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#### Practice guidelines

## Exercise in the management of polycystic ovary syndrome: A position statement from Exercise and Sports Science Australia



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#### ABSTRACT

Polycystic ovary syndrome (PCOS) is the most prevalent endocrine condition amongst females of reproductive age, leading to lifelong cardiometabolic, reproductive, psychological, and dermatologic symptoms as well as a reduced quality of life. Lifestyle interventions, which can include structured exercise programmes delivered by appropriately trained exercise professionals such as clinical exercise physiologists, are considered first-line strategies in PCOS management due to their therapeutic effects on various health outcomes and quality of life. This position statement builds on the 2023 International Evidence-based Guideline for the Assessment and Management of PCOS and describes the role of the exercise professional in the context of the multidisciplinary care team which includes physicians and allied health professionals. This position statement aims to equip exercise professionals with a broad understanding of the pathophysiology of PCOS, how it is diagnosed and managed in clinical practice, and evidence- and consensus-based recommendations for physical activity and exercise in PCOS management. In line with the physical activity recommendations for the general public, individuals with PCOS should aim to undertake between 150 to 300 min of moderate-intensity or 75 to 150 min of vigorous-intensity aerobic activity per week, or an equivalent combination of both spread throughout the week. Additionally, muscle-strengthening activities on two non-consecutive days per week are recommended to maintain health and prevent weight gain. For further health benefits and to achieve modest weight loss, individuals with PCOS should aim for a minimum of 250 min of moderate-intensity or 150 min of vigorous-intensity aerobic activity per week, or an equivalent combination of both spread throughout the week, plus muscle-strengthening activities on two non-consecutive days per week. Adolescents with PCOS should aim for a minimum of 60 min moderate- to vigorous-intensity activity each day, incorporating muscle- and bone-strengthening activities three times per week. Finally, exercise professionals should consider the significant psychological burden, including weight stigma, and the high prevalence of comorbidities amongst individuals with PCOS and take appropriate measures to deliver safe and efficacious exercise interventions.

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#### 1. Background

#### 1.1. Definition

Polycystic ovary syndrome (PCOS) is the most common endocrine condition in women of reproductive age, 1 and can manifest lifelong reproductive (infertility, oligomenorrhea, and hyperandrogenism), cardiometabolic (impaired glucose tolerance, insulin resistance, type 2 diabetes mellitus, and cardiovascular disease risk), psychological (anxiety and depression, disordered eating, low self-esteem, and body image distress) and dermatologic (acne, facial hirsutism, and androgenic alopecia) symptoms, leading to reduced quality of life (Fig. 1).<sup>2</sup> The updated 2023 International Evidence-based Guideline for the Assessment and Management of PCOS,<sup>3</sup> which build on past consensus Rotterdam criteria, recommends that PCOS should be diagnosed using specific criteria. In adults, this requires the presence of two of i) clinical/biochemical hyperandrogenism, ii) ovulatory dysfunction, or iii) polycystic ovaries on ultrasound or elevated anti-mullerian hormone (AMH) levels, after other causes of these features have been excluded.

#### 1.2. Aetiology

PCOS is a complex multigenic condition that can manifest when predisposing and protective genetic variants interact with environmental factors.<sup>4,5</sup> Such factors include suboptimal lifestyle behaviours including prolonged sedentary behaviour (e.g., sitting at work),<sup>6</sup> lack of regular physical activity, suboptimal intake of core food groups (e.g. fibre, protein, and micronutrients), and the overconsumption of energy-dense and highly processed foods such as sugar-sweetened beverages.<sup>7</sup> Importantly, other non-modifiable factors such as ethnicity<sup>8,9</sup> and family history<sup>10</sup> have also been shown to affect the manifestation and severity of PCOS symptoms. Excess weight, which results from a combination of modifiable and non-modifiable risk factors, also exacerbates PCOS symptoms as the degree of insulin resistance and androgen excess increases with obesity and affects the clinical features of PCOS. <sup>11</sup>

#### 1.2.1. Insulin resistance

Whilst not part of the diagnostic criteria, insulin resistance is a central aetiological characteristic of PCOS affecting approximately 75 % of lean women with PCOS and up to 95 % of women with PCOS and obesity. <sup>12</sup> It is proposed that insulin resistance and hyperinsulinemia increase ovarian androgen production and decrease hepatic sex-hormone binding globulin (SHBG) leading to excess levels of androgen hormones, also termed hyperandrogenism. <sup>13</sup> In fact, hyperandrogenic PCOS phenotypes have the highest prevalence of insulin resistance, with one study reporting a prevalence of 80 % in PCOS phenotypes with hyperandrogenism and oligomenorrhoea, and 65 % in phenotypes with hyperandrogenism and polycystic ovaries, compared to only 38 % in normoandrogenic PCOS phenotypes. <sup>14</sup>

Beyond its bidirectional relationship with androgen excess, insulin resistance is also an underlying feature of many cardiometabolic comorbidities associated with PCOS, such as metabolic-associated fatty liver disease, <sup>15</sup> diabetes, <sup>16,17</sup> and cardiovascular disease, independent of body weight. <sup>18</sup> Consequently, international screening guidelines for cardiometabolic risk in PCOS recommend regular assessment of obesity, glucose tolerance, lipid profiles, and hypertension (Table 1).<sup>3</sup>

#### 1.2.2. Androgen excess and ovarian dysfunction

Androgens and oestrogens have historically been classified as sex hormones and contribute to the regulation of various bodily functions including reproduction, energy homeostasis, and psychological wellbeing. <sup>19</sup> Amongst females, androgens play a key role in the maintenance of reproductive, cardiometabolic, and musculoskeletal health as

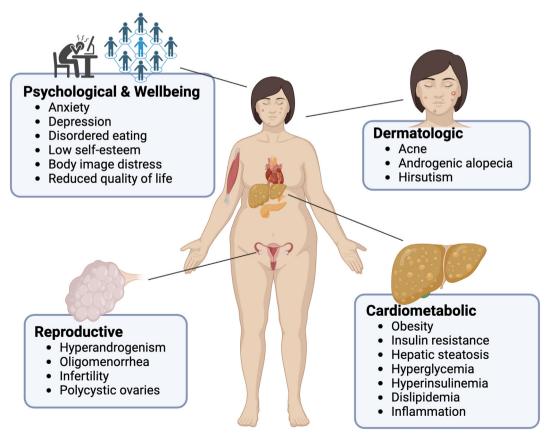


Fig. 1. Common symptoms in PCOS.

 Table 1

 Cardiometabolic screening recommendations for women with PCOS.

Metabolic morbidity	Who should be screened?	Screening recommendation	Screening frequency	Special consideration
Obesity	All women at the time of PCOS diagnosis	<ul><li>Weight and height to calculate BMI</li><li>Ideally, waist circumference</li></ul>	Every 6–12 months	
Impaired glucose tolerance/type 2 diabetes	All women at the time of PCOS diagnosis	<ul> <li>Fasting glucose or HbA1c in lowrisk women or</li> <li>OGTT in higher-risk women (BMI &gt; 25 kg/m² or in Asians &gt; 23 kg/m², history of abnormal glucose tolerance, or family history of diabetes)</li> </ul>	Every 1–3 years based on risk factors for diabetes	<ul> <li>An OGTT should be offered to all women with PCOS planning a pregnancy or seeking fertility treatment.</li> <li>If not performed preconception, an OGTT should be offered at &lt; 20 week gestation, and all women with PCOS should have an OGTT at 24–28 week gestation.</li> </ul>
Dyslipidaemia	All women (regardless of weight) after age 20. Adolescents who present with overweight or obesity at the time of PCOS diagnosis	Fasting lipid profile (cholesterol, LDL, HDL, and TG levels)	Repeat measurement should be guided based on results or global CVD risk. ACC/AHA guidelines recommend at least every 4–6 years	
Hypertension	All women at the time of PCOS diagnosis	Blood pressure	Annually or more frequently based on global CVD risk.	

ACC/AHA, American College of Cardiology/American Heart Association; BMI, body mass index; CVD, cardiovascular disease; HbA1c, haemoglobin A1c; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; OGTT, oral glucose tolerance test; PCOS, polycystic ovary syndrome; TG, triglycerides.

well as cognition.<sup>20</sup> Whilst healthy levels of sex hormones are critical for healthy ageing, four in five women with PCOS present with androgen excess,<sup>21</sup> making it the most common feature of PCOS.<sup>22</sup> Women with androgen excess/hyperandrogenism, can often manifest various clinical signs including hirsutism, acne, or androgenic alopecia.<sup>23</sup> Biochemically, hyperandrogenism is characterised by abnormally elevated androgen levels, including testosterone, pro-androgens, and enzymes which convert pro-androgens to bioactive androgens.<sup>24</sup> The source of the excess androgen production lies in the ovary and is directly stimulated by insulin and gonadotropins such as luteinising hormone.<sup>25</sup> Additionally, hyperandrogenism is associated with and contributes to the development of polycystic ovary morphological traits such as theca interstitial hyperplasia and multiple semi-developed follicles in the ovaries.<sup>26</sup>

#### 1.2.3. Mental health and quality of life

In addition to presenting with clear physiological and, at times, morphological signs and symptoms, PCOS also increases the risk of developing mental health conditions, such as anxiety, depression, and disordered eating.<sup>27</sup> In fact, a previous meta-analysis showed that women with PCOS are at least three times more likely to have symptoms of depression or anxiety when compared to women without PCOS.<sup>28</sup> Whilst multiple factors contribute to this observation, excess weight, infertility, alopecia, and hirsutism have been shown to be associated with psychological distress in women with PCOS.<sup>29,30</sup> Furthermore, there is also a higher risk for disordered eating partly due to: a) the higher prevalence of obesity, where early management strategies involve dietary modification, and b) PCOS being specific to females of reproductive age, where eating disorders are most prevalent.<sup>31</sup>

PCOS is a multi-system disorder affecting both physical and mental components of health and as a result, women with PCOS often report reduced health-related quality of life (HR-QoL).<sup>32</sup> The relationship between PCOS and reduced HR-QoL is partly explained by its association with body mass index (BMI), increasing age, and infertility.<sup>32</sup> Importantly, further studies are required to not only determine which components of QoL are most affected by PCOS, but also which interventions are most effective for improving QoL.

#### 2. Evidence on the role of exercise in the management of PCOS

#### 2.1. Definitions of physical activity and exercise

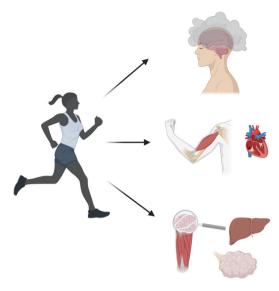
Physical activity is defined as any bodily movement generated by the skeletal muscles which results in energy expenditure. Examples of physical activity include active commuting and gardening. Exercise is

physical activity that is planned, structured and repetitive, which is often undertaken to improve or maintain health, wellbeing, and/or performance. This section details the known effects of structured exercise, rather than physical activity more broadly, on various PCOS-related outcomes (Fig. 2).

#### 2.2. Effect of exercise on insulin resistance

The well-established link between PCOS and insulin resistance has resulted in various studies examining the acute and chronic insulinsensitising effects of exercise amongst this population, which appear to be independent of weight loss.<sup>33</sup> Skeletal muscle is known to play a crucial role in exercise-induced glucose uptake by stimulating the translocation of the glucose transporter type 4 (GLUT4) to the plasma membrane to promote glucose uptake. 34,35 GLUT4 is regulated by insulin and belongs to a family of glucose transporter proteins that facilitate the transport fo glucose across the plasma membrane.<sup>36</sup> Studies have emphasised the role of adenosine monophosphate-activated protein kinase (AMPK), which can be activated through exercise in an intensityand volume-dependent manner, <sup>37</sup> in regulating the post-exercise increase in glucose uptake and insulin sensitivity. 38–40 Furthermore, it has been shown that after an acute bout of exercise, women with PCOS exhibit increased activation of skeletal muscle insulin signalling<sup>41</sup> with changes in insulin gene expression and metabolic signalling similar to those in healthy women. 42 However, the results of other studies have suggested that PCOS can impair the pathways through which exercise induces metabolic improvements.<sup>43–45</sup> Thus, additional mechanistic and interventional studies in PCOS are needed to investigate this further.46

Whilst there is a plausible mechanistic basis for supporting the role of exercise as an insulin-sensitising therapy in PCOS, empirical evidence has demonstrated mixed results. For example, some systematic reviews and meta-analyses in individuals with PCOS showed that exercise improved homeostatic model of insulin resistance (HOMA-IR), <sup>47,48</sup> a rudimentary measure of insulin resistance, whilst others demonstrated conflicting findings. <sup>49,50</sup> Despite the mechanistic data supporting exercise as a therapy for improving insulin resistance, the incongruent findings from clinical studies in PCOS suggest that other factors may influence its efficacy, such as exercise prescription parameters (exercise intensity, volume, and type), timing of follow-up assessments, and participant characteristics. Notably, improvements in skeletal muscle insulin sensitivity dissipate ~72 h after the last exercise session, <sup>51</sup> suggesting that regular physical activity and/or exercise is essential for long-term management of insulin resistance and overall metabolic health.



#### Mental health and wellbeing

- ↓ Symptoms of depression
- ↓ Symptoms of anxiety
- ↓ Body image distress
- 1 Quality of life

#### Anthropometry and performance

- ↑ Cardiorespiratory fitness
- ↑ Muscular strength and endurance
- 1 Weight management
- ↓ Waist circumference
- 1 Lean muscle mass maintenance

#### Metabolic and reproductive

- ↓ Hyperinsulinaemia
- ↑ Glucose control
- ↑ Mitochondrial function
- Ovulatory function
- Menstrual regularity

Fig. 2. Demonstrated effects of exercise on health and wellness outcomes in PCOS.

#### 2.3. Effect of exercise on androgen excess and ovarian function

Amongst women with PCOS, exercise has been demonstrated to improve free androgen levels by increasing SHBG concentrations, which binds to circulating testosterone and regulates its bioavailability.<sup>52</sup> Additionally, exercise can also lower hyperinsulinaemia,<sup>48</sup> commonly present in women with PCOS, which may also impact androgen levels. In this regard, high insulin levels may inhibit the hepatic production of SHBG, increasing serum-free testosterone.<sup>53</sup> However, the precise mechanisms by which exercise modulates SBHG, including through its effects on insulin levels, remain unclear.<sup>54</sup>

Both insulin and insulin-like growth factor 1 (IGF-1) play significant roles in enhancing ovarian steroidogenesis, the process by which hormones, including testosterone, are produced in the ovaries, thus contributing to hyperandrogenism in individuals with PCOS. <sup>55–58</sup> Analyses undertaken for the 2023 International Evidence-based Guideline for the Assessment and Management of PCOS showed that when compared to minimal intervention, exercise alone or combined with diet improved fasting insulin. <sup>59</sup> Conversely, biochemical measures of hyperandrogenism, such as free androgen index, and testosterone remained unchanged. <sup>59</sup> Given only few small randomised controlled trials have investigated this relationship, it is difficult to form evidence-based conclusions. However, it may be that other factors, such as differing time-course changes in the respective outcomes, affect the relationship between insulin and hyperandrogenism or that the magnitude of improvement in insulin was not sufficient to elicit concomitant improvements in hyperandrogenism.

Exercise has also been found to positively affect ovarian function in individuals with PCOS. 52,60 These improvements are linked to reduced hormonal imbalances and improvements in lean muscle mass and/or body fat, resulting in increased ovulation rates and regular menstrual cycles.<sup>60</sup> In fact, a previous randomised trial showed that a 4-month individualised exercise programme involving both aerobic and resistance components led to significantly improved menstrual regularity and reduced upper body fat percentage whilst hormone profiles remained unchanged.<sup>61</sup> Thus, exercise-induced improvements in menstrual regularity may be more closely related to improvements in body composition rather than hormonal changes. However, because other reports have shown that exercise can also normalise ovarian morphology independent of body composition changes by regulating ovarian sympathetic innervation, 62,63 further research is required to elucidate the molecular mechanisms underlying exercise-induced improvements in ovarian function in PCOS.

#### 2.4. Effect of exercise on cardiometabolic health, weight, and body composition

The effects of exercise on cardiometabolic health outcomes in PCOS have been investigated in various systematic reviews. 47-50,64,65 The available evidence is consistent regarding exercise eliciting modest improvements in waist circumference, <sup>48–50</sup> which is often used as a surrogate measure of visceral fat in clinical practice. However, lipid profiles and body weight have improved in some<sup>48,60</sup> but not all metaanalyses. 50 Similarly, whilst fasting insulin appears to improve in most meta-analyses, fasting blood glucose does not. 48-50 This may be due. in part, to early compensatory mechanisms resulting in hyperinsulinaemia to maintain normal glucose levels, which as peripheral insulin resistance improves through exercise, elevated insulin levels also decrease. In fact, fasting blood glucose levels for most studies included in systematic reviews investigating the effects of exercise in PCOS lie within normal ranges. 49 Additionally, differences in exercise parameters, including intervention length, modality, volume, intensity, and frequency, may also influence the efficacy of such interventions. For example, whilst some studies have implemented interventions that adhered to populational physical activity guidelines minus musclestrengthening components, <sup>59</sup> few studies <sup>66,67</sup> have implemented interventions meeting the physical activity recommendations for additional health benefits<sup>68</sup> or achieving meaningful weight loss (between 5 to 10 % of body weight). 69 Importantly, whilst weight loss is beneficial for improving PCOS symptoms, exercise has been shown to improve central adiposity and reduce cardiovascular disease risk independent of meaningful weight loss. 70 This point is further emphasised by recent epidemiological findings demonstrating a 17-36 % reduction in cardiovascular disease incidence amongst individuals with obesity who undertook aerobic physical activity.<sup>71</sup>

Skeletal muscle mitochondrial function, which partly reflects substrate metabolism and energy production capacity, has been shown to be impaired in those with insulin resistance and PCOS. Exercise has been demonstrated to improve mitochondrial function and content, which can lead to improved metabolic health. For example, a previous study demonstrated that 12 weeks of aerobic exercise training improved and partly restored mitochondrial function, alongside enhancing skeletal muscle insulin sensitivity in women with PCOS and obesity. Although it is not feasible to directly assess mitochondrial improvements in clinical practice, surrogate markers such as cardiorespiratory fitness may be useful. Cardiorespiratory fitness reflects the capacity of the respiratory and circulatory systems to supply oxygen

to skeletal muscle mitochondria for energy production.<sup>74</sup> In the context of metabolic disease, cardiorespiratory fitness is inversely associated with both insulin resistance and ectopic fat accumulation.<sup>75</sup> Importantly, various meta-analyses have demonstrated that aerobic exercise, involving either moderate-intensity continuous training (MICT) or high-intensity interval training (HIIT), can improve cardiorespiratory fitness in women with PCOS by approximately one metabolic equivalent (~3.5 mL/kg/min).<sup>48,49</sup> A cardiorespiratory fitness difference of one metabolic equivalent is associated with a 13 % risk reduction in all-cause mortality and a 15 % reduction in the incidence of cardiovascular disease.<sup>76</sup>

#### 2.5. Effect of exercise on mental health and quality of life

Exercise is known to be an effective strategy for improving symptoms of depression and anxiety<sup>77</sup> and QoL in various populations.<sup>78,79</sup> Whilst the effect of exercise on mental health outcomes and QoL has been relatively understudied in PCOS, available data suggests that those with PCOS that are more physically active report fewer symptoms of depression compared to their inactive counterparts.<sup>80</sup> Although it is currently unclear what type, intensity, or duration of exercise may be most effective for improving the abovementioned outcomes, preliminary evidence indicates that exercise in general may be an effective strategy for improving mental health outcomes in women with PCOS.

A systematic review in women with PCOS reported that interventions involving exercise alone or in combination with other lifestyle therapies reduced symptoms of anxiety and depression in half of the fifteen included studies. <sup>81</sup> Exercise also resulted in improvements in multiple domains of HR-QoL across all studies. However, it is important to note that the diagnosis of a mental health condition was not an inclusion or exclusion criteria for the studies included in the review. In individuals with PCOS that have a diagnosed mental health condition or that display elevated symptoms of depression or anxiety, the available evidence suggests that a multi-component intervention that integrates exercise with psychological treatment (e.g., cognitive behavioural therapy or medication) may be indicated and could have greater potential for improving mental health outcomes.

The abovementioned systematic review also showed that interventions involving exercise alone or in combination with other lifestyle therapies improved various domains of the PCOS Questionnaire, <sup>81</sup> a QoL tool designed to measure HR-QoL in those with PCOS. <sup>82</sup> The results of the systematic review reported that of the eight studies that implemented the PCOS Questionnaire, interventions involving exercise significantly improved domains related to emotions, infertility, and weight. Furthermore, a previous study also emphasised the positive effects of regular exercise on body image distress measured via the Body Dysmorphic Disorder Examination Questionnaire. <sup>83</sup> Given that significant weight loss is seldom achieved and sustained, these findings indicate that exercise may improve women's perception of their body without significant weight loss. However, further appropriately powered studies involving clearly defined exercise protocols are required to elucidate this interaction.

#### 3. Recommendations for the implementation of exercise interventions

#### 3.1. Guideline development process

The exercise recommendations provided in this position statement were informed by the 2023 International Evidence-based Guideline for the Assessment and Management of PCOS. These recommendations were derived from evidence or consensus and are presented in Table 2.<sup>3</sup> A comprehensive description of methodological approach used to derive such recommendations has been published elsewhere.<sup>84,85</sup> Given the relative lack of available evidence on the efficacy of exercise programmes for improving PCOS-related outcomes, the Guideline Development Group also considered high-quality mechanistic literature on PCOS and international exercise/physical activity recommendations for the general population.

#### 3.2. The role of exercise within the multidisciplinary care of PCOS

In the context of multidisciplinary care for the management of PCOS, exercise professionals, such as clinical exercise physiologists, play a unique and important role by assessing physical capacity and providing safe, effective, and individualised exercise interventions, with the aim of managing cardiometabolic risk factors and improving PCOS symptoms. To this end, individuals with PCOS may be referred to an exercise professional by their coordinating physician for specific reasons including, but not limited to, weight management, fertility concerns, psychological concerns, or other symptom management. As PCOS management centres on holistic multidisciplinary care involving a team of medical (e.g., primary care physician, gynaecologist, endocrinologist) and allied health professionals (e.g., dietician, psychologist, exercise physiologist) along with the patient, exercise professionals should actively maintain correspondence with the coordinating physician and relevant allied health professionals to ensure the safety and efficacy of the exercise interventions being delivered, particularly when multiple lifestyle and medical interventions are being prescribed concomitantly.

Lifestyle interventions involving optimising dietary intake and increasing physical activity/exercise are primary early therapeutic strategies for managing PCOS-related symptoms and associated cardiometabolic risk factors.<sup>3</sup> The 2023 International Evidence-based Guideline for the Assessment and Management of PCOS recommends that lifestyle intervention (involving exercise alone or multicomponent diet combined with exercise and behavioural strategies) should be recommended for all women with PCOS, for improving metabolic health, including central adiposity and lipid profile.<sup>3</sup>

Given the available evidence surrounding its benefits, clinicians should focus on recommending healthy eating and physical activity advice to all individuals with PCOS to optimise general health, QoL, body composition, and weight management, which may include maintaining weight, preventing weight gain, or modest weight loss. <sup>86</sup> Whilst it is not essential for an individual with PCOS having no apparent co-morbidities to see an exercise professional before changing physical activity patterns or beginning exercise, findings from a previous systematic review amongst participants with PCOS demonstrated that exercise interventions were most effective when they were supervised. <sup>48</sup> However, the Guideline Development Group acknowledged that this may be unfeasible in resource-limited environments. <sup>59</sup>

#### 3.3. Exercise-related treatment goals in PCOS

In line with the 2023 International Evidence-based Guideline for the Assessment and Management of PCOS, lifestyle management goals should be co-developed in partnership with individuals with PCOS, preferably during the initial consultation and with an emphasis on the individual's preferences, given that there is a lack of evidence to recommend one form of exercise over another. 59,85 Patients should be educated on the benefits of exercise for PCOS, which go beyond weight management and include improved physical health, mental health, and wellbeing. Importantly, amongst those without excess weight, both in adolescence and at key life points, including menopause, clinicians should focus on maintaining a healthy lifestyle and preventing excess weight gain. In this context, behavioural goals, rather than goals centred on clinical outcomes, may be particularly useful. For example, goals may be assigned on achieving a specified amount of steps per day or minutes of physical activity per day/week, for which, if achieved, ensuing benefits on PCOS symptoms may also be realised.<sup>87</sup> Where appropriate, the exercise professional should also provide education to the patient on physical activity selfmonitoring, including using fitness tracking devices and technologies for monitoring exercise intensity and quantifying step counts; as monitoring goal progress has been demonstrated to be an effective self-regulation strategy for goal attainment.<sup>88</sup> Self-monitoring could be considered an adjunct to support and promote active lifestyles and minimise sedentary behaviours.

**Table 2**Physical activity and exercise recommendations from The International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome.<sup>84</sup>

Category of recommendation	Recommendation	Quality/grade		
EBR	Lifestyle intervention (exercise alone or multicomponent diet combined with exercise and behavioural strategies) should be recommended			
	for all women with PCOS, for improving metabolic health including central adiposity and lipid profile.	$\oplus$ OOO		
EBR	Healthcare professionals and women could consider that there is a lack of evidence supporting any one type and intensity of exercise being	***		
	better than another for anthropometric, metabolic, hormonal, reproductive, or psychological outcomes.	$\oplus$		
CR	Healthy lifestyle behaviours encompassing healthy eating and/or physical activity should be recommended in all women with PCOS to optimise general health, quality of life, body composition and weight management (maintaining weight, preventing weight gain and/or modest weight loss).			
CR	Any physical activity consistent with population guidelines will have health benefits, and within this, healthcare professionals should advise sustainable physical activity based on individual preferences and goals.	***		
CR	Healthcare professionals should encourage and advise the following in concordance with general population physical activity guidelines:	***		
	• All adults should undertake physical activity as doing some physical activity is better than none.			
	<ul> <li>Adults should limit the time spent being sedentary (e.g., sitting, screen time) as replacing sedentary time with physical activity of any intensity (including light intensity) provides health benefits.</li> </ul>			
CR	For the prevention of weight gain and maintenance of health, adults (18–64 years) should aim for a minimum of 150–300 min of moderate-intensity or 75–150 min of vigorous-intensity aerobic activity per week or an equivalent combination of both spread throughout the week, plus muscle-strengthening activities (e.g., resistance/flexibility) on two non-consecutive days per week.			
CR	For the promotion of greater health benefits, including modest weight loss and prevention of weight regain, adults (18–64 years) should aim for a minimum of 250 min of moderate-intensity or 150 min of vigorous-intensity aerobic activity per week or an equivalent combination of both spread throughout the week, plus muscle-strengthening activities (e.g., resistance/flexibility) on two non-consecutive days per week.			
CR	Adolescents should aim for at least 60 min of moderate- to vigorous-intensity physical activity per day, including activities that strengthen muscle and bone, at least three times per week.	****		

EBR, evidence-based recommendations: Evidence sufficient to inform a recommendation made by the guideline development group. CR, consensus recommendations: In the absence of adequate evidence, a consensus recommendation has been made by the guideline development group, also informed by evidence from the general population.

- **♦♦♦♦**, strong recommendation for the option;
- \*\*\*, conditional recommendation for the option;
- \*\*, conditional recommendation for either the option or the comparison;
- , conditional recommendation against the option.
- DDDD, very confident that the true effect lies close to that of the estimate of the effect;
- ####O, moderate confidence in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is different;
- ###CO, limited confidence in the effect estimate: The true effect may be substantially different from the estimate of the effect;
- $\oplus \bigcirc\bigcirc\bigcirc$ , very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Amongst patients with excess weight, and with their permission, exercise professionals may provide education on the benefits of weight management for significant clinical improvements, whilst being conscious of weight stigma. If the goal is to achieve weight loss, exercise professionals should work closely with dietitians and assist with the prescription of a tailored energy deficit plan which is considerate of individual energy requirements, body weight, physical activity levels, as well as short- and long-term goals. Examples of such approaches have recently been summarised and can be found elsewhere. 86 Additionally, there is evidence to suggest that ectopic fat can be reduced in the absence of clinically significant weight loss amongst individuals with metabolic disorders, <sup>89</sup> and as a result, the value of reducing central adiposity, a clinical marker of ectopic fat accumulation, should also be emphasised. In this regard, the clinician, through a shared decisionmaking process with patient, may instead measure waist circumference as a clinical surrogate for visceral/ectopic fat and prescribe goals according to this outcome whilst being conscious of the overall goal of achieving behaviour change and promoting a healthy lifestyle.

Concerning exercise-specific therapeutic benefits, improving cardiorespiratory fitness should be emphasised as an integral part of the treatment plan due to its association with metabolic health, 70,74,75 and reduced cardiovascular risk. Additionally, the available literature suggests that cardiorespiratory fitness often improves with exercise (particularly aerobic exercise) and that such improvements can occur independent of significant weight loss. Furthermore, muscular strength can also be improved relatively quickly in exercise-naïve individuals with PCOS and may also be targeted as a therapeutic goal. Finally, individuals with PCOS may benefit from their anabolic body constitution when it comes to physical performance (cardiorespiratory fitness and muscular strength) as supported by an increased occurrence of PCOS amongst female athletes. These benefits should be emphasised to encourage individuals with PCOS to be physically active and take part in regular exercise.

#### 3.4. Clinical assessment and exercise prescription recommendations

Prior to commencing exercise, exercise professionals should undertake a risk assessment using a validated screening tool, such as the Adult Pre-Exercise Screening System (APSS), 92 to determine the safety of commencing a structured exercise intervention, particularly if there is risk of injury or presence of comorbidities. Where clinically indicated and with consent from the individual, the exercise professional may choose to co-develop goals in the initial consultation and undertake a comprehensive assessment which includes anthropometric, cardiovascular, physical capacity, and patient-reported outcome measures, such as the Modified Polycystic Ovary Syndrome Questionnaire. 93 Because many cardiometabolic risk factors would likely be assessed by the coordinating physician/nurse as per the international screening guidelines for cardiometabolic risk in PCOS (Table 1),<sup>3</sup> the exercise professional should prioritise assessments that are available to them whilst being considerate of their resources and expertise (Fig. 3). Assessment and reassessment of cardiorespiratory fitness and muscular strength, power, and endurance, may be effective strategies to increase exercise selfefficacy given their responsiveness to exercise interventions, particularly amongst those who are physically inactive or exercise-naïve.<sup>94</sup> For specific guidance on assessing cardiorespiratory or muscular strength, power, and endurance, exercise professionals can refer to the American College of Sports Medicine Guidelines for Exercise Testing and Prescription. 95 Given individuals with PCOS are more likely to report low self-esteem and a higher prevalence of eating disorders,<sup>3</sup> the exercise professional may also assess these or related outcomes, where clinically indicated, through the use of tools such as the Multidimensional Body-Self Relations Questionnaire-Appearance Scales (body image distress), Modified Weight Bias Internalization Scale (internalised weight stigma and bias) and/or the Eating Disorder Examination Questionnaire (disordered eating).

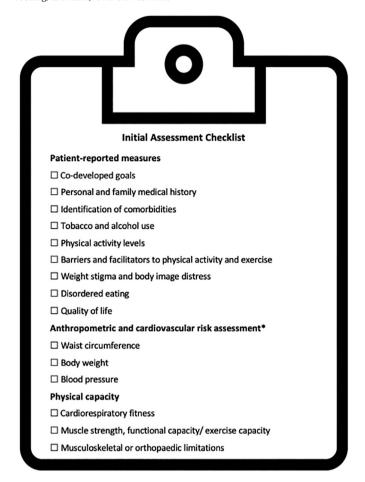


Fig. 3. PCOS assessment checklist for exercise professionals.

\*All outcome measures are to be taken where clinically indicated and after informed consent has been acquired from the patient, particularly for anthropometric measures.

For the prevention of weight gain and maintenance of health, adults with PCOS should aim for a minimum of 150-300 min of moderate-intensity or 75–150 min of vigorous-intensity aerobic activity or an equivalent combination of both spread throughout the week, plus musclestrengthening activities (e.g., resistance training) on two non-consecutive days per week. To achieve greater health benefits, including modest weight loss and prevention of weight regain, individuals with PCOS should aim for a minimum of 250 min/week of moderate-intensity or 150 min/week of vigorous intensity aerobic activity or an equivalent combination of both, plus muscle-strengthening activities (e.g., resistance training) on two non-consecutive days per week. Additionally, given the high prevalence of insulin resistance and the negative consequences of hyperinsulinemia on PCOS symptoms, exercise should be undertaken daily or at minimum every two days to enhance insulin action. Adolescents with PCOS should aim for at least 60 min of moderate- to vigorous-intensity physical activity daily, including activities that strengthen muscle and bone, at least three times per week.

It is important to acknowledge that whilst the recommendations included in this position statement provide benchmarks for which all individuals with PCOS should aim to achieve, some patients may present with low physical capacity. <sup>96</sup> As such, exercise professionals should follow core exercise programming principles by prescribing individually tailored and progressive programmes. <sup>94</sup> For additional guidance on prescribing aerobic or muscle strengthening exercises to their patients, exercise professionals can refer to the American College of Sports Medicine Guidelines for Exercise Testing and Prescription <sup>95</sup> whilst considering the unique challenges individuals with PCOS face when undertaking lifestyle interventions as described in Section 4 of this position statement. Furthermore,

exercise professionals should discuss barriers and facilitators to optimise engagement and adherence to physical activity and exercise. This includes discussing psychological factors (e.g., body image concerns, fear of injury, fear of failure, mental health), personal safety concerns, environmental factors, physical limitations, socioeconomic factors, sociocultural factors, and personal motivators for change.<sup>3</sup> The value of broader family engagement should also be considered.

#### 4. Special considerations for exercise in PCOS

#### 4.1. Medications

Whilst lifestyle intervention remains a primary early therapeutic strategy for PCOS management,<sup>3</sup> it is not uncommon for individuals with PCOS to be prescribed medications to help manage their insulin resistance and weight, including metformin and glucagon-like peptide-1 receptor agonists amongst others.<sup>97</sup> In such cases, the exercise professional should monitor for adverse drug-exercise interactions (e.g., hypoglycaemic or hypotensive events) during and after exercise as necessary. Furthermore, patients with PCOS may also be prescribed statins to help manage their cholesterol levels. Given the association between statins and muscle pain,<sup>98</sup> and that exercise and medication may lead to additive effects, patients with PCOS undertaking pharmacotherapy should be monitored for exercise-related adverse events and referred for a medication review where necessary.

Individuals with PCOS are at an increased risk for developing moderate to severe anxiety and depressive symptoms<sup>28</sup> and other mental health conditions.<sup>31</sup> As such, they may be prescribed antidepressant and antipsychotic medication. These medications have been associated with weight gain of approximately 5 %.<sup>99</sup> The exercise professional should discuss the potential utility of carefully tailored exercise prescriptions for mitigating such side effects.

#### 4.2. Concomitant lifestyle interventions

Given the deleterious effects of excess weight on PCOS symptoms and where weight loss is an agreed goal,  $^{11}$  the 2023 International Evidence-based Guideline for the Assessment and Management of PCOS recommends weight loss of 5–10  $\%.^3$  Aerobic exercise alone involving  $\sim\!60$  min of moderate-to-vigorous intensity exercise on five or more days of the week is reported to elicit modest weight loss.  $^{69}$  However, such exercise volume may be difficult to achieve for many. As such, combining exercise with dietary interventions involving reduced energy intake may be a more feasible strategy given this approach has been demonstrated to yield greater weight loss than either exercise or diet alone.  $^{100}$ 

Whilst the current dietary recommendations for women with PCOS emphasise adhering to a balanced diet in line with general population guideline for healthy eating, the use of hypocaloric diets in PCOS has been reported with some success. <sup>101</sup> Exercise professionals should be aware of the use of such interventions and adjust their prescriptions accordingly. For example, if an energy deficit is primarily achieved through dietary intervention, the exercise professional may choose to prioritise resistance training as this approach has been shown to preserve lean muscle mass during energy restriction in populations with overweight or obesity <sup>102</sup>; similar results have been reported in PCOS when resistance training was combined with aerobic exercise. <sup>103</sup> Additionally, given its cardioprotective benefits, cardiorespiratory fitness may be improved in a time-efficient manner by incorporating HIIT, where tolerated, as an adjunct therapy <sup>49,90</sup> whilst targeting weight loss through dietary intervention.

Although weight management/loss is an often-targeted therapeutic goal in PCOS management, adhering to a balanced diet can improve various outcomes, such as reproductive outcomes, which may not be entirely explained by weight change. 104 As such, there may be instances where individuals with PCOS may be following diets which aim to restrict the consumption of certain macronutrients (e.g., low-carbohydrate diets)

or foods such as refined sugar (e.g., Mediterranean diet) for the purpose of improving overall health and wellbeing. <sup>105</sup> In such instances, and where there is a risk for hypoglycaemic events from exercise, the exercise professional should work closely with the patient to provide education on managing such events through carbohydrate consumption.

Psychological and mindfulness-based interventions are often implemented to improve various outcomes not related to weight. These include improved self-efficacy relating to healthy lifestyle behaviours, wellbeing, symptoms of anxiety and depression, and body image concerns. 106,107 In such instances, the exercise professional should work closely with the wider medical team as adjunctive psychological interventions may lead to greater improvements in the aforementioned outcomes as well as potentially assisting with physical activity uptake and long-term adherence. 108 Importantly, it is not uncommon for individuals with disordered eating to undertake dysfunctional exercise, defined as a pathological relationship with exercise resulting in physical and/or psychological health impairment. 109 In such cases, exercise professionals should work closely with and consult the wider medical team (including psychologists) to provide appropriate care.

#### 4.3. Multiple or severe comorbidities

Individuals with PCOS are at an increased risk of obesity, <sup>110</sup> type 2 diabetes, <sup>111</sup> osteoarthritis, <sup>112</sup> moderate and severe depressive and anxiety symptoms, <sup>28</sup> disordered eating, <sup>31</sup> and reduced QoL. <sup>32</sup> Screening for such conditions should be conducted, and their broader management should be considered within the context of PCOS management. For example, as many individuals with PCOS often experience weight stigma and body image distress, <sup>3</sup> the exercise professional should carefully consider how best to design and implement their exercise intervention. This approach may require the incorporation of the traditional exercise prescription principles such as Frequency, Intensity, Time, and Type (FITT), with other factors such as location (gym, home, etc.,) and setting (group exercise versus one-on-one). Location and setting are particularly important to consider as individuals with obesity selectively avoid sports and exercise settings due to a fear of weight stigma and self-discrimination, and therefore may benefit from exercise in a "safe" space such as at home.

In the presence of one or more comorbidity (e.g., type 2 diabetes, <sup>113</sup> obesity, <sup>69</sup> metabolic-associated fatty liver disease, <sup>114</sup> hypertension <sup>115</sup>), specific exercise guidelines for the relevant condition should be reviewed. Where there are multiple exercise recommendations for different comorbidities, the exercise prescription should be individually tailored to incorporate all guidelines, where possible, whilst making necessary modifications to exercise volume, intensity, and modality as required to ensure safety. However, there may be instances in which one condition may limit effective exercise prescription for another condition (e.g., knee osteoarthritis limiting exercise capacity, thereby rendering the patient unable to achieve the sufficient volume of exercise to achieve weight loss). In such instances, the exercise professional should prioritise the exercise-limiting symptoms in the initial phase of their management plan. With regard to underlying mental health conditions such as disordered eating, exercise professionals should be mindful that patients with a history or risk of disordered eating or body image dysmorphia may require a focus on behaviour-change goals (examples provided in Section 3.3) as an alternative to a weight loss focus.3

#### 5. Summary

PCOS is a common endocrine condition in women that contributes to lifelong reproductive, cardiometabolic, psychological, and dermatologic symptoms and a reduced QoL. PCOS can impact weight stigma, self-esteem, body image, and disordered eating behaviours, which all need to be considered. Lifestyle therapy, involving exercise and diet, is considered a primary early intervention therapy in PCOS. The available

evidence, including mechanistic studies, shows that exercise can improve a variety of cardiometabolic health outcomes in PCOS, including insulin sensitivity, central obesity, and cardiorespiratory fitness. Thus, the exercise professional plays a unique and important role in PCOS management by conducting appropriate assessments and providing safe and effective exercise interventions, particularly amongst women with PCOS and additional comorbidities.

In line with general population guidelines, women with PCOS should aim for a minimum of 150-300 min of moderate-intensity or 75-150 min of vigorous-intensity aerobic activity per week or an equivalent combination of both spread throughout the week, plus musclestrengthening activities on two non-consecutive days per week to maintain health and prevent weight gain. For the promotion of greater health benefits, including modest weight loss and prevention of weight regain, women with PCOS should aim for a minimum of 250 min of moderate-intensity or 150 min/week of vigorous-intensity aerobic activity per week or an equivalent combination of both spread throughout the week, plus muscle-strengthening activities on two non-consecutive days per week. Adolescents should aim for a minimum of 60 min of moderate- to vigorous-intensity activity each day, incorporating muscle- and bone-strengthening activities three times per week. The exercise professional should employ a person-centred approach that includes involving the individual in the healthcare decision-making. When employing practical behavioural strategies to promote physical activity, the exercise professional should consider the individual's local, cultural, and socioeconomic circumstances, as well as personal preferences, comorbidities, physical capacity, and broader management goals.

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None.

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#### References

- Deswal R et al. The prevalence of polycystic ovary syndrome: a brief systematic review. J Hum Reprod Sci 2020;13(4):261-271.
- Teede H, Deeks A, Moran L. Polycystic ovary syndrome: a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan. BMC Med 2010;8:41.
- Teede HJ et al. Recommendations from the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome. Fertil Steril 2023;120(4):767-793.
- Escobar-Morreale HF, Luque-Ramírez M, San Millán JL. The molecular-genetic basis
  of functional hyperandrogenism and the polycystic ovary syndrome. *Endocr Rev*2005;26(2):251-282.
- Escobar-Morreale HF. Polycystic ovary syndrome: definition, aetiology, diagnosis and treatment. Nat Rev Endocrinol 2018;14(5):270-284.
- Kazemi M et al. Comparison of dietary and physical activity behaviors in women with and without polycystic ovary syndrome: a systematic review and meta-analysis of 39471 women. Hum Reprod Update 2022;28(6):910-955.
- Dicken SJ, Batterham RL. The role of diet quality in mediating the association between ultra-processed food intake, obesity and health-related outcomes: a review of prospective cohort studies. *Nutrients* 2021;14(1).
- Chan JL et al. Racial and ethnic differences in the prevalence of metabolic syndrome and its components of metabolic syndrome in women with polycystic ovary syndrome: a regional cross-sectional study. Am J Obstet Gynecol 2017;217(2):189.e1–189.e8.
- 9. Kazemi M et al. Comprehensive evaluation of disparities in cardiometabolic and reproductive risk between Hispanic and White women with polycystic ovary syndrome in the United States: a systematic review and meta-analysis. *Am J Obstet Gynecol* 2022;226(2):187-204.e15.
- Vink JM et al. Heritability of polycystic ovary syndrome in a Dutch twin-family study. J Clin Endocrinol Metab 2006;91(6):2100-2104.
- Moran LJ, Norman RJ, Teede HJ. Metabolic risk in PCOS: phenotype and adiposity impact. Trends Endocrinol Metab 2015;26(3):136-143.
- Stepto NK et al. Women with polycystic ovary syndrome have intrinsic insulin resistance on euglycaemic-hyperinsulaemic clamp. Hum Reprod 2013;28(3):777-784.
- Diamanti-Kandarakis E, Dunaif A. Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications. *Endocr Rev* 2012;33
  (6):981-1030.
- Moghetti P et al. Divergences in insulin resistance between the different phenotypes of the polycystic ovary syndrome. J Clin Endocrinol Metab 2013;98(4):E628-E637.
- Asfari MM et al. Association of non-alcoholic fatty liver disease and polycystic ovarian syndrome. BMJ Open Gastroenterol 2020;7(1).
- Yan Q et al. The incidence of gestational diabetes mellitus among women with polycystic ovary syndrome: a meta-analysis of longitudinal studies. BMC Pregnancy Childbirth 2022;22(1):370.
- Persson S et al. Higher risk of type 2 diabetes in women with hyperandrogenic polycystic ovary syndrome. Fertil Steril 2021;116(3):862-871.
- Kakoly NS et al. The impact of obesity on the incidence of type 2 diabetes among women with polycystic ovary syndrome. Diabetes Care 2019;42(4):560-567.
- Fiacco S, Walther A, Ehlert U. Steroid secretion in healthy aging. Psychoneuroendocrinology 2019;105:64-78.
- Davis SR, Wahlin-Jacobsen S. Testosterone in women—the clinical significance. Lancet Diabetes Endocrinol 2015;3(12):980-992.
- Chiaffarino F et al. Prevalence of polycystic ovary syndrome in European countries and USA: a systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol 2022;279:159-170.
- Nisenblat V, Norman RJ. Androgens and polycystic ovary syndrome. Curr Opin Endocrinol Diabetes Obes 2009;16(3):224-231.
- Cussen L et al. Approach to androgen excess in women: clinical and biochemical insights. Clin Endocrinol (Oxf) 2022;97(2):174-186.
- Rodriguez Paris V, Bertoldo MJ. The mechanism of androgen actions in PCOS etiology. Med Sci (Basel) 2019;7(9).
- Rosenfield RL, Ehrmann DA. The pathogenesis of polycystic ovary syndrome (PCOS): the hypothesis of PCOS as functional ovarian hyperandrogenism revisited. Endocr Rev 2016;37(5):467-520.
- Hague WM et al. The prevalence of polycystic ovaries in patients with congenital adrenal hyperplasia and their close relatives. Clin Endocrinol (Oxf) 1990;33(4): 501-510
- Tay CT et al. Psychiatric comorbidities and adverse childhood experiences in women with self-reported polycystic ovary syndrome: an Australian populationbased study. Psychoneuroendocrinology 2020;116:104678.
- Cooney LG et al. High prevalence of moderate and severe depressive and anxiety symptoms in polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod 2017;32(5):1075-1091.
- Chaudhari AP, Mazumdar K, Mehta PD. Anxiety, depression, and quality of life in women with polycystic ovarian syndrome. *Indian J Psychol Med* 2018;40(3): 239-246
- Sundararaman PG, Shweta, Sridhar GR. Psychosocial aspects of women with polycystic ovary syndrome from South India. J Assoc Physicians India 2008;56:945-948.
- Lee I et al. Increased odds of disordered eating in polycystic ovary syndrome: a systematic review and meta-analysis. Eat Weight Disord 2019;24(5):787-797.

- Tabassum F et al. Impact of polycystic ovary syndrome on quality of life of women in correlation to age, basal metabolic index, education and marriage. PLoS One 2021:16(3):e0247486.
- Hutchison SK et al. Effects of exercise on insulin resistance and body composition in overweight and obese women with and without polycystic ovary syndrome. J Clin Endocrinol Metab 2011;96(1):E48-E56.
- DeFronzo RA et al. Synergistic interaction between exercise and insulin on peripheral glucose uptake. J Clin Invest 1981;68(6):1468-1474.
- Kristiansen S, Hargreaves M, Richter EA. Exercise-induced increase in glucose transport, GLUT-4, and VAMP-2 in plasma membrane from human muscle. Am J Physiol 1996;270(1 Pt 1):E197-E201.
- 36. Huang S, Czech MP. The GLUT4 glucose transporter. *Cell Metab* 2007;5(4):237-252.
- Torma F et al. High intensity interval training and molecular adaptive response of skeletal muscle. Sports Med Health Sci 2019;1(1):24-32.
- Kjobsted R et al. TBC1D4 is necessary for enhancing muscle insulin sensitivity in response to AlCAR and contraction. *Diabetes* 2019;68(9):1756-1766.
- 39. Kjobsted R et al. AMPK and TBC1D1 regulate muscle glucose uptake after, but not during, exercise and contraction. *Diabetes* 2019;68(7):1427-1440.
- Kjobsted R et al. Enhanced muscle insulin sensitivity after contraction/exercise is mediated by AMPK. *Diabetes* 2017;66(3):598-612.
- Dantas WS et al. GLUT4 translocation is not impaired after acute exercise in skeletal muscle of women with obesity and polycystic ovary syndrome. Obesity (Silver Spring) 2015;23(11):2207-2215.
- Dantas WS et al. Acute exercise elicits differential expression of insulin resistance genes in the skeletal muscle of patients with polycystic ovary syndrome. Clin Endocrinol (Oxf) 2017;86(5):688-697.
- Hansen SL et al. Mechanisms underlying absent training-induced improvement in insulin action in lean, hyperandrogenic women with polycystic ovary syndrome. *Diabetes* 2020;69(11):2267-2280.
- Harrison CL et al. The impact of intensified exercise training on insulin resistance and fitness in overweight and obese women with and without polycystic ovary syndrome. Clin Endocrinol (Oxf) 2012;76(3):351-357.
- Stepto N et al. Exercise and insulin resistance in PCOS: muscle insulin signalling and fibrosis. *Endocr Connect* 2020;9(4):346-359.
- Stepto NK et al. Exercise recommendations for women with polycystic ovary syndrome: is the evidence enough? Sports Med 2019;49:1143-1157.
- Dos Santos IK et al. The effect of exercise as an intervention for women with polycystic ovary syndrome: a systematic review and meta-analysis. *Medicine (Balti-more)* 2020;99(16):e19644.
- Kite C et al. Exercise, or exercise and diet for the management of polycystic ovary syndrome: a systematic review and meta-analysis. Syst Rev 2019;8(1):51.
- Breyley-Smith A et al. The effect of exercise on cardiometabolic risk factors in women with polycystic ovary syndrome: a systematic review and meta-analysis. Int J Environ Res Public Health 2022;19(3).
- Richards CT et al. HIIT'ing or MISS'ing the optimal management of polycystic ovary syndrome: a systematic review and meta-analysis of high- versus moderateintensity exercise prescription. Front Physiol 2021;12:715881.
- Ryan BJ et al. Moderate-intensity exercise and high-intensity interval training affect insulin sensitivity similarly in obese adults. J Clin Endocrinol Metab 2020;105(8).
- Patten RK et al. High-intensity training elicits greater improvements in cardio-metabolic and reproductive outcomes than moderate-intensity training in women with polycystic ovary syndrome: a randomized clinical trial. *Hum Reprod* 2022;37(5): 1018-1029
- Pugeat M et al. Pathophysiology of sex hormone binding globulin (SHBG): relation to insulin. J Steroid Biochem Mol Biol 1991;40(4–6):841-849.
- Simó R et al. Novel insights in SHBG regulation and clinical implications. Trends Endocrinol Metab 2015;26(7):376-383.
- Ipsa E et al. Growth hormone and insulin-like growth factor action in reproductive tissues. Front Endocrinol (Lausanne) 2019;10:777.
- Poretsky L et al. Insulin receptor mediates inhibitory effect of insulin, but not of insulin-like growth factor (IGF)-I, on IGF binding protein 1 (IGFBP-1) production in human granulosa cells. J Clin Endocrinol Metab 1996;81(2):493-496.
- 57. Poretsky L et al. Insulin-like growth factor II (IGF-II) inhibits insulin-like growth factor binding protein I (IGFBP-1) production in luteinized human granulosa cells with a potency similar to insulin-like growth factor I (IGF-I) and higher than insulin. J Clin Endocrinol Metab 1996;81(9):3412-3414.
- 58. Nestler JE et al. Insulin stimulates testosterone biosynthesis by human thecal cells from women with polycystic ovary syndrome by activating its own receptor and using inositolglycan mediators as the signal transduction system. J Clin Endocrinol Metab 1998;83(6):2001-2005.
- Mousa A, Tay CT, Teede H. Technical Report for the 2023 International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome, Monash University, 2023.
- Benham JL et al. Role of exercise training in polycystic ovary syndrome: a systematic review and meta-analysis. Clin Obes 2018;8(4):275-284.
- 61. Nybacka Å et al. Serum antimüllerian hormone in response to dietary management and/or physical exercise in overweight/obese women with polycystic ovary syndrome: secondary analysis of a randomized controlled trial. Fertil Steril 2013;100 (4):1096-1102.
- Redman LM, Elkind-Hirsch K, Ravussin E. Aerobic exercise in women with polycystic ovary syndrome improves ovarian morphology independent of changes in body composition. Fertil Steril 2011;95(8):2696-2699.
- 63. Manni L et al. Effect of exercise on ovarian morphology and expression of nerve growth factor and alpha(1)- and beta(2)-adrenergic receptors in rats with steroid-induced polycystic ovaries. J Neuroendocrinol 2005;17(12):846-858.

- 64. Patten RK et al. Exercise interventions in polycystic ovary syndrome: a systematic review and meta-analysis. Front Physiol 2020;11:606.
- Santos IKD et al. Effect of high-intensity interval training on metabolic parameters in women with polycystic ovary syndrome: a systematic review and metaanalysis of randomized controlled trials. PLoS One 2021;16(1):e0245023.
- 66. Konopka AR et al. Defects in mitochondrial efficiency and H2O2 emissions in obese women are restored to a lean phenotype with aerobic exercise training. Diabetes 2015:64(6):2104-2115.
- Wil X et al. Improvement of anti-Müllerian hormone and oxidative stress through regular exercise in Chinese women with polycystic ovary syndrome. Hormones (Athens) 2021-20(2)-339-345
- Bull FC et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med 2020;54(24):1451-1462.
- Johnson NA et al. Physical activity in the management of obesity in adults: a position statement from Exercise and Sport Science Australia. J Sci Med Sport 2021;24 (12)-1245-1254
- Sabag A, Little JP, Johnson NA. Low-volume high-intensity interval training for cardiometabolic health. J Physiol 2022;600(5):1013-1026.
- Sabag A et al. Timing of moderate to vigorous physical activity, mortality, cardiovascular disease, and microvascular disease in adults with obesity. Diabetes Care 2024;47(5):890-897
- 72. Moreno-Asso A et al. Non-cell autonomous mechanisms control mitochondrial gene dysregulation in polycystic ovary syndrome. J Mol Endocrinol 2021;68(1):63-76.
- Malamouli M et al. The mitochondrial profile in women with polycystic ovary syndrome: impact of exercise. J Mol Endocrinol 2022;68(3):R11-r23.
- Ross R et al. Importance of assessing cardiorespiratory fitness in clinical practice: a case for fitness as a clinical vital sign: a scientific statement from the American Heart Association. Circulation 2016;134(24):e653-e699.
- Sabag A et al. The association between cardiorespiratory fitness, liver fat and insulin resistance in adults with or without type 2 diabetes: a cross-sectional analysis. BMC Sports Sci Med Rehabil 2021;13(1):40.
- Kodama S et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. Iama 2009:301(19):2024-2035.
- Singh B et al. Effectiveness of physical activity interventions for improving depression, anxiety and distress: an overview of systematic reviews. Br J Sports Med 2023:57:1203-1209.
- Toval A et al. Effects of physical exercise on health-related quality of life in coronary heart disease patients. A systematic review and meta-analysis. Eur J Prev Cardiol 2023;30(Supplement\_1).
- Sabag A et al. The effect of exercise on quality of life in type 2 diabetes: a systematic review and meta-analysis. Med Sci Sports Exerc 2023;55(8):1353-1365.
- Banting LK et al. Physical activity and mental health in women with polycystic ovary syndrome. BMC Womens Health 2014;14(1):51.
- 81. Patten RK et al. Effectiveness of exercise interventions on mental health and healthrelated quality of life in women with polycystic ovary syndrome: a systematic review. BMC Public Health 2021;21(1):2310.
- Cronin L et al. Development of a health-related quality-of-life questionnaire (PCOSQ) for women with polycystic ovary syndrome (PCOS). J Clin Endocrinol Metab 1998;83(6):1976-1987.
- 83. Liao LM et al. Exercise and body image distress in overweight and obese women with polycystic ovary syndrome: a pilot investigation. Gynecol Endocrinol 2008;24
- Teede HJ et al. International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome 2023, 2023, 2023
- Colombo GE et al. Comparison of selected exercise training modalities in the management of PCOS: a systematic review and meta-analysis to inform evidence-based guidelines. JSAMS Plus 2023;2:100024.
- Colombo GE, Pirotta S, Sabag A. Diet and exercise in the management of polycystic ovary syndrome: practical considerations for person-centered care. Semin Reprod Med 2023:41(01/02):026-036.
- Brennan L et al. Lifestyle and behavioral management of polycystic ovary syndrome. J Womens Health (Larchmt) 2017;26(8):836-848.
- Harkin B et al. Does monitoring goal progress promote goal attainment? A metaanalysis of the experimental evidence. Psychol Bull 2016;142(2):198-229.
- Sabag A et al. The effect of a novel low-volume aerobic exercise intervention on liver fat in type 2 diabetes: a randomized controlled trial. Diabetes Care 2020;43 (10):2371-2378.

- 90. Sultana RN et al. The effect of low-volume high-intensity interval training on body composition and cardiorespiratory fitness: a systematic review and meta-analysis. Sports Med 2019;49(11):1687-1721.
- Hirschberg AL. Female hyperandrogenism and elite sport. Endocr Connect 2020;9 (4):R81-r92.
- Norton K et al. New Australian standard for adult pre-exercise screening. Sport Health 2012:30:12-18
- 93. Barnard L et al. Quality of life and psychological well being in polycystic ovary syndrome. Hum Reprod 2007;22(8):2279-2286.
- McNicol AJ et al. The effects of increased absolute training intensity on adaptations to endurance exercise training. J Sci Med Sport 2009;12(4):485-489. Liguori G, A.C.o.S. Medicine. ACSM's Guidelines for Exercise Testing and Prescription,
- Lippincott Williams & Wilkins, 2020.
- Donà S, Bacchi E, Moghetti P. Is cardiorespiratory fitness impaired in PCOS women? A review of the literature. J Endocrinol Invest 2017;40(5):463-469. Bednarz K et al. The role of Glp-1 receptor agonists in insulin resistance with con-
- comitant obesity treatment in polycystic ovary syndrome. Int J Mol Sci 2022;23(8). Selva-O'Callaghan A et al. Statin-induced myalgia and myositis: an update on patho-
- genesis and clinical recommendations. Expert Rev Clin Immunol 2018;14(3):215-224. Alonso-Pedrero L, Bes-Rastrollo M, Marti A. Effects of antidepressant and antipsy-
- chotic use on weight gain: a systematic review. Obes Rev 2019;20(12):1680-1690.
- Franz MJ et al. Weight-loss outcomes: a systematic review and meta-analysis of weight-loss clinical trials with a minimum 1-year follow-up. J Am Diet Assoc 2007:107(10):1755-1767.
- 101. Jarrett BY, Lujan ME. Impact of hypocaloric dietary intervention on ovulation in obese women with PCOS. Reproduction 2016;153(1):R15-R27.
- 102. Lopez P et al. Resistance training effectiveness on body composition and body weight outcomes in individuals with overweight and obesity across the lifespan: a systematic review and meta-analysis. Obes Rev 2022;23(5):e13428.
- 103. Thomson RL et al. 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.
- Shang Y et al. Dietary modification for reproductive health in women with polycystic ovary syndrome: a systematic review and meta-analysis. Front Endocrinol (Lausanne) 2021:12:735954.
- 105. Mei S et al. Mediterranean diet combined with a low-carbohydrate dietary pattern in the treatment of overweight polycystic ovary syndrome patients. Front Nutr 2022:9:876620.
- Young CC et al. Outcomes of a mindfulness-based healthy lifestyle intervention for adolescents and young adults with polycystic ovary syndrome. J Pediatr Adolesc Gynecol 2022;35(3):305-313.
- Stefanaki C et al. Impact of a mindfulness stress management program on stress, anxiety, depression and quality of life in women with polycystic ovary syndrome: a randomized controlled trial. Stress 2015;18(1):57-66.
- Schneider J et al. The role of mindfulness in physical activity: a systematic review. Obes Rev 2019;20(3):448-463.
- Quesnel DA et al. Medical and physiological complications of exercise for individuals with an eating disorder: a narrative review. J Eat Disord 2023;11(1):3.
- 110. Lim SS et al. Overweight, obesity and central obesity in women with polycystic ovary syndrome: a systematic review and meta-analysis. Hum Reprod Update 2012:18(6):618-637.
- 111. Gambineri A et al. Polycystic ovary syndrome is a risk factor for type 2 diabetes: results from a long-term prospective study. Diabetes 2012;61(9):2369-2374.
- Kluzek S et al. Accelerated osteoarthritis in women with polycystic ovary syndrome: a prospective nationwide registry-based cohort study. Arthritis Res Ther 2021;23(1):225.
- Kanaley JA et al. Exercise/physical activity in individuals with type 2 diabetes: a consensus statement from the American College of Sports Medicine. Med Sci Sports Exerc 2022:54(2):353-368.
- Keating SE et al. Exercise in the Management of Metabolic-Associated Fatty Liver Disease (MAFLD) in adults: a position statement from Exercise and Sport Science Australia. Sports Med 2023;53(12):2347-2371.
- 115. Sharman JE et al. Exercise and Sport Science Australia position stand update on exercise and hypertension. J Hum Hypertens 2019;33(12):837-843.