI: 27.7 ± 6.44 (kg/m ²). EA group: Age: 29.7 ± 4.3 (years). BMI: 29.1 ± 8.83 (kg/m ²). Control group: Age: 30.1 ± 4.2 (years). BMI: 26.8 ± 5.56 (kg/m ²).	Physical exercise group: 16 week aerobic ex., self-selected pace; at least 3 days/week; at least 30 min at faster than normal walking pace; weekly call to advise increase of ex.; 16-week follow-up (32 week). Low frequency EA group: low-frequency electro-acupuncture. Control group: No intervention.	VO ₂ max (0.002) Free Testosterone (0.014) DHEAS (0.039)
Nidhi et al, 2012 ²²	RCT - 90 PCOS into Yoga (n=35) and control (n=36). Exercise group: Age: 16.22 ± 1.13 (years). BMI: 20.30 ± 1.92 (kg/m ²). Control group: Age: 16.22 ± 0.93 (years). BMI: 21.22 ± 2.99 (kg/m ²).	Yoga: Suryanamaskara, asana, pranayama, and meditation 1 hour per day each day for 12 weeks.	Fasting Insulin (<0.001) Fasting Blood Glucose (<0.001) HOMA-IR (<0.05) Lipid profile: TRIG (<0.001) TC (<0.001) HDL (<0.001) LDL (0.001)
Roessler et al, 2013 ²³	RCT - 17 sedentary PCOS into two groups (n=8 and n=9). Exercise group: Age: 31.0 ± 3.0 (years). BMI: 36.7 ± 2.8 (kg/m ²). Control group: Age: 32.3 ± 2.6 (years). BMI: 36.0 ± 2.3 (kg/m ²).	16 weeks of intervention: eight weeks high-intensity aerobic exercise (3 days per week with two days of indoor cycling and one of brisk walking or running) was followed by eight weeks of Group counselling or vice versa.	Weight (0.023) BMI (0.024) Waist (0.002) VO ₂ max (<0.001)
Nidhi et al, 2013 ²⁴	RCT - 90 PCOS into Yoga (n=35) and control (n=36). Exercise group: Age: 16.22 ± 1.13 (years). BMI: 20.36 ± 2.06 (kg/m ²). Control group: Age: 16.22 ± 0.93 (years). BMI: 21.10 ± 2.98 (kg/m ²).	Yoga: Holistic yoga module: asana, pranayama, relaxation techniques, meditation, and lectures on yogic lifestyle and stress management through yogic counselling.	MFG score (0.002) LH (0.005) LH/FSH ratio (0.015) Total Testosterone (0.014).

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Author, Publication year	Design, Sample size, Demographics	Intervention	Significant outcome measures
Nybacka et al, 2013 ²⁵	RCT - 57 overweight/obese PCOS into Diet only group (n=19), Exercise group (n=19) and diet and exercise group (n=19). Exercise group: Age: 31.3 ± 4.8 (years). BMI: 34.8 ± 5.2 (kg/m ²). Diet and EX group: Age: 31.8 ± 4.9 (years). BMI: 38.1 ± 7.0 (kg/m ²). Diet group: Age: 29.9 ± 5.5 (years). BMI: 35.4 ± 4.9 (kg/m ²).	Exercise: Walking (with or without poles), aerobics, jogging, swimming, and muscle strength training, with a moderate to vigorous exertion level, performed two to three times per week and a duration of 45–60 minutes.	BMI (<0.05) body fat (<0.05) Mean follicle number (<0.01)
Gaeini et al, 2014 ²⁶	RCT - 40 PCOS into trained and sedentary control groups. Age: 23.5 ± 5.0 (years) BMI: 18.86–32.03 (kg/m ²)	Aerobic sport activity (running) for 12 weeks and 3 sessions weekly during 25–30 min. 60–85% intensity.	Body weight (<0.0001) DHEAso4 (0.023) Menstrual cycle (<0.0001) Follicles Number in left Ovary (0.005) Follicles Number in right Ovary (0.041)
Almenning et al, 2015 ²⁷	RCT - 31 PCOS into three group: HIIT n=10, strength training group n=11 and control group n=10. Age: 27.2 ± 5.5 (years) BMI: 26.7 ± 6.0 (kg/m ²)	HIIT group: High-intensity interval training (walking/running and/or cycling). Strength training (8 dynamic strength drills with a resistance/machines) Control group: recommended > 150 min of weekly	Fat mass (0.70) Fat mass (0.39) VO2max (<0.01) Insulin (0.02) HOMA-IR (0.01) DHEAS (0.71) Lipid profile: HDL (0.04)
Turan et al, 2016 ²⁸	RCT - 30 PCOS into Exercise group (n=14) and control group (n=16). Age: 24.45 ± 2.8 (years). Exercise group: BMI: 21.8 ± 1.0 (kg/m ²). Control group: BMI: 21.9 ± 1.1 (kg/m ²).	8-week aerobic and resistance ex; 3 day/week for 50–60 min; treadmill and step, resistance band; supervised. Control group: no exercise.	WC (< 0.05) VO2max (< 0.05)
Vizza et al, 2016 ²⁹	RCT - 15 PCOS into PRT group (n = 8) and control group (n = 7). Age: 27 ± 5 (years). BMI: 37.8 ± 11.4 (kg/m ²).	12 week Progressive resistance training: cycle or treadmill/calisthenics and resistance exercise (lat pull down, leg curl, seated row, leg press, calf raise, chest press, split squat, shoulder press, biceps curl, triceps extension and abdominal curl). Control group: usual lifestyle.	Body weight (0.01) BMI (0.04) Waist Circumference (0.03) Lean mass (0.01) Fat-free mass (0.005) PCOSQ domain scores: Emotions (0.003) Weight (0.04) Infertility problems (0.03) HRQoL (SF-36): Physical functioning (0.02) Vitality (0.02)

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Author, Publication year	Design, Sample size, Demographics	Intervention	Significant outcome measures
			Social functioning (0.002) Role emotional (0.009) Mental health (0.009) DASS-21 domains: Depression (0.01) Anxiety (0.03) Exercise self-efficacy scale (0.04)
Vasheghani-Farahani et al, 2017 ³⁰	RCT - 40 PCOS into exercise group (n=20) and control group (n=20). Exercise group: Age: 27.7 ± 4.2 (years). BMI: 28.8 ± 5.88 (kg/m ²). Control group: Age: 29 ± 5.39 (years). BMI: 25.7 ± 2.15 (kg/m ²).	Walk with a medium intensity (64 to 76% of maximum heart rate) for 30 minutes per day and at least 5 days per week.	WC (<0.001) Insulin (0.016) HOMA-IR (.009)
Costa et al, 2018 ³¹	RCT - 27 PCOS into exercise group (n = 14) and control group (n = 13). Exercise group: Age: 27.6 ± 4.5 (years). BMI: 32 ± 4.2 (kg/m ²). Control group: Age: 24.4 ± 5.0 (years). BMI: 33.6 ± 5.1 (kg/m ²).	Progressive aerobic exercise: walking and/or jogging. Control group: no intervention.	Control HRQL: Physical functioning (0.004) General health (0.012) Mental health (0.042) BMI (<0.001) WC (<0.001) VO ₂ max (<0.001) Lipid profile: Total cholesterol (0.043)
Esmael et al, 2019 ³²	RCT - 30 obese PCOS into Group A (Pulsed Electromagnetic Field) n=15 and Group B (aerobic exercise) n=15. Exercise group: Age: 26.46 ± 2.74 (years). BMI: 34.64 ± 3.21 (kg/m ²). Control group: Age: 26.4 ± 3.97 (years). BMI: 34.36 ± 1.24 (kg/m ²).	Aerobic exercise: 40 mins/session, 3 sessions per week for 12 weeks. Pulsed electromagnetic field. Following specifications: Speed range (0.8 mph to 16 mph). Elevation range (0% to 15%). Power (220v, 60Hz, 15amp).	Weight (0.001) BMI (0.001) LH:FSH ratio (0.001)
Kirthika et al, 2019 ³³	RCT - 30 PCOS into Exercise group (n=15) and Control group (n=15).	AE: 45 minutes of brisk jogging in a treadmill at 6km/hour speed. ASE: active stretching exercises for the upper limb, lower limb and trunk muscles. Each stretch was held for 20 seconds and 10 repetitions for each group of muscle daily for 12 weeks.	PCOSQ-50 (<0.001) LH:FSH ratio (<0.001) Free Testosterone (<0.001) HOMA-IR (<0.001)
Ribeiro et al, 2019 ³⁴	RCT - 87 PCOS into CAT (n = 28), IAT (n = 29) and control group (n = 30). CAT group: Age: 29.1 ± 5.3 (years). BMI: 28.4 ± 5.6 (kg/m ²). IAT group: Age: 29.0 ± 4.3 (years). BMI: 28.7 ± 4.8 (kg/m ²). Control group: Age: 28.5 ± 5.8 (years). BMI: 29.1 ± 5.2 (kg/m ²).	Group IAT: Treadmills. Group CAT: Treadmills. Control group: No intervention.	WC (0.05 – CAT and IAT) Testosterone (0.001- CAT, 0.05- IAT) SF-36 questionnaire: Physical role functioning (0.05- CAT, 0.001-IAT) Physical functioning (0.001-CAT, 0.05-IAT) General health perception (0.001- CAT and IAT) Vitality (0.001-CAT and IAT)

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Author, Publication year	Design, Sample size, Demographics	Intervention	Significant outcome measures
			Social role functioning (0.001-CAT and IAT) Emotional role functioning (0.00-CAT, 0.05-IAT) Mental health (0.001-CAT and IAT)
Samadi et al, 2019 ³⁵	30 PCOS (15/group) AHIT+ metformin group and metformin only group. Exercise group: Age: 80.2 ± 25.29 (years). BMI: 32.80 ± 4.49 (kg/m ²). Control group: Age: 83.4 ± 0.26 (years). BMI: 34.08 ± 4.45 (kg/m ²).	12-week aquatic HIIT; 3 days/week for 30 min with 4 x 4min intervals, each with 8 rounds of 20 s max II w/10 s rest, and 1 min rest between each 4 min bout; HRM. Metformin (1500 mg) taken daily for 3 consecutive days for weeks.	BMI (0.032) Fat mass (0.015) FSH (0.012) 12 Free Testosterone (0.001) SHBG (0.000) HOMA-IR (0.032) Hirsutism severity (0.000)
Tiwari et al, 2019 ³⁶	RCT - 66 PCOS into two groups: exercise with oral placebo and exercise with oral metformin. Exercise group: Age: 24.46 ± 4.76 (years). BMI: 26.32 ± 3.68 (kg/m ²). Control group: Age: 24.33 ± 3.89 (years). BMI: 25.23 ± 4.64 (kg/m ²).	6-month marching in place; 3 days/week for 30 min; monitored by investigator for first 3 months to ensure HR ≥ 120 bpm.	BMI (<0.001) WC (<0.001) MFG score (0.005) Serum Testosterone (0.203)
Patel et al, 2020 ³⁷	RCT - 31 PCOS (13 yoga and 9 no ex). Exercise group: Age: 30.9 ± 1.2 (years). BMI: 35.1 ± 1.5 (kg/m ²). Control group: Age: 31.2 ± 2.3 (years). BMI: 35.4 ± 3.3 (kg/m ²).	3-month supervised mindful yoga; 3 days/week for 1 h; yoga: pranayama, vinyasa flows, restorative asana, mindfulness, meditation; follow-up 3 month post-study.	Free Testosterone (0.0413) BAI score (0.0365) BDI-II score (<0.001)
Ribeiro et al, 2020 ³⁸	RCT - 87 PCOS divided into three groups: CAT (n=28), IAT (n=29) and CG (n=30). CAT Group: Age: 29.1 ± 5.3 (years). BMI: 28.4 ± 5.6 (kg/m ²). IAT Group: Age: 29.0 ± 4.3 (years). BMI: 28.7 ± 4.8 (kg/m ²). Control group: Age: 28.5 ± 5.8 (years). BMI: 29.1 ± 5.2 (kg/m ²).	CAT and IAT group: 16-week CAT or IAT performed on a treadmill three times per week, lasting equally and progressively from 30 minutes in the first week, to 50 minutes in the last wk. Control group: CG were asked to maintain their usual daily physical activity profile.	WC (0.045) Body fat percentage (0.034) Lipid profile: Cholesterol (≤0.001) LDL (0.030) Testosterone (≤0.001) FAI (0.037)
Wu et al, 2020 ³⁹	RCT - 38 PCOS into exercise (n=19) and control (n=19). Exercise Group: Age: 32.7 ± 3.2 (years). BMI: 23.8 ± 3.0 (kg/m ²). Control Group: Age: 23.8 ± 3.0 (years). BMI: 24.1 ± 3.2 (kg/m ²).	12-week exercise program: 1-h training consisting of a 15-min warm-up, 30-min bicycle ergometer at V02AT achieved at the initial symptom-limited CPET, and a 15-min cool-down (four times per week).	BMI (0.029) V02max (0.032)

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Author, Publication year	Design, Sample size, Demographics	Intervention	Significant outcome measures
Zehsaz et al, 2020 ⁴⁰	RCT - 30 sedentary obese PCOS. Exercise group: Age: 31.07 ± 2.49 (years). BMI: 33.12 ± 0.92 (kg/m ²). Control group: Age: 30.73 ± 0.67 (years). BMI: 33.30 ± 0.21 (kg/m ²).	Endurance training: 6 sessions per week (Treadmill walking/running): 45 min per session of aerobic exercise at an intensity of 60–75% of age-predicted MHR (~ 300 kcal/day). The training sessions started at 40% MHR and gradually increased to 60–75% MHR by week 12.	Weight (0.004) BMI (0.004) WC (0.001) Fat % (0.001) Glucose (0.001) Insulin (0.001) HOMA-IR (0.001)
Benham et al, 2021 ⁴¹	RCT - 47 PCOS into HIIT group (n=16), CAET group (n=14) and control group (n=17). HIIT: Age: 29.1 ± 4.1 (years). BMI: 31.4 ± 8.6 (kg/m ²). CAET: Age: 29.5 ± 4.6 (years). BMI: 31.9 ± 9.0 (kg/m ²). Control group: Age: 29.1 ± 5.4 (years). BMI: 31.6 ± 8.2 (kg/m ²).	HIIT: 10 cycles of 30 seconds high-intensity (90% heart rate reserve or 9-10 on modified Borg scale) alternating with 90 seconds of low-intensity aerobic exercise. CAET: 40 min of moderate-intensity Aerobic exercise (50%–60% HRR, or 4 or 6 or 10 on modified Borg scale). Control group: instructed to maintain usual level of physical activity for the entirety of the intervention period and at the completion of study, they were offered three sessions with a personal trainer.	BMI (0.01) WC (<0.01) Fasting Glucose (0.02)

RCT: Randomised control trial, PCOS: Polycystic ovary syndrome, BW: Body weight, BF%: Body fat percentage, WC: Waist circumference, BMI: Body mass index, SHBG: Sex-hormone binding globulin, FAI: Free androgen index, MHR: Maximum heart rate, ET: Exercise therapy, PRT: Progressive resistance training, CHO: Carbohydrates, EA: Electro-acupuncture, LH: Luteinizing hormone, FSH: Follicle-stimulating hormone, FT: Free testosterone, IAT: Intermittent aerobic training, CAT: Continuous aerobic training, HIIT: High-intensity interval training, HRM: Heart rate max, CG: Control group, CPET: Cardiopulmonary exercise test, HDL-C: High-density lipoprotein-cholesterol, LDL-C: Low-density lipoprotein-cholesterol, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HOMA-IR: Homeostatic model assessment for insulin resistance, TC: Total cholesterol, DHEAS: Dehydroepiandrosterone, TRIG: Triglycerides, PCOSQ: Polycystic ovary syndrome questionnaire, HRQOL (SF-36): Health-related quality of life questionnaire (short form-36), BAI: Beck anxiety inventory, BDI-II: Beck's depression inventory-II, DA: Diet and aerobic exercise, DC: Diet and combined resistance-aerobic exercise, VO2max: Maximal oxygen consumption.

Table-3: The TESTEX Scale scoring.

Author and publication year	Eligibility criteria specified	Randomization specified	Allocation concealed	Groups similar at baseline	Blinding of assessors	Outcome measures in >85% participants (a)	Intention to treat analysis (b)	Between-group statistical comparisons reported	Point measures & measures of variability for all reported outcome measures	Activity monitoring in control group	Relative exercise intensity remained constant	EX volume & energy expenditure	Total
Hoeger et al, 2004 ¹⁴	1	1	1	1	0	1	0	2	1	1	1	1	11
Bruner et al, 2006 ¹⁵	1	1	1	1	0	0	0	2	1	1	1	1	10
Vigorito et al, 2007 ¹⁶	1	0	1	1	1	3	0	2	1	0	1	1	12
Orio et al, 2008 ¹⁷	1	0	0	1	1	3	0	2	1	1	1	1	12
Thomson et al, 2008 ¹⁸	1	1	0	1	0	2	0	2	1	1	1	1	11
Moro et al, 2009 ¹⁹	1	0	0	1	0	0	0	2	1	0	1	1	7
Stener-Victorin et al, 2009 ²⁰	1	1	1	1	0	1	0	2	1	0	1	1	10
Jedel et al, 2011 ²¹	1	1	1	1	0	3	1	2	1	1	1	1	14

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Author and publication year	Eligibility criteria specified	Randomization specified	Allocation concealed	Groups similar at baseline	Blinding of assessors	Outcome measures in >85% participants (a)	Intention to treat analysis (b)	Between-group statistical comparisons reported	Point measures & measures of variability for all reported out measures	Activity monitoring in control group	Relative exercise intensity remained constant	EX volume & energy expenditure	Total
Nidhi et al, 2012 ²²	1	0	0	0	1	1	0	2	1	1	1	1	9
Roessler et al, 2013 ²³	1	0	0	1	0	0	0	2	1	1	1	1	8
Nidhi et al, 2013 ²⁴	1	1	1	1	1	1	0	2	1	1	1	1	12
Nybacka et al, 2013 ²⁵	1	1	1	1	0	1	0	2	1	1	1	1	11
Gaeini et al, 2014 ²⁶	1	0	0	1	0	0	0	2	1	0	1	1	7
Almenning et al, 2015 ²⁷	1	1	0	1	0	3	0	2	1	1	1	1	12
Turan et al, 2016 ²⁸	1	1	0	1	0	1	0	2	1	0	1	1	9
Vizza et al, 2016 ²⁹	1	1	1	1	0	3	1	2	1	0	1	1	13
Vasheghani-Farahani et al, 2017 ³⁰	1	1	1	1	0	1	0	2	1	0	1	1	10
Costa et al, 2018 ³¹	1	1	0	1	0	2	0	2	1	0	1	1	10
Esmael et al, 2019 ³²	1	1	1	1	1	2	0	1	1	1	1	1	12
Kirthika et al, 2019 ³³	1	1	1	1	0	1	1	2	1	1	1	1	12
Ribeiro et al, 2019 ³⁴	1	1	1	1	0	2	0	2	1	0	1	1	11
Samadi et al, 2019 ³⁵	1	0	0	0	0	0	0	2	1	0	1	1	6
Tiwari et al, 2019 ³⁶	1	1	1	1	1	1	0	2	1	1	1	1	12
Patel et al, 2020 ³⁷	1	1	1	1	1	3	0	2	1	0	1	1	13
Ribeiro et al, 2020 ³⁸	1	1	1	1	0	2	0	2	1	0	1	1	11
Wu et al, 2020 ³⁹	1	0	0	1	0	0	0	2	1	0	1	1	7
Zehsaz et al, 2020 ⁴⁰	1	0	1	1	1	1	0	2	1	0	1	1	10
Benham et al, 2021 ⁴¹	1	1	1	1	0	3	1	2	1	1	1	1	14

TESTEX: Tool for the assessment of study quality and reporting in exercise

of bias for blinding outcome assessment, and a low risk of bias for blinding participants or personnel (Table 4, Figure 3).



PRISMA 2009 Flow Diagram

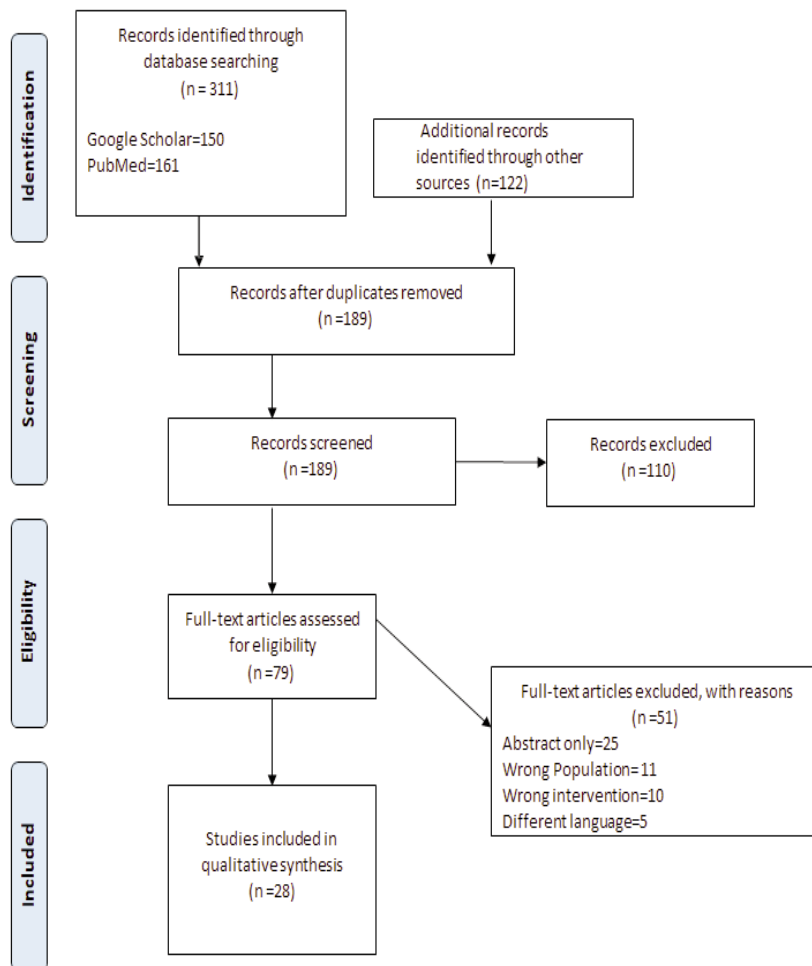


Figure-2: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart.

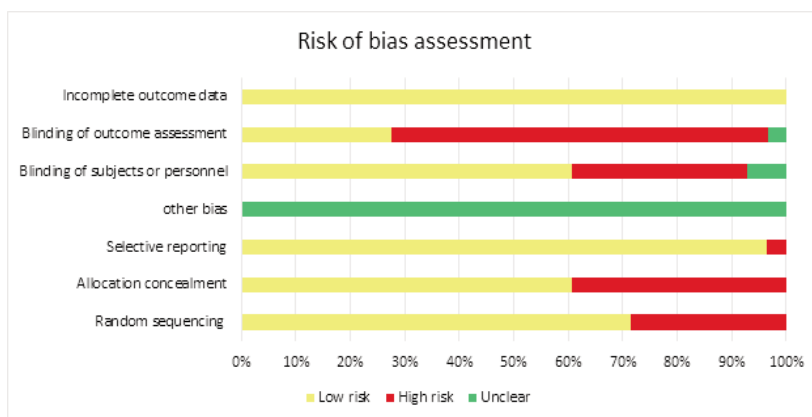


Figure-3: Risk of bias assessment

Discussion

The current systematic review provides evidence from the last 20 years, with 1367 subjects, for the sole purpose of reinforcing the need to use exercise as an intervention option for managing PCOS. It is known that lifestyle modification, the first line of management of PCOS, includes exercise⁴². The RCTs in the current review included sample sizes ranging from 12 to 94 participants, where only one study had 94 participants. Six studies included 84-90 participants, while others ranged from 12-66 participants, while the study with the least number of participants had 12 subjects. The effectiveness of different exercise training among PCOS patients was evaluated, and mode, frequency, intensity, and duration of exercise regimes were studied. The effects of exercise on metabolic functions, cardiovascular functions, reproductive functions, psychological wellbeing, and anthropometrics were studied.

Statistically significant post-intervention outcome values compared to the values taken at baseline were observed across all the 28 studies. The majority of studies reported improvement in insulin sensitivity, reduction in IR, and improvement in blood lipid profile. IR, insulin sensitivity, lipid profile, free testosterone, total testosterone, SHBG, DHEA, androstenedione, FAI, oestradiol, prolactin, anti-müllerian hormone (AMH), and adiponectin showed favourable outcomes. Exercise improved menstrual condition and reduced the number of ovarian follicles. For the restoration of ovarian function, insulin sensitivity needs to be improved. Homeostatic model assessment for insulin resistance (HOMA-IR) is an indicative tool used to assess IR, and different exercise interventions were studied for effectiveness in reducing IR. Seven studies reported significantly lower HOMA-IR after aerobic, HIIT, PRT and yoga interventions^{22, 27, 28, 30, 33, 35, 40}.

Fasting insulin and fasting glucose were reported to be significantly improved in 5 studies, while TG, TC, HDL and LDL

Table-4: Assessment of risk of bias.

Study	Random sequencing	Allocation concealment	Selective reporting	Other bias	Blinding of subjects or personnel	Blinding of outcome assessment	Incomplete outcome data
Hoeger et al, 2004 ¹⁴	✓	✓	✓	?	✓	✗	✓
Bruner et al, 2006 ¹⁵	✓	✓	✓	?	✓	✗	✓
Vigorito et al, 2007 ¹⁶	✗	✓	✓	?	?	✓	✓
Orio et al, 2008 ¹⁷	✗	✗	✗	?	✗	✓	✓
Thomson et al, 2008 ¹⁸	✓	✗	✓	?	✓	✗	✓
Moro et al, 2009 ¹⁹	✓	✗	✓	?	✗	✗	✓
Stener-Victorin et al, 2009 ²⁰	✓	✓	✓	?	✓	✗	✓
Jedel et al, 2011 ²¹	✓	✓	✓	?	✓	✗	✓
Nidhi et al, 2012 ²²	✗	✗	✓	?	✗	✓	✓
Roessler et al, 2013 ²³	✗	✗	✓	?	✗	✗	✓
Nidhi et al, 2013 ²⁴	✓	✓	✓	?	✓	✓	✓
Nybacka et al, 2013 ²⁵	✓	✓	✓	?	✗	✗	✓
Gaeini et al, 2014 ²⁶	✗	✗	✓	?	✗	✗	✓
Almenning et al, 2015 ²⁷	✓	✗	✓	?	✓	✗	✓
Turan et al, 2016 ²⁸	✓	✗	✓	?	✗	✗	✓
Vizza et al, 2016 ²⁹	✓	✓	✓	?	✓	✗	✓
Vasheghani-Farahani et al, 2017 ³⁰	✓	✓	✓	?	✓	✗	✓
Costa et al, 2018 ³¹	✓	✗	✓	?	✓	✗	✓
Esmael et al, 2019 ³²	✓	✓	✓	?	✓	✓	✓
Kirthika et al, 2019 ³³	✓	✓	✓	?	✓	✗	✓
Ribeiro et al, 2019 ³⁴	✓	✓	✓	?	✓	✗	✓
Samadi et al, 2019 ³⁵	✗	✗	✓	?	✗	✗	✓
Tiwari et al, 2019 ³⁶	✓	✓	✓	?	✓	✓	✓
Patel et al, 2020 ³⁷	✓	✓	✓	?	✓	✓	✓
Ribeiro et al, 2020 ³⁸	✓	✓	✓	?	✓	✗	✓
Wu et al, 2020 ³⁹	✗	✗	✓	?	✗	✗	✓
Zehsaz et al, 2020 ⁴⁰	✗	✓	✓	?	✓	✓	✓
Benham et al, 2021 ⁴¹	✓	✓	✓	?	?	?	✓

✓ - Low risk. ✗ - High risk. ?- Unclear.

significantly improved in 6 studies^{15, 16, 18, 19, 22, 27, 30, 31, 40, 41}). All the improvements were either in the presence or absence of weight loss. In 10 weeks of HIIT, there was no weight reduction, but several other features changed significantly, like improved IR, reduced AMH, and fat percentage. Without weight loss, HIIT significantly improved the cardiometabolic profile among the PCOS population²⁷. Aquatic HIIT significantly reduced BMI, FSH, FT, SHBG, HOMA-IR, and hirsutism severity, and improved menstrual cycle³⁵.

PCOS women with increased BMI tend to have metabolic manifestations with increased risk of IR and cardiovascular diseases, thus impacting the hormonal control related to ovulation. Several studies reported that aerobic exercise improves various biomarkers related to health, with 12 weeks of aerobic exercise showing significant improvements in weight loss, FSH, oestrogen, antral follicle count, AMH, and adiponectin. These outcomes correlated significantly with the improvement in reproductive function. In women with anovulation, significant improvements in the ovarian process and a restoration of the menstrual cycle were seen. Several parameters of the Polycystic Ovary Syndrome Questionnaire-50 (PCOSQ-50) and the ratio of LH and FSH and free serum testosterone were reported to have significantly improved. Besides, 16 weeks of aerobic exercise improved menstrual frequency and hyperandrogenism. The visceral adiposity index also significantly improved. Furthermore, high-sensitivity C-reactive protein (hs-CRP) and HOMA-IR decreased. The data showed that in PCOS women, the regulation of lipolysis by the main endocrine hormones as impaired, but the lipolytic defects can be partly reversed by aerobic exercise training independent of changes in body fat mass and sex hormones. It was reported that aerobic fitness and insulin sensitivity significantly increased independent of weight loss. Also, reduction in the total number of follicles was observed after aerobic exercise for 16 weeks. Continuous aerobic training (CAT) and intermittent aerobic training (IAT) also significantly lowered the anthropometric profile, while also improving the condition of hyperandrogenism. In contrast, only IAT training reduced FAI, while CAT improved the lipid profile. Six months of HIIT and CAT showed improvement in fasting glucose, BMI, and lipid profile compared to the control group^{15-21, 25, 26, 28, 30-34, 36, 38-41}.

PRT was reported to have improved several HRQOL domains, particularly vitality, physical functioning, social functioning, role emotional, and mental health. It also decreased BMI and WC, thus improving body composition. PCOSQ showed that exercise improved

weight and infertility issues. Depression was also treated as DASS score showed improved depression, anxiety and exercise self-efficacy scale scores²⁹.

Yoga intervention was reported to have significantly lowered free testosterone and DHEA levels without weight reduction. Additionally, yoga showed betterment in measures of anxiety and depression. It was reported that this improvement seemed long-lasting even when the treatment ended. A holistic yoga programme also significantly reduced AMH, LH, testosterone, and hirsutism, while menstrual frequency, body weight and FSH remained unchanged. Some studies though reported that weight reduction is the most significant way to restore ovulation in obese women with PCOS. Several studies reported exercise-induced reductions in cardiometabolic risk factors without significant weight loss, suggesting the notion that in the future, the sole interest of exercise programmes should not be weight reduction, and more research is needed for a concrete basis^{22, 24, 37}.

Limitations: Several RCTs included in the review had weaknesses related to the inadequate blinding of patients and examiners, failure to evaluate the outcome measures in some RCTs, and failure to either implement or mention the ITT analysis and mention of any adverse effect. Only a few studies had follow-ups. Most RCTs focused on aerobic exercise, and only a handful of studies studied the effects of HIIT, PRT and yoga.

Strength: The systematic review provides detailed knowledge of the impact of physical therapy or exercise on several different parameters and characteristic symptoms of PCOS.

Future recommendations: More trials are needed to be conducted on the interventions mentioned in the current review that will open a wide range of research area to establish the most efficient therapeutic programme for the PCOS population. Considering how IR and hyperandrogenism are involved in the pathophysiology of PCOS, future studies should focus on them.

Conclusion

Evidence suggests that exercise potentially benefits PCOS women by reducing and improving various risk factors, like IR and hyperandrogenism. Exercise regimes, such as aerobic exercise, HIIT, PRT and yoga, significantly reduce the complications associated with PCOS. However, with the present data, it cannot be concluded which exercise regime is superior and more significant than the other regimes.

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