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Advancing Knowledge of Exercise as a Therapeutic Management Strategy for Women with Polycystic Ovary Syndrome

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by

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None of us got where we are alone.
Harvey MacKay

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ABSTRACT

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy among premenopausal women with a prevalence that ranges 15-21%. The estimated financial burden in the United States for evaluating and treating premenopausal women with PCOS was over $8 billion in 2020. PCOS etiology is complex and poorly understood, as is the optimal treatment and management. Endocrine Society Clinical Practice Guidelines recommend exercise as first-line treatment. Yet, the optimal exercise type and "dosing" are not defined. As last reported for women with PCOS, less than 60% are regularly physically active and more than 25% are sedentary. Additionally, little to no published data exist about their perceived exercise barriers/benefits and exercise outcome expectations. The overall objective of this dissertation was to gain knowledge to begin developing exercise interventions for women with PCOS. The research used multiple methods with three specific aims: 1) Explore the relationships among biopsychosocial characteristics, perceived exercise benefits and barriers, exercise outcome expectations, and depressive symptoms among premenopausal women with PCOS; 2) Explore the relationships among, anthropometric attributes, hormonal concentrations, lipid profiles, and fitness levels of premenopausal women with PCOS; and 3) Identify supports (people, services, technology, and/or behavioral change strategies) that may promote initiation and maintenance of exercise in premenopausal women with PCOS. Findings from Aim 1 revealed that many women with PCOS present with low health-related

quality-of-life, high depressive symptoms, and neutral exercise outcome expectations with more perceived exercise barriers than benefits. Phenotypically, the women who participated in Aim 2 were obese (BMI 32.2 ± 8.3m^2/kg, percent body fat 41.1 ± 8.1%) with high levels of free testosterone (6.4 ± 4.0 pg/mL). Self-reported level of physical activity was negatively correlated with BMI (r_s=-0.64, p=0.04) and waist-to-hip ratio (r_s=-0.76, p=0.01). Cardiovascular endurance was negatively correlated with free testosterone (r_s=-.70, p=0.02) and depressive symptoms (r_s=-0.69, p=0.02 and positively correlated with health-related quality-of-life (r_s=0.62, p=0.04). All women who participated in Aim 3 reported external types of motivation when considering exercise, such as incentives, and a preference for a structured PCOS-knowledgeable support system to help initiate and sustain exercise. Additionally, the self-determination theory was useful toward identifying unmet psychological needs, that if met, could promote internal self-regulation.

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LIST OF ABBREVIATIONS

AMH ....Anti-Mullerian Hormone

BMI .... Body Mass Index

CAB .... Community Advisory Board

CI ....Confidence Interval

cm..centimeter

DEXA.. Dual Energy X-ray Absorptiometry

EOE .... Exercise Outcome Expectation

HBM .... Health Belief Model

HDL.. High Density Lipoprotein

HRQoL ....Health-related Quality-of-Life

IRB ....Institutional Review Board

Kg.. kilogram

LDL.. Low Density Lipoprotein

m^2..Meters Squared

MOEEQ................................. Modified Outcome Expectations for Exercise Questionnaire

PAR-Q .... Physical Activity Readiness Questionnaire

PCOS..Polycystic Ovary Syndrome

PHQ-8 ....Personal Health Questionnaire

RAPA..Rapid Assessment of Physical Activity

RT .... Resistance Training

SDT ....Self Determination Theory

SHBG .... Sex Hormone Binding Globulin

T_F .... Free Testosterone

TG .... Triglycerides

T_T .... Total Testosterone

UofSC.. University of South Carolina

US .... United States

VO_2 Max .... Maximum Volume of Oxygen

CHAPTER 1

INTRODUCTION

The nurse scientist functions as a bridge between research and practice. Specifying a phenomenon of interest, nurse scientists innovatively seek strategies and interventions to improve health outcomes and the human holistic health experience. The phenomenon of interest explored in this dissertation was polycystic ovary syndrome (PCOS), specifically PCOS-specific health-related quality-of-life (HRQoL) and exercise as therapeutic management for women with PCOS. As a vulnerable and underserved female population (Bratka et al., 2017), women with PCOS deserve acknowledgement of their unique concerns and promotion of effective strategies that produce positive health outcomes.

PCOS is the most common endocrinopathy and the leading cause of infertility among premenopausal women (Azziz, 2019). The prevalence of PCOS in the United States (U.S.) ranges from 15 to 21% (Greenwood et al., 2018; Blagojevic et al., 2017; Brakta et al., 2017). The estimated total financial burden in the U.S. for evaluating and treating premenopausal women with PCOS was over $8 billion in 2020 (Riestenberg et al., 2021). Clinical features of PCOS include obesity, impaired glucose tolerance, insulin resistance, and dyslipidemia, which are associated with an increased risk cardiovascular, metabolic, and oncological conditions (Legro et al., 2013). Psychological sequelae are also problematic, as women with PCOS are eight times more likely to report symptoms of anxiety and depression as compared to other women (Cooney et al. 2017).

The etiology of PCOS is complex and poorly understood. The Endocrine Society and the National Institutes of Health endorse the 2003 Rotterdam Criteria for diagnosing PCOS because these criteria include an assessment of ovarian morphology, making it more comprehensive than other criteria (such as the NIH 1991 criteria) (Azziz 2019; Legro et al., 2013). According to the Rotterdam Criteria, PCOS is diagnosed when two or more of the following conditions are met: ovulatory dysfunction, ultrasound evidence of polycystic ovaries, and clinical and/or biochemical signs of hyperandrogenism, such as elevated testosterone, hirsutism, acne, alopecia, and/or visceral obesity (Legro et al., 2013). PCOS includes four phenotypes with distinct combinations of the Rotterdam criteria (Sachdeva et al., 2019). Phenotype A, also known as full-blown PCOS, includes ovulatory dysfunction, polycystic ovaries, and hyperandrogenism. Phenotype B includes ovulatory dysfunction and hyperandrogenism. Phenotype C includes polycystic ovaries and hyperandrogenism, and phenotype D includes polycystic ovaries and ovulatory dysfunction. This variability of symptom expression can result in missed and delayed diagnosis and treatment (Teede et al., 2014).

Optimal treatment and management of PCOS typically involves a multi-pronged approach of targeted medications and weight-management lifestyle changes.

Accordingly, the Endocrine Society Clinical Practice Guidelines on the Diagnosis and Treatment of PCOS recommend exercise as first-line treatment yet details about what type of exercise are not included (Legro et al., 2013). Based on a 2011 systematic review of aerobic exercise (e.g., walking, cycling) for women with PCOS, the PCOS Australian Alliance adult guidelines advised at least 150 minutes per week of moderate intensity physical activity, of which 90 minutes should be moderate-to-high intensity aerobic activity, to maintain health and/or help prevent chronic comorbid conditions by reducing body weight (Teede et al., 2011). The literature at that time had only examined the isolated use of aerobic exercise or aerobic exercise with diet. Therefore, any recommendations for resistance training are absent from the PCOS Australian Alliance guidelines. Also, the sole focus was weight loss without attention to other potential improvements from exercise, such as improved insulin sensitivity and altered hormonal milieu, which would further reduce risk of common chronic co-morbid conditions, such as diabetes and cardiovascular disease (Conte et al., 2015; Westcott 2012).

Despite recommendations for exercise as a first-line treatment for PCOS (Fauser et al., 2011), there is evidence that exercise is not routinely recommended (Dokras et al., 2017). Findings from a survey of reproductive endocrinologists revealed that only 41.6% recommended physical activity changes (Dokras et al., 2017). This is not surprising for a several reasons. The PCOS Australian Alliance guidelines are not referenced in the diagnostic criteria, creating challenges for physicians when prescribing mode of exercise and dose. In addition, the scientific literature interchanges the terms physical activity and exercise, causing confusion as to what activities promote PCOS-specific therapeutic management.

Despite the known benefits of regular physical activity for overall health and well-being, the prevalence of women with PCOS who meet the physical activity guidelines of 150 minutes per week of moderate-to-vigorous intensity activity is less than 60% (Lamb et al., 2011). Preliminary findings from our team and those by others suggest that women with PCOS have unique barriers to exercise, which include poor body image, depression, social anxiety, and stigma-related stress that may contribute to low exercise uptake (Wright et al., 2020; Thomson et al., 2016). Conte and colleagues (2015) called for more research to identify psychosocial influences on exercise habits and strategies to promote adoption and maintenance of exercise among women with PCOS.

Study Purpose

There is a need to promote exercise as a therapeutic option for women with PCOS to manage symptoms and decrease their risk of chronic comorbid conditions and discover effective behavioral strategies to initiate and maintain the behavior. The purposes of this research were to identify the biopsychosocial characteristics, exercise perceptions, and fitness profiles among women with PCOS and to develop motivational supports (people, services, technology, and/or behavioral change strategies) using a person-centered, participatory approach. The rationale for conducting this research was that exercise tailored to the needs of the population may be more readily initiated and maintained. The specific aims of this study were to: 1) explore the relationships among biopsychosocial characteristics, perceived exercise benefits and barriers, exercise outcome expectations, and depressive symptoms among premenopausal women with PCOS; 2) explore the relationships among anthropometric attributes, hormonal concentrations, lipid profiles, and fitness levels and their impact on HRQoL and depressive symptoms among premenopausal women with PCOS; and 3) identify supports (people, services, technology, and/or behavioral change strategies) that may promote initiation and maintenance of exercise in premenopausal women with PCOS. The knowledge gained by this study provided insight into the biopsychosocial aspects and benefits and barriers to exercise and identified meaningful and relevant means to promote exercise as a therapeutic option for symptom management and chronic disease risk reduction among women with PCOS.

The research was innovative in that it employed multiple research methods to challenge the current clinical approach to manage PCOS, which is primarily a pharmaceutical model. This research was the first known study to explore exercise outcome expectations among women with PCOS. The research was also the first to include a community advisory board (CAB) of women with PCOS to identify relevant and meaningful supports (strategies, technology, and/or services) to promote the use of exercise as a therapeutic option for symptom management and risk reduction of other chronic conditions.

Theoretical Framework

The research was guided by the biopsychosocial approach. Developed by Dr. George Engel in 1977, the biopsychosocial approach is a conceptual model that posits research on health and illness must consider psychological and social factors along with the biological factors (Engel, 1977). As depicted in Figure 1.1, biological, psychological, and social factors exist along a continuum of natural systems over time within a contextual environment, which includes the broad patterns of shared culture, norms, policies, and values (Lehman, et al., 2017). The biopsychosocial approach expands the traditional reductionist biomedical model by its assumption that health and illness are influenced by psychological and social considerations.

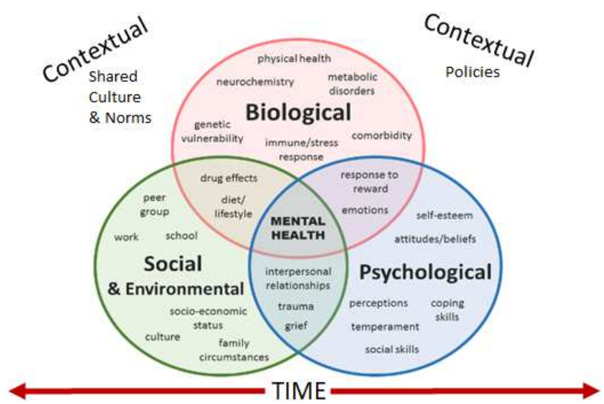

Figure 1.1

The biopsychosocial model of health and illness, adapted from Physiopedia (2021)

Critics of this model cite merging of biopsychosocial factors as a limitation because it blurs the lines between each component (Benning, 2015). They proffer that lines-of-responsibility become vague among professionals and boundaries become unclear between disciplines. Thus, psychological and socioenvironmental factors may be difficult to integrate seamlessly in patient care. Additionally, the model may create difficulty among practitioners or researchers when deciding which factors should be considered, especially when considering individuals living in an ever-changing world.

However, the biopsychosocial framework also has several strengths. This model offers a holistic and inclusive approach toward defining overall mental health. Mental health is both the absence of psychological conditions and the presence of psychological well-being (Kubzansky et al., 2018). This approach aligns with the World Health Organization which defines health as complete well-being, not just the absence of disease (WHO, 2006). In the U.S., over half of the population live with one or more chronic health conditions (Boersma et al., 2020). Long-term conditions such as PCOS are associated with biopsychosocial processes that can lead to depression and other comorbidities. Psychoneuroendocrinology is an interdisciplinary approach to exploring the relationships between endocrine pathways, the nervous system, and human behaviors. This approach to understanding the development of depressive symptoms is relevant in the context of PCOS, as it is an endocrine disorder involving a hypothalamus-pituitary-gonadal axis dysfunction, which can both affect the endocrine system and result in psychological symptoms (Mikhael et al., 2019). The biopsychosocial model emphasizes the need for both multidisciplinary care and self-management.

To explore relationships between constructs of the conceptual model, three theoretical frameworks were used to guide and inform this exploratory, descriptive study: the health belief model (aim 1), a physiological model of PCOS (aim 2), and the self-determination theory (aim 3).

Methodology

Aim 1: Explore the effects of exercise benefits and barriers, exercise outcome expectations, and depressive symptoms on biopsychosocial characteristics among women with PCOS.

Theoretical Model. The Health Belief Model (HBM) explains and predicts health behaviors as an expression of attitudes and beliefs. As one of the most widely applied theories of health behavior prediction (Glanz & Bishop, 2012), the HBM theorizes that health-related behavior, such as physical activity, depends on the perception of severity of the illness, susceptibility or likelihood of risk factors or co-morbid conditions, benefits of physical activity, and barriers to physical activity. Thus, the HBM, operationalized as a series of individual variables, accounts for variance in the choice of health behaviors (Abraham & Sheeran, 2015).

PCOS is a chronic condition that creates need for symptom management and poses risks for other co-morbid conditions with the most common being depression (Fauser et al., 2011). The constructs of severity of illness and susceptibility to future complications were examined using the Polycystic Ovary Syndrome Questionnaire (PCOSQ-50). The PCOSQ-50 indicates overall HRQoL for the purposes of examining impact of PCOS on perceived quality-of-life and determining motivational cues for symptom management (Nasiri-Amiri et al., 2016). Perceived exercise barriers and facilitators were measured with the Exercise Benefits/Barriers Scale (EBBS). The EBBS identifies perceived intrinsic and extrinsic improvements or rewards (benefits) as well as tangible and psychological costs of, or obstacles to, exercise (barriers) (Sechrist et al., 1987). The construct of exercise outcome expectations was measured using the Modified Outcome Expectations for Exercise Questionnaire (MOEEQ). The MOEEQ helps identify health beliefs related to exercise. Individual characteristics (as measured by a demographic questionnaire), psychosocial determinants, and structural variables can all modify the four major constructs of the HBM (Abraham & Sheeran, 2015). See Figure 1.2.

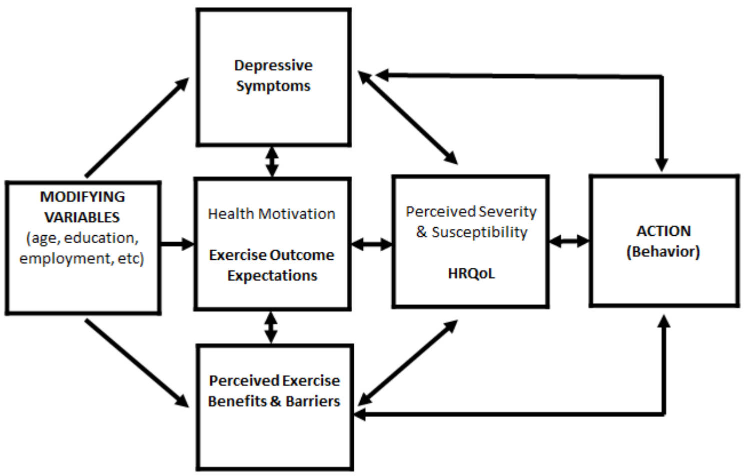

Figure 1.2

Modified health belief model to define PCOS-specific health-related behavior

Setting, Sample, and Recruitment. The University of South Carolina (UofSC) Institutional Review Board provided an "exempt" determination for the study. Participants (n = 935) were recruited through two PCOS-specific Facebook pages over one week in December 2020. Inclusion criteria were women aged 18-42 with a self-report of PCOS (identified with one question). If eligible, women were invited to complete a cross-sectional internet-based survey with questionnaires that assessed PCOS-specific HRQoL, exercise barriers and facilitators, exercise outcome expectations, and depressive symptoms (Table 1.1). Social media posts included a Qualtrics (Provo, Utah) electronic link to a website that provided additional detail about the study. A CAPTCHA verification question was used to prevent automated attempts. Participants had the option to enter a drawing to win one of eight $50 gift cards.

Table 1.1

Descriptions of Aim 1 measures, including psychometric properties

Expected Outcomes	Measure	Description	Psychometrics
Demographics	Demographic Questionnaire	8-item personal descriptive data (including age, educational attainment, employment, marital status, etc.)	N/A
Biopsychosocial Characteristics	PCOS Health-Related Quality of Life Questionnaire (PCOSQ-50)	50-item PCOS-specific measure that includes emotions, body hair, body weight, infertility, & menstrual problems	Construct Validity = 0.92 Test-retest Reliability = 0.91 (Nasiri-Amiri et al., 2018)
Exercise Benefits and Barriers	Exercise Benefits/Barriers Scale	43-item questionnaire assessing ideas about exercise	Validity = 0.95 Test-retest Reliability = 0.89 (Sechrist et al., 1987)
Exercise Outcome Expectations	Modified Outcome Expectations for Exercise Questionnaire (MOEEQ)	15-item tool exploring potential exercise outcomes expectations	Construct Validity = 0.66 Test-retest Reliability = 0.85 (Resnick et al., 2000)
Depressive Symptoms	Personal Health Questionnaire (PHQ-8)	8-item screening tool measuring severity of depressive symptoms	Construct Validity = 0.75 Internal Reliability = 0.81 (Kroenke et al., 2009)

Data Collection and Management. Survey data were collected in Qualtrics and transferred to IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA) and then cleaned and analyzed.

Data Analysis. Descriptive statistics, frequencies or mean ± standard deviations, were computed for each variable. The score for the exercise benefits and barriers subscale was calculated by dividing the total mean score for benefits by the total mean score for barriers to provide a ratio. Backward confounder variable selection procedures were used to develop the final model. Linear regression analyses were used to determine the impact of exercise benefits and barriers, exercise outcome expectations, and depressive symptoms on PCOS-specific HRQoL. Normality, linearity, and heteroskedasticity checks performed on the data confirmed that all model assumptions were met.

Aim 2: Explore the relationships among anthropometric attributes, hormonal concentrations, lipid profiles, and fitness levels of premenopausal women with PCOS and their impact on HRQoL and depressive symptoms.

The second aim, theoretically supported by the physiological model of PCOS and the importance of biopsychosocial constructs for exercise initiation and maintenance, provided proof-of-concept knowledge about precisely measured anthropometric techniques, hormonal and lipid profiles, and fitness testing and fitness levels among a convenience sample of 15 women with PCOS.

Theoretical Model. The etiology of PCOS remains largely unknown, but mounting evidence suggests that PCOS is a complex multigenic disorder with strong epigenetic and environmental influences, including diet and lifestyle factors. The physiological model of PCOS begins with these factors and then depicts the interrelationships and reciprocal interactions of PCOS features and their sequelae (Figure 1.3). Even though the etiology is unclear, the model provides points from which to explore and advance knowledge.

The first limitation of this physiological model is the relationship between some variables are hypothetical. Physiological models are typically used to predict and simplify complex systems. Often, the model becomes too simplified and cannot incorporate all details of the phenomenon. For example, PCOS is associated with psychological variables, such as depression and stigma-related stress, constructs that are not easy to define or measure, yet they likely influence some of the biological variables. By measuring only physiological variables, the influence of psychological or social variables is not delineated.

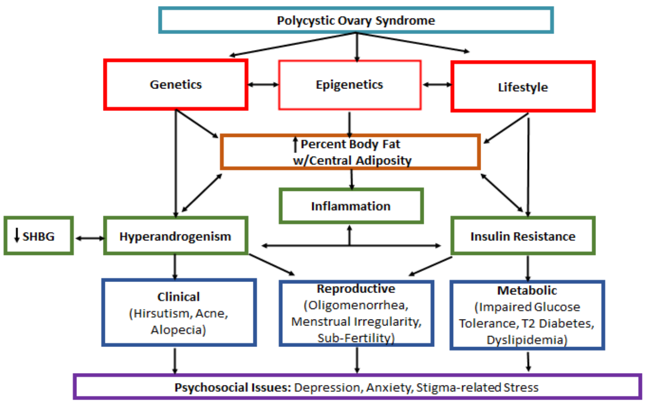

Figure 1.3

Adapted physiological model of PCOS with permission (Hiam et al., 2019)

However, this physiological model has several strengths. The model is the most complete to date (Witchel et al., 2019) and includes the recent areas of research of epigenetics and inflammation. The physiological model identifies key biological variables involved in the process of PCOS that are objective and measurable, and these measurements are easy to repeat across further future studies.

Setting, Sample, and Recruitment. Research protocols were approved by the Institutional Review Board of the UofSC. Participants (n=15) were recruited using flyers, social media, and snowball methods. Inclusion criteria were a woman with a verified PCOS diagnosis between the ages of 18-42 years. Exclusion criteria were medically induced menopause, hypertension or heart disease, orthopedic injury, or pregnancy.

Potential participants were pre-screened via telephone or email using the Physical Activity Readiness Questionnaire (PAR-Q) to identify exclusion criteria. When potential participants met requirements, they were invited to schedule an early morning fasting appointment at the Clinical Exercise Research Center housed within the Arnold School of Public Health at the UofSC. Upon arrival, the purpose, benefits, and risks of the study were explained, and any questions or concerns were addressed. Participants then signed the informed consent document.

Data Collection and Management. Participants completed the following steps with trained personnel: body measurements, venipuncture for hormonal and lipid profiles, surveys, dual energy x-ray absorptiometry (DEXA), oxygen consumption testing (VO_2 max), and muscular fitness and flexibility testing. Following the venipuncture participants had a light snack prior to participating in the fitness testing. The measurements used are detailed in Table 1.2.

Anthropometric and fitness data were recorded on a form and transferred to SPSS. Survey data was directly input into the same software. Venipuncture specimens were transported to the laboratory of Lexington Medical Center to be processed and analyzed. Specimen results were de-identified and confidentially faxed to the UofSC College of Nursing Research Office, and then transferred to IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA) database. Participants were given a $50 gift card as an incentive.

Data Analysis. Descriptive statistics (frequencies, mean ± standard deviations) were computed and compared with categorical descriptors based on the scientific literature.

Due to the small sample size, the data did not meet normality assumptions. As a result, the nonparametric test Spearman rank correlation was used. Correlation analyses were

Table 1.2

Descriptions of anthropometric, laboratory, and fitness measures used for Aim 2

Expected Outcomes	Measure	Description	Psychometrics
Body Mass Index	Weight(kg) / Height(m^2)	Measure using bodyweight and height to estimate overweightness	Sensitivity = 50% Specificity = 90% Validity = 0.82 (Buss, 2014)
Waist-to-Hip Ratio	Waist(cm) / Hip(cm)	Measure using waist and hip circumferences to estimate visceral adiposity and risk of chronic disease	Test-retest Reliability = 0.84 (Reidpath et al., 2013)
Percent Body Fat	Dual Energy Xray Absorptiometry (DEXA)	Measuring of bone mineral density using spectral imaging to determine percent body fat	Reliability = 0.99 (Kutac et al., 2019)
Lean Muscle Mass	Dual Energy Xray Absorptiometry (DEXA)	Measuring of bone mineral density using spectral imaging to determine lean muscle mass	Reliability = 0.99 (Kutac et al., 2019)
Total Testosterone	T_T	Androgenic hormone marker for PCOS	N/A
Free Testosterone	T_F	Bioavailable androgenic hormone	N/A
Sex hormone binding globulin	SHBG	Hormone that binds and transports androgenic hormone	N/A
Total Cholesterol	$Chol_T$	Waxy, fat like substance in body cells, used as a marker of heart health	N/A
High Density Lipoprotein	HDL	Molecules that help remove cholesterol from arteries	N/A
Low Density Lipoprotein	LDL	Main source of cholesterol buildup and blockage in the arteries	N/A
Triglycerides	TG	Type of fat in the blood, used as a marker of heart health, especially in women	N/A
VO_2 Max	Modified Bruce Treadmill Test	Protocol with extended warm-up that allows estimation of maximal oxygen consumption	Reliability = 0.94 (Bruce, 1971)
Upper Body Strength	Modified Push Up Test	Measure of upper body muscular endurance involving knee position and repeatedly lifting upper body for one minute	Test-Retest Reliability = 0.99 (Benny & Mahar, 2001)
Core Strength	Curl Up Test	Measure of abdominal muscular endurance involving partial sit-ups to metronome (40b·min)	Test-Retest Reliability = 0.98 (Diener et al, 1995)
Flexibility	Sit-and-Reach Test	Measure of low back and hamstring extensibility involving stretching forward in a seated position	Criterion-Related Validity = 0.46 – 0.67 (Mayorga-Vega et al., 2014)
Demographics	Demographic Questionnaire	8-item personal descriptive data (including age, educational attainment, employment, marital status, etc.)	N/A

PCOS-Specific Health-Related Quality of Life	PCOS Health-Related Quality of Life Questionnaire (PCOSQ-50)	50-item PCOS-specific measure that includes emotions, body hair, body weight, infertility, & menstrual problems	Construct Validity = 0.92, Test-Retest Reliability = 0.91 (Nasiri-Amiri et al., 2018)
Self-Reported Physical Activity Participation	Rapid Assessment of Physical Activity (RAPA)	9-item questionnaire assessing physical activity level and participation with resistance and flexibility exercise	Positive Predictive Value = 94%, Negative Predictive Value = 100% (Topolski et al., 2006)
Exercise Benefits and Barriers	Exercise Benefits/Barriers Scale	43-item questionnaire assessing ideas about exercise	Validity = 0.95 Test-retest Reliability = 0.89
Exercise Outcome Expectations	Exercise Outcome Expectations Scale	15-item tool exploring potential exercise outcomes expectations	Construct Validity = 0.66 Test-retest Reliability = 0.85 (Resnick et al., 2000)
Depressive Symptoms	Personal Health Questionnaire (PHQ-8)	8-item screening tool measuring severity of depressive symptoms	Construct Validity = 0.75, Internal Reliability = 0.81 (Kroenke et al., 2009)

performed to explore associations between fitness, the independent variable operationalized by cardiorespiratory endurance, muscular strength, and flexibility, and the dependent variables of anthropometric characteristics (body mass index and waist-to-hip ratio) and hormonal and lipid concentrations.

Aim 3: Identify supports (people, services, technology, and/or behavioral change strategies) that may promote the initiation and maintenance of exercise in premenopausal women with PCOS.

A Community Advisory Board (CAB) of women with PCOS, informed by data from the previous two aims and guided by the self-determination theory, discussed exercise barriers, as well as identified motivational supports (people, services, technology, and/or behavioral change strategies) that may promote exercise initiation and maintenance as a therapeutic management strategy for PCOS.

Theoretical Model. Self-determination theory (SDT), as introduced by Ryan and Deci (2000), is an organismic and dialectical metatheory for the study of human motivation, personality development, and well-being. The underlying assumption of SDT is that humans (as active organisms) are naturally self-directed and empowered but require social supports to develop and maintain natural potential and well-being. SDT predominantly focuses on a taxonomy of motivations and three innate psychological needs.

Motivation is the willingness and energy to enact a behavior and it exists in three forms: 1) amotivation (relative lack of intention to engage in a behavior), 2) extrinsic motivation (external reward-driven behavior), and 3) intrinsic motivation (inherent satisfaction to perform a behavior). Extrinsic motivation comprises four categories (external regulation, introjected, identified regulation, and integrated), with each differing by type of external reward. For example, external regulation is performing a behavior to obtain an award or avoid a punishment, whereas, identified regulation is performing a behavior to achieve an external outcome such as weight loss. The types of motivation exist on a continuum between non-self-determined and self-determined behaviors (see Figure 4). Each type of motivation is further classified by causality orientations: controlled (goals or outcomes associated with external sources) or autonomous (goals or outcomes from within self). Internalization is the process by which behaviors become relatively more autonomously regulated over time.

According to Ryan and Deci (2000), a psychological need is an “energizing state that, if satisfied, conduces toward health and well-being but, if not satisfied, contributes to pathology and ill-being" (p. 74). The three innate psychological needs are autonomy (freedom to choose a behavior), competence (ability to be effective in one's interaction with the environment and perform and master a behavior), and 3) relatedness (sense of belonginess). According to this theory, satisfying these psychological needs leads to autonomous internalization of behaviors. Thus, the extent to which people meet these psychological needs dictates position on the continuum (Figure 1.4).

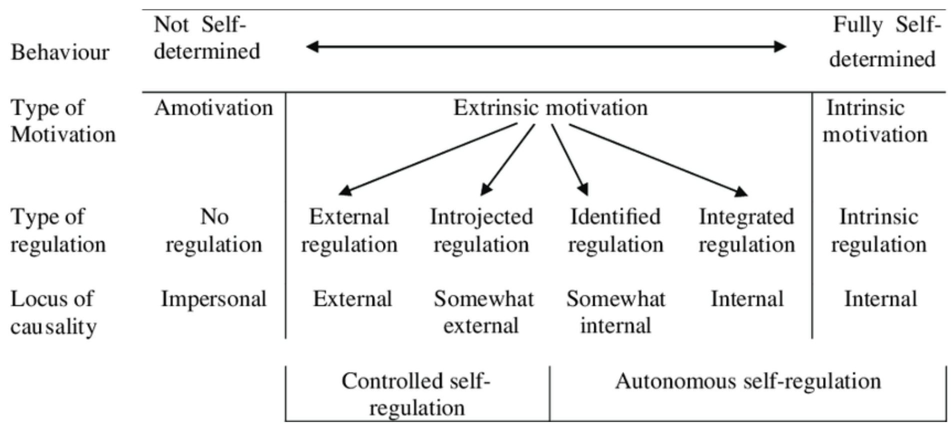

Figure 1.4

Self-determination continuum with motivational styles, loci of causality, and regulation processes as adapted from Deci and Ryan (2000)

Setting, Sample, and Recruitment. A Community Advisory Board (CAB) of 7 women with PCOS was formed to discuss exercise benefits and identify supports (people, services, technology, and/or behavioral change strategies) that may promote exercise initiation and maintenance as a therapeutic management strategy for PCOS. CAB guidelines and responsibilities were created by the researcher and shared with all members. The CAB used the Zoom platform to meet virtually three times over the months of June and July 2021. IRB approval was not necessary as CAB members were collaborative research partners, not research participants.

Data Collection and Management. CAB meetings were recorded and transcribed using the confidential research transcription services offered by the Zoom platform. CAB members received a $20 gift card for each meeting attended to acknowledge their time and expertise.

Data Analysis. Data were analyzed by two independent researchers using low inference content analysis (Vaismoradi et al., 2013). The iterative process of open (line-by-line) and axial (identifying relationships in line-by-line) coding produced a coding scheme. Using the coding scheme, major themes were identified via clustering and data reduction and discussed for consensus among the two researchers. The themes and supporting data were incorporated into a summary document that delineated the CAB's final recommendations. Rigor was strengthened through the continuous reassessment and reiteration of coding and fact checking with the CAB members.

Summary

The purposes of this research were to identify the biopsychosocial characteristics and fitness profiles of women with PCOS and to identify potential motivational supports (people, services, technology, and/or behavioral change strategies) using a person-centered, participatory approach.

In chapter 1, completed research was introduced through a summary of the relevant scientific literature, purpose, aims, and methodology. Chapter 2 is a scoping review of the literature to assess evidence for resistance training as therapeutic management for women with PCOS. This manuscript was published in the *International Journal of Exercise Science* (Wright et al., 2121). Chapters 3, 4, and 5 consist of three manuscripts reporting the research findings from this dissertation work. The Chapter 3 manuscript reports the impact of exercise perceptions and depressive symptoms on PCOS-specific health-related quality-of-life and was submitted to *Women's Health* and is currently in the peer review process. The Chapter 4 manuscript reports on associations between PCOS phenotypes and biomarkers with fitness profiles and is prepared for submission to *Clinical Endocrinology*. The Chapter 5 manuscript reports on supports (people, services, technology, and/or behavioral change strategies) that may assist with the initiation and maintenance of exercise as therapeutic management for women with PCOS. The manuscript presents qualitative analysis of meeting transcriptions created by the PCOS Community Advisory Board and was submitted to *Health Education & Behavior.* Chapter 6 consists of study conclusions and recommendations for practice, education, and future research.

CHAPTER 2

RESISTANCE TRAINING AS THERAPEUTIC MANAGEMENT IN WOMEN WITH PCOS: WHAT IS THE EVIDENCE?[1]

[1] Wright, P. J., Corbett, C. L., Pinto, B. M., Dawson, R. M., & Wirth, M. D. 2021. *International Journal of Exercise Science, 14*(3), 840-854. Reprinted here with permission of publisher.

ABSTRACT

Polycystic ovary syndrome (PCOS), the most common chronic endocrinopathy and the leading cause of infertility in women, has significant clinical consequences, including cardiovascular, endocrinological, oncological, and psychological co-morbidities. Endocrine Society Clinical Practice Guidelines on the Diagnosis and Treatment of PCOS recommend exercise and physical activity as first-line treatment to combat chronic disease risk. However, details about what type of exercise are not provided. Given the known beneficial effects of resistance training on the management of other chronic diseases, the purpose of this scoping review was to evaluate the scientific evidence about the physical and psychosocial effects of resistance training among women with PCOS. Studies were identified through a systematic search of PubMed, SPORTDiscus, and CINAHL databases. Peer-reviewed research studies published between January 2011 and January 2021 that evaluated a resistance training intervention for premenopausal women with PCOS were included. Studies that offered multi-component programs were excluded. Nine articles met the inclusion criteria of which seven were sub-studies of one larger clinical trial. One article reported findings from a small randomized controlled trial and the last article reported feasibility study findings. Each intervention yielded positive results across a wide range of outcome variables; however, the studies had small sample sizes and assessed different outcome variables. Evidence regarding the effects of resistance training on health outcomes for women with PCOS is positive but preliminary. Adequately powered clinical trials are required to confirm health benefits, answer research questions as to therapeutic dose, and discover behavioral strategies to promote resistance training for therapeutic management.

KEYWORDS: polycystic ovarian syndrome, metabolic syndrome, strength training, symptom management

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common chronic endocrinopathy and the leading cause of infertility in women (Azziz, 2019). Based on conservative estimates, 5 million women in the United States (US) have PCOS (NIH, 2020). According to the 2003 Rotterdam diagnostic criteria, the most widely used criteria, PCOS is diagnosed when two or more of the following conditions are met: ovulatory dysfunction or ultrasound evidence of polycystic ovaries, and clinical and/or biochemical signs of hyperandrogenism (Legro et al., 2013). The Endocrine Society endorses the 2003 Rotterdam Criteria because these criteria require a more comprehensive evaluation than other criteria, as it is the only criteria to include ovarian morphology (Legro et al., 2013). Women with PCOS are at risk for insulin resistance, obesity (specifically, visceral adiposity), dyslipidemia, and endometrial disturbances, thereby increasing the likelihood of comorbidities such as metabolic syndrome, cardiovascular disease, and endometrial cancer (Dumetrescu et al., 2015). Psychological morbidities are also significant, as women with PCOS are eight times more likely to have anxiety and depression than women without PCOS (Sadeega et al., 2018; Cinar et al., 2011). Given its various definitions and phenotypes, as well as significant and varied comorbidities, optimal treatment and management typically involves a multi-pronged approach of targeted medications and weight-management lifestyle changes.

Accordingly, the Endocrine Society Clinical Practice Guidelines on the Diagnosis and Treatment of PCOS recommend exercise and physical activity as first-line treatment to combat chronic disease risk (Legro et al., 2013) yet details about what type of exercise are not included. Based on a 2011 systematic review of aerobic exercise (e.g., walking, cycling) for women with PCOS, the PCOS Australian Alliance adult guidelines advised at least 150 minutes per week of moderate-intensity physical activity, of which 90 minutes should be moderate-to-high intensity aerobic activity, to maintain health and/or help prevent chronic comorbidities by reducing body weight (Alliance PA, 2011). The literature at that time had only examined the isolated use of aerobic exercise or aerobic exercise with diet; therefore, any recommendations for resistance training are absent from these guidelines (Westcott, 2012).

Resistance training (RT) is the anaerobic category of exercise involving the repeated movements against unaccustomed loads to stimulate a stronger muscle contraction (Westcott, 2012). There is a wealth of research describing the beneficial effects of RT on symptoms and management of several chronic diseases such as diabetes, cardiovascular disease, and cancer (Ciccolo & Nosrat, 2016). Since muscle contraction involves both mechanical and metabolic properties (Williams et al., 2007), this exercise modality is associated with increased functional strength (Williams & Stewart, 2009), improved insulin sensitivity, quicker rapid glucose uptake (Westcott, 2012), clinically decreased blood pressure over time, and increased basal metabolic rate (responsible for approximately two thirds of total energy expenditure) (Williams et al., 2007). These benefits are the reasons cardiac rehabilitation programs now include RT (Navalta et al., 2019). Additionally, in a study by Schmitz et al. (2003) a sample of women aged 30-50 years lost more visceral fat than men after an intervention of RT

(Schmitz et al., 2003). Visceral fat, a type of fat stored in the abdomen, is a typical PCOS symptom and associated with risk of metabolic syndrome, diabetes, and hypertension (dos Santos et al., 2020; Williams et al., 2007). Thus, the myogenic or muscular adaptations induced by RT are often accompanied by a range of physiological (metabolic) and functional adaptations that may be clinically important among women with PCOS.

A recent systematic review and meta-analysis also reported on the "discordant and limited findings on exercise characteristics" that could lead to more complete and detailed exercise guidelines for women with PCOS (dos Santos et al., 2020). This study reported on ten exercise interventions: eight aerobic, one RT, and one high-intensity training. The findings revealed high heterogeneity for major outcomes of reproductive function (menstrual cycle, ovulation, and fertility) and minor outcomes such as body composition. The research team noted low certainty evidence for little to no effect of exercise on reproductive hormones and moderate certainty evidence that aerobic exercise reduced body mass index (BMI) in women with PCOS (dos Santos et al., 2020). Many studies, however, do not delineate what type of body mass is lost (fat weight vs lean mass). If the women are losing lean muscle mass, the basal metabolic rate slows, producing diminishing returns over time. Aerobic exercise was also credited for improved cardiorespiratory function, whereas resistance training increased functional strength (dos Santos et al., 2020). The authors recommended further research on the benefits of the unique characteristics of exercise with more consideration for RT (dos Santos et al., 2020).

Additionally, evidence exists that some women with PCOS are often dissatisfied with the typical medical model, including pharmaceutical treatment (e.g., metformin and birth control pills). These women report actively seeking alternative therapeutic management strategies such as acupuncture and herbal remedies (Wright et al., 2020). Despite the high prevalence and serious clinical implications of PCOS throughout the woman's lifespan, no standard long-term treatment prevails, and current medications are only moderately effective at controlling symptoms and preventing complications (Legro et al., 2013). However, non-pharmacological therapeutic management strategies such as RT are relatively unexplored in women with PCOS. Exercise as therapeutic management will be defined as planned and structured movement designed to attenuate clinical symptoms of PCOS and reduce associated risk of comorbidities over the long-term. The objective of this scoping review was to present current literature specific to the isolated use of RT and delineate evidence of its effectiveness in this population. To the best of our knowledge, this is the first scoping review on this topic in the United States.

METHODS

The search strategy was based on the Arksey and O'Malley (2002) framework for scoping reviews. A search of PubMed, CINAHL, and SPORTDiscus was conducted. Search strategies for all databases were adapted from the PubMed search strategy (see Table 1). Database searches were limited to the last 10 years (January 2011 – January 2021), as this time span is relevant given the publication of the Australian physical activity guidelines in 2011 and the Endocrine Society Clinical Practice Guidelines in 2013. The search was also limited to full-text articles written in English. MeSH and TIAB terms were used for the database search (Table 2.1). This research was carried out fully in accordance to the ethical standards of the *International Journal of Exercise Science* (Navalta et al.,2019).

Table 2.1.

Concepts with MeSH and TIAB terms used for the database search

Concept	MeSH Term	TIAB Terms
Polycystic Ovary Syndrome	Polycystic Ovary Syndrome	PCOS*
		Polycystic ovar*
Resistance Training	Resistance Training	Resistance exercise*
		Resistance training
		Progressive resistance training
		Strength training
		Strengthening
		Weight bearing
		Weightlifting
		Weight training
		Exercise band
		Medicine ball

Protocol

Articles were deemed eligible for review if they were published in a peer-reviewed journal between January 2011 and January 2021, reported the results of research that evaluated a RT intervention, and involved a sample of premenopausal women with PCOS. In all studies, the diagnosis of PCOS was determined by the 2003 Rotterdam Criteria and confirmed by either the participant's general practitioner or specialist. Studies that offered multi-component programs (nutrition, aerobic exercise, and counseling) were excluded to assess the effects of the isolated use of RT. No studies were excluded based on age.

The reviewer documented the number of articles at each stage of the screening process using the PRISMA flow diagram (see Figure 2.1). Each eligible article was then reviewed for general content, results, and contribution to the literature.

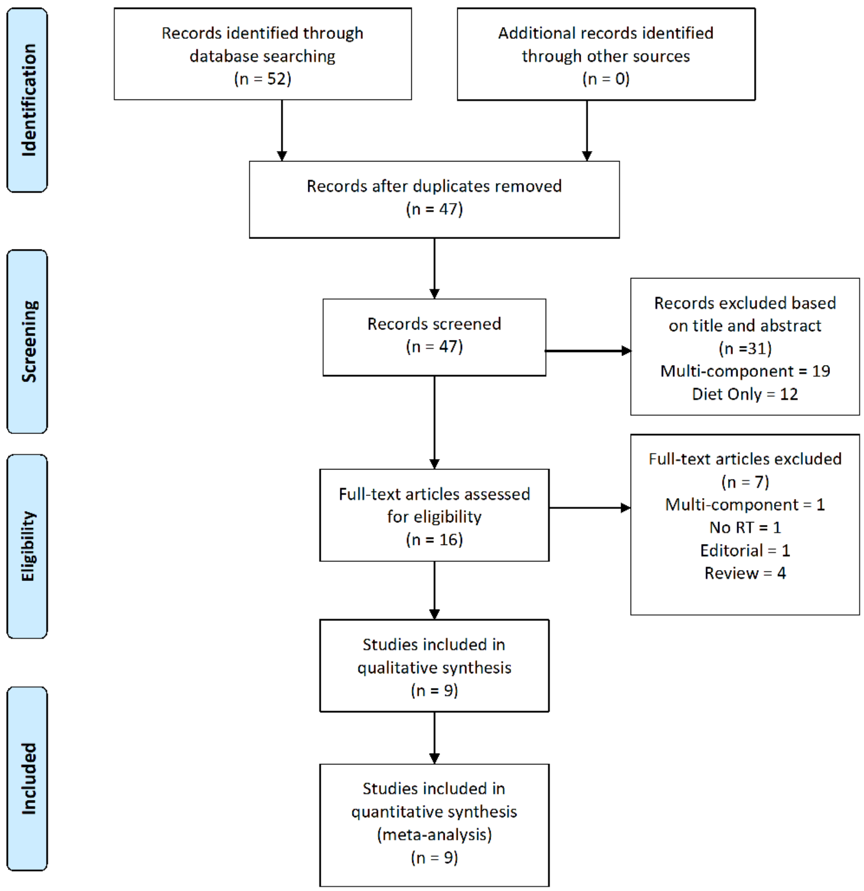

Figure 2.1.

PRISMA flowchart.

As shown in Table 2.2, the following data were extracted from each article: study purpose, design, sample, intervention, measures, and results. We also present the potential benefits of RT for women with PCOS and offer recommendations for future research.

The Johanna Briggs Institute's Critical Appraisal Checklist (2021) was used to assess the methodological quality of each study.

RESULTS

Of the 52 articles identified from the selected databases, five were removed as duplicates and 31 were removed based on titles and abstracts that indicated exclusion criteria. Of the remaining 16 articles, full-text reviews yielded nine articles that matched criteria (see Figure 2.1). Of these nine articles, seven were from the same parent study, a nonrandomized case-control study. The other two articles featured a randomized controlled trial and a nonrandomized feasibility study. Thus, these nine articles represent three separate interventions. The geographic location of these studies included Brazil, Norway, and Australia. Brazil was the site for the parent study (and hence, its six associated studies).

Refer to Table 2.3 for the summary of the Johanna Briggs Institute's Critical Appraisal Checklists using the research designs of three RT interventions.

Study sample sizes ranged from 15 to 73 participants; all participants were overweight or obese, sedentary, premenopausal women with PCOS in the age range of 18-42. In one randomized controlled trial, the participants' age range was not mentioned; however, 26 years old was the mean age for the intervention group (Almenning et al., 2015).

Table 2.2

Summary of resistance training studies from January 2009-July 2020.

The studies in the bold outlined box are sub-studies of a larger trial.

ARTICLE	PURPOSE	STUDY DESIGN	SAMPLE	INTERVENTION	MEASURES	RESULTS (Women w/PCOS)
Kogure et al., 2019	PRT: obesity indices & telomere content	nonrandomized control trial	PCOS = 73 No PCOS = 97 Age Range: 18-37	4 months RT (progressive linear periodization); 3 1hr sess/week	anthropometrics, telomere length, HOMA-IR, hormone panel	↓ WC, ↓ WHtR
Kogure et al., 2018	PRT: muscle strength	nonrandomized control	PCOS = 45 No PCOS = 52 Age Range: 18-37	4 months RT (progressive linear periodization); 3 1hr sess/week	anthropometrics, max strength, HOMA-IR, hormone panel	↑ max strength ↓ %BF, ↑ LMM ↓ testosterone ↓ glycemia
Miranda-Furado et al., 2016	PRT: telomere content & metabolism	nonrandomized control	PCOS = 45 No PCOS = 52 Age Range: 18-37	4 months RT (progressive linear periodization); 3 1hr sess/week	Telomere content, anthropometrics, homocysteine, fasting insulin, hormone panel	↓ telomere length ↓ WC, ↓ %BF ↓ testosterone, ↓ sex hormone binding globulin, ↓ free androgen index, ↑ androstendione ↑ homocysteine ↓ glycemia
Ramos et al., 2016	PRT: QOL	nonrandomized control	PCOS = 43 No PCOS = 51 Age Range: 18-37	4 months RT (progressive linear periodization); 3 1hr sess/week	QOL (SF-36), anthropometrics, BP, HOMA-IR, hormone panel	↑ functional capacity ↓ WC ↓ testosterone ↑ androstenedione
Ribeiro et al., 2016	PRT: autonomic	nonrandomized control	PCOS = 27	4 months RT (progressive linear	HR variability, ovarian volume,	↓ testosterone

	modulation of HR variability & endocrine function		No PCOS = 26 Age Range: 18-37	periodization); 3 1hr sess/week	follicle size & #, %BF, HOMA-IR, hormone panel	
Kogure et al., 2015	PRT: LMM	nonrandomized control	PCOS = 45 No PCOS = 52 Age Range: 18-37	4 months RT (progressive linear periodization); 3 1hr sess/week	Anthropometrics, hormone panel	↓ WC, ↑ LMM ↓ testosterone ↑ androstenedione ↓ sex hormone binding globulin ↓ glycemia
Lara et al., 2015	PRT: sexual function & emotional status	nonrandomized control	PCOS = 43 No PCOS = 51 Age Range: 18-37	4 months RT (progressive linear periodization); 3 1hr sess/week	Sexual function	↑ desire, ↑ excitement, ↑ lubrication. ↓ pain, ↓ depression, ↓ anxiety
Vizza et al., 2016	Assess feasibility of large scale PRT intervention for women w/PCOS	Feasibility nonrandomized control	PRT = 8 Control Group = 7 Age Range: 18-42	3 months RT; 2 supervised sess/wk + 2 home-based sess/wk of 1hr ea	recruitment, attrition, adherence, adverse events, assessment completion, isometric strength, cyclicity, anthropometrics, HbA1C, insulin, glycemia, CRP, hormone panel	FB better recruitment Adherence better w/supervision No adverse events ↓ BW, ↓ WC, ↑ LMM ↑ lower body strength ↓ HbA1C,↑ glycemia ↓ scores for depression, anxiety ↑exercise self-efficacy
Almenning al., 2015	HIT & ST: metabolic, cardiovascular, & hormonal outcomes	3-arm randomized control trial	HIT = 8 ST = 8 PA = 9 Age Range: UNK	10 weeks HIT, ST, or PA; HIT/ST 3 sess/wk; PA ≥ 150min/wk mod-intensity exercise	HOMA-IR, T chol, TG, CRP, cardiovascular markers, insulin, anthropometrics, hormone panel	↓ BF% ↓ anti-Mullerian hormone

*Abbreviations: **%BF** = percent body fat, **BMI** = body mass index, **CRP** = c-reactive protein, **FB** = Facebook, **HIT** = high intensity training, **HR** = heart rate, **HbA1C** = glycated hemoglobin test, **HOMA-IR** = homeostatic model assessment of insulin resistance, **LMM** = lean muscle mass, **PA** = physical activity, **PCOS** = polycystic ovary syndrome,**PRT** = progressive resistance training, **QOL** = quality of life, **ST** = strength training **TG** = triglycerides, **T chol** = total cholesterol, **UNK** = unknown, **WC** = waist circumference, **WHtR** = waist to height ratio

Table 2.3.

Summary of the Johanna Briggs Institute's Critical Appraisal Checklist using the RT intervention research designs.

Checklist Item	Kogure et al., 2015 (19)	Almenning et al., 2015 (2)	Vizza et al., 2016 (37)
Is it clear in the study what is the 'cause' and what is the 'effect' (i.e. there is no confusion about which variable comes first)?	Yes	Yes	Yes
Were the participants included in any comparisons similar?	Yes	Yes	Yes
Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	No Both groups received RT	Yes 3-arm parallel	Yes
Was there a control group?	Yes	Yes	Yes
Were there multiple measurements of the outcome both pre and post the intervention/exposure?	Yes	Yes	Yes
Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	Yes	Yes	Yes
Were the outcomes of participants included in any comparisons measured in the same way?	Yes	Yes	Yes
Were outcomes measured in a reliable way?	Yes	Yes	Yes
Was appropriate statistical analysis used?	Yes	Yes	Yes
Overall Appraisal	Include	Include	Include

Note: The same research design was implemented in the six sub-studies, thus matching that of Kogure et al., 2015 (18, 19, 20, 22, 25, 32, 33).

In all three studies, the diagnosis of PCOS was confirmed by the participants' primary care providers (Almenning et al., 2015; Kogure et al., 2015; Vizza et al., 2016) and in two studies, PCOS was diagnosed using the 2003 Rotterdam criteria (Almenning et al., 2015; Kogure et al., 2015). The larger randomized controlled trial and its associated studies (all based on secondary analysis of the parent study) included a control group of premenopausal sedentary and overweight or obese women who did not have PCOS (Kogure et al., 2015). The study by Vizza et al. (2016) included all women with PCOS; however, one group (n =8) received progressive RT and the control group (n = 7) did not receive an intervention. The feasibility study included only women with PCOS but compared three types of exercise: high intensity training (n = 8), strength training (n = 8), and physical activity (n = 7) (Almenning et al., 2015) (see Table 2 for descriptions of each program). High intensity training differs from strength training in terms of higher intensity and shorter duration. For example, high-intensity training involves shorter, more intense unsustainable bursts of physical activity, combined with short periods of rest, such as running sprints on the treadmill followed by a quick recovery period. In contrast those in the strength training group received an intervention consistent with progressive linear periodization, which involves anaerobic activity only at a slower pace. Physical activity is a type of aerobic (versus anaerobic) exercise defined by the World Health Organization (2020) as any body movement that requires more energy than rest.

Terms used in the three interventions for RT include progressive resistance training and strength training. The protocol for all interventions was the same, that of progressive linear periodization. Periodization is a commonly used RT method involving planned manipulation of training variables (load, sets, and repetitions) to maximize neuromuscular adaptations to unaccustomed load or stressors. The linear model is based on changing exercise volume and load across several predictable mesocycles. Based on a 12-month period, the program is referred to as a macrocycle; the 2 subdivisions are the mesocycle (3-4 months) and the microcycle (1-4 weeks) (Legro et al., 2013). All the studies included interventions that progressed through a microcycle and into a mesocycle.

The overall purpose of the studies was to examine the impact of RT among overweight or obese and sedentary premenopausal women with PCOS. The parent study and its six associated studies (one large non-RCT) each emphasized a different primary variable: lean muscle mass (Kogure et al., 2015), sexual function (Lara et al., 2015), autonomic regulation of heart rate variability (Ribeiro et al., 2016), quality of life (Ramos et al., 2016), telomere content (Miranda-Furtado et al., 2016), muscle strength (Kogure et al., 2018), and obesity indices (Kogure et al., 2019). The study by Vizza et al. (2016) was designed to assess the feasibility of executing a randomized controlled trial of progressive RT in women with PCOS. Although the primary outcomes were recruitment and attrition, adherence, adverse events and completion of assessments, secondary outcomes were also collected and included a range of biopsychosocial variables. Almenning et al. (2015) aimed to measure metabolic (e.g., total cholesterol), cardiovascular (e.g., resting heart rate), and hormonal (e.g., free androgen index) outcomes from 10 weeks of strength training, high intensity training, or physical activity. Table 2 provides more detail as to purpose, study design, sample, intervention, measures, and results.

Anthropometrics

Although each article focused on a different primary outcome, the articles also shared common secondary outcomes. For example, each study revealed a significant decrease in percent body fat due specifically to reduced visceral fat, thus decreased waist circumference. Visceral fat, that is abdominal adiposity, is an important predictor of obesity-related health risks such as cardiovascular and metabolic disorders (Jansen et al., 2004). Visceral fat has also been implicated in the etiology of insulin resistance in PCOS (Hutchinson et al., 2011). Additionally, each RT intervention produced a significant increase in lean muscle mass among women with PCOS when compared with other women with PCOS who served as control and with women without PCOS. The decrease in percent body fat plus the increase in lean muscle mass equaled no change in body mass index for women with PCOS in the RT intervention groups.

Metabolic

A common metabolic outcome measured in all studies was fasting glucose. This measure decreased with statistical significance after a program of RT in all studies. Interestingly, RT produced a significantly lower fasting glucose in women with PCOS as compared to women without PCOS who engaged in the same RT program (Kogure et al., 2015).

Hormonal

Each study involved biochemical assays to obtain a hormonal panel on each participant. The selected hormonal tests for each study's panel differed with only two common variables: serum testosterone and sex hormone binding globulin (SHBG). Serum testosterone significantly decreased after a program of resistance training in two studies (Vizza et al., 2017; Kogure et al., 2015) and did not change at all in the feasibility study (Almenning et al., 2015), which was attributed to difficulty with interpretation within a small-scale study. Women with PCOS often present with below normal levels of

SHBG, a glycoprotein that serves to limit exposure to androgen (Qu & Donnelly, 2020). Interestingly, the three main studies indicated mixed results: a decrease without statistical significance (Vizza et al., 2016), an increase with statistical significance (Kogure et al., 2015), and no change at all (Almenning et al, 2011).

Almenning et al. (2015) was the only study to consider anti-Mullerian hormone (AMH), a glycoprotein often used as a measure of certain aspects of ovarian function. Evidence has shown that increasing the level of AMH improves fertility due to its inhibitory effect on follicular sensitivity to follicle-stimulating hormone (Broer et al, 2014). In the study by Almenning et al. (2015), women with PCOS had a significant decrease in AMH after a program of resistance training, high intensity training, and physical activity.

DISCUSSION

Endocrine Society Clinical Practice Guidelines on the Diagnosis and Treatment of PCOS recommend exercise and physical activity as first-line treatment to combat the risk of chronic comorbidities. However, detail about the type of exercise is not provided. The scientific literature includes information about cardiovascular or aerobic activity, but notably lacks attention to RT. Given the known beneficial effects of RT on the management of other chronic diseases, RT may provide therapeutic management for PCOS.

A scoping review of three databases over the last ten years revealed nine articles that involved three interventions. The primary outcomes of each intervention shared broad categories of anthropometric, hormonal, cardiovascular, and fitness variables.

Common outcome measures across all three interventions that resulted in positive and significant changes after RT included waist circumference, percent bodyfat, lean muscle mass, testosterone, sex hormone binding globulin, and fasting glucose. Kogure et al. (2019) and Vizza et al. (2016) measured waist circumference as an operational definition for central adiposity, whereas Almenning et al. (2015) used percent bodyfat to operationalize total body fat mass. Although percent bodyfat is the best measure for overall obesity, central adiposity is associated with a greater risk for chronic disease (Flegal et al., 2009). Further, a distinction must be made between types of body mass. The body mass index is a function of bodyweight and height. Schmitz et al. (2003) found that sedentary, overweight women lost a significant amount of visceral fat after a RT intervention. In Kogure et al. (2015), findings revealed that women with PCOS had no change in body mass index; however, lean muscle mass increased. Logistically, this indicates a loss of fat mass. The increase in muscle mass increases the basal metabolic rate, which is responsible for up to two-thirds of total energy expenditure in healthy adults (Williams et al., 2007). In this scenario, the body fat percentage is relevant and the better indicator of a healthier metabolism (Schmitz et al., 2003). The example of body mass measurements illustrates the current paucity of data that can be equivocally compared now or with future results. More research is needed to develop a solid knowledge base and determine relationships between variables.

RT protocols were detailed in each intervention, with each program significantly differing in terms of load, frequency, intensity, and supervision, indicating that the state of the science is still in an exploratory phase. However, each RT program was associated with reduced body fat as an outcome in women with PCOS, and primarily due to reduced abdominal adiposity. This outcome is promising, as a modest weight loss of 5-10% of total body weight is likely to produce health benefits, such as improved insulin sensitivity and total cholesterol (Wing et al., 2011). Interestingly, findings from two studies indicated improved depressive symptom scores (Vizza et al., 2016; Lara et al., 2015), also a positive outcome for women with PCOS who have a high rate of depressive symptoms (Wright et al., 2020).

Research that examines the hormonal response to RT does exist; however, most of the studies involve men or trained athletes (Kraemer & Ratamess, 2005). Several positive hormonal outcomes unique to RT have been documented, all of which create a cascade of events that support energy production, improved insulin sensitivity, and increased strength (Alvidrez & Kravitz, 2021). A hypothesis still under investigation and of relevance to women with PCOS is the possible upregulation of androgen receptors due to RT (Hunter et al., 2017). Although RT may or may not directly affect SHBG, two factors do increase SHBG, and both are positive outcomes of RT: reduced visceral adiposity and improved insulin resistance (Westcott, 2012). An increase in SHBG helps bind the excess bioavailable testosterone (Qu & Donnelly, 2020).

Overall, the effect of RT on the hormonal profiles of women with PCOS is mixed among the three interventions discovered during this scoping review. As such, it remains unknown at this time if RT can alter certain hormones. If RT does alter the hormone panel of women with PCOS, the variation of response to anaerobic stress would depend on exercise frequency and intensity and program duration. More research is necessary that targets a range of selected hormonal variables among larger samples of women with PCOS who complete more detailed RT programs.

Additional useful data gleaned from the feasibility study by Vizza et al. (2016) were the success of Facebook as a recruitment tool and the increased adherence with supervised exercise sessions. The researchers concluded that a randomized control trial of RT for women with PCOS would be feasible, as evidence reveals that this mode of exercise can elicit a therapeutic effect on a wide range of health outcomes. The authors noted challenges recruiting women with PCOS to participate in their feasibility study. However, the authors further stated that this challenge is expected in clinical research, especially in interventions that require behavioral change.

The geographic location of these studies included Brazil, Norway, and Australia. To date, the US has not been a site for research trials investigating RT as a therapeutic management strategy for PCOS in premenopausal women. Few studies have shown differences between geographical location or race; however, the existing data remains inconclusive as to significant differences in the prevalence of PCOS across geographical location, racial, or ethnic groups (Wolf et al., 2018).

Also inconclusive is the effect of culture on the perception of RT. In a qualitative study by Moghadam et al., (2018), women of Persian descent expressed stigma-related concerns due to perceived masculine characteristics of PCOS and RT. Wright et al., (2020) found the same sentiment among women with PCOS in the US about femininity, along with stigma associated with being overweight or obese. Myre et al. (2019) examined barriers to RT among women without PCOS and found that these women also endorsed a masculine stereotype to RT. Additionally, women without PCOS, who were overweight or obese, described stigmatizing concerns due to body size (Hurley et al., 2018). Many women with PCOS have both hirsutism and overweightness or obesity, leading them to avoidance of body-conscious activities and social situations (Myre et al., 2019). Stigma related to weight issues is a barrier to health-seeking behaviors (Flegal et al., 2009). Further research is needed to discover innovative strategies to mitigate negative perceptions of RT and the harmful consequences of stigma-related stress.

The evidence about the effects of RT on health outcomes for women with PCOS is largely preliminary, but positive, and none of the studies showed an absence of benefit. The nine identified articles that reported on studies involving RT to determine effects on health outcomes for women with PCOS were representative of only three interventions: a nonrandomized case control study (a parent study with six sub-studies), a small, randomized controlled trial, and a nonrandomized feasibility study. Except for one study (Kogure et al., 2015), sample sizes were small, thus limiting the generalizability to the broader PCOS population. Although detailed protocols were described, robust trials are needed to determine the minimum dose of RT to produce optimal health outcomes, including the potential symptom management benefits and contribution toward risk reduction of other chronic diseases. Other limitations of these studies included no assessment of prior physical activity or nutrition (Vizza et al., 2016; Almenning et al., 2015; Kogure et al., 2015) and the use of indirect measures of insulin resistance (Almenning et al., 2015; Kogure et al., 2015). Additional research with adequately powered clinical trials are required to establish health benefits, answer research questions as to therapeutic dose, and discover sustainable behavioral change strategies for women with PCOS. Lastly, if RT is deemed appropriate and effective as a therapeutic treatment strategy for women with PCOS, further investigation of facilitators and barriers to exercise unique to women with PCOS is necessary. This information would strengthen any proposed intervention.

CHAPTER 3

THE IMPACT OF EXERCISE PERCEPTIONS AND DEPRESSIVE SYMPTOMS ON PCOS-SPECIFIC HEALTH-RELATED QUALITY-OF-LIFE[1]

[1] Wright, P. J., Corbett, C. L., Pinto, B. M., Dawson, R. M., & Wirth, M. D. Submitted to *Women's Health*. 7/17/21.

ABSTRACT

Background: Exercise among women with polycystic ovary syndrome (PCOS) is low although recommended as first-line management. The purpose of this study was to explore the effects of exercise perceptions and depressive symptoms on health-related quality-of-life (HRQoL).

Methods: A survey link was posted on PCOS Facebook groups. Premenopausal women with PCOS (n=935) answered questionnaires about demographics, PCOS-specific HRQoL, exercise benefits and barriers, exercise outcome expectations, and depressive symptoms. Data were collected using Qualtrics, transferred to SPSS, and statistically analyzed using descriptive analysis and linear regression.

Results: Respondents were 32.0 ± 10.6 years of age, mostly White (72%), well-educated (56% earned a college degree), and employed full-time (65%). The mean scores were as follows: 2.7 ± 0.1 for HRQoL, 2.4 ± 0.8 for exercise outcome expectations (EOE), and 12.4 ± 5.8 for depressive symptoms. The benefit/barrier ratio was 0.90 ± 0.05. HRQoL increased 0.32 points for every additional perceived exercise benefit and 0.61 points for every additional exercise outcome expectation (EOE). HRQoL was reduced by 1.19 points for every additional perceived exercise barrier and 2.82 points for every additional one-point increase of the depressive symptoms score.

Conclusions: Respondents reported low HRQoL, greater exercise barriers than benefits, neutral EOEs, and high depressive symptoms. These results suggest that promoting exercise benefits, overcoming exercise barriers, and addressing management of depressive symptoms are important foci of future efforts to improve HRQoL among women with PCOS.

Keywords: health-related quality-of-life, polycystic ovary syndrome, exercise barriers, exercise facilitators, outcome expectations, depression, depressive symptoms

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy and the leading cause of infertility among premenopausal women (Azziz, 2019). The prevalence of PCOS in the United States (US) ranges from 15-21% (Greenwood et al., 2018; Blagojevic, et al., 2017; Brakta et al., 2017). The estimated total financial burden in the US for evaluating and treating premenopausal women with PCOS was over $5 billion in 2014 (Bratka et al., 2017; Bahar, 2017). Clinical features of PCOS include obesity, impaired glucose tolerance, insulin resistance, and dyslipidemia, which are associated with an increased risk of cardiovascular, metabolic, and oncological conditions (Legro et al., 2013). Psychological sequelae are also problematic, as women with PCOS are eight times more likely to have anxiety and depression as compared to other women (Cinar et al., 2011; Fauser et al., 2012).

Despite the high prevalence and serious clinical implications of PCOS throughout the woman's lifespan, no standard long-term treatment prevails, and current medications are only moderately effective at controlling symptoms and preventing complications (Legro et al., 2013). Evidence suggests that some women with PCOS are dissatisfied with the typical medical model, including the use of pharmaceuticals (e.g., metformin and oral contraceptives). These women reported actively seeking alternative therapeutic management strategies (e.g., acupuncture and herbal remedies) (Wright et al., 2020). Yet a survey of reproductive endocrinologists revealed that only 42% recommended that women engage in physical activity behavior (Dokras et al., 2017), even though the Endocrine Society Clinical Practice Guidelines of PCOS recommend exercise as first line treatment for PCOS (Legro et al., 2013).

A cross-sectional study conducted in 2011 surveyed 150 premenopausal women with PCOS recruited from multiple clinics (Lamb et al., 2011). The authors reported that 59% met the recommended physical activity guidelines of 150 minutes of moderate-to-vigorous activity per week (Lamb et al., 2011). This statistic is comparable to the report by the Centers for Disease Control and Prevention (2020) concerning all women in the US.

Given the clinical profile and risks associated with PCOS and the known benefits of regular physical activity, more research is needed to identify both psychosocial influences on exercise habits and strategies to promote adoption and maintenance of exercise (Conte et al., 2015) among women with PCOS. According to current evidence, women with PCOS have unique barriers to exercise, which include poor body image, depression, and stigma-related stress that may contribute to low exercise uptake (Wright et al., 2020; Thomson et al., 2016). According to the Health Belief Model (HBM), exploration of exercise benefits/barriers, along with biopsychosocial characteristics and exercise outcome expectations, is critical toward designing meaningful and sustainable evidence-based exercise interventions for premenopausal women with PCOS (Abraham & Sheeran, 2015). The purpose of this descriptive, exploratory cross-sectional study was to explore the impact of perceived exercise benefits and barriers, exercise outcome expectations, and depressive symptoms on PCOS-specific health-related quality-of-life (HRQoL) using multiple regression analyses.

CONCEPTUAL FRAMEWORK

The Health Belief Model (HBM) explains and predicts health behaviors as an expression of attitudes and beliefs. As one of the most widely applied theories of health behavior prediction (Glanz & Bishop, 2012), the HBM theorizes that health-related behavior depends on the perception of severity (of the illness or the risk of illness), susceptibility or likelihood of risk factors or co-morbid conditions, benefits of the behavior, and barriers to that behavior. Thus, the HBM, operationalized as a series of individual variables, accounts for variance in the choice of health behaviors (Abraham & Sheeran, 2015).

PCOS is a chronic condition that creates need for symptom management and poses risks for other co-morbid conditions with the most common being depression. The constructs of severity of illness and susceptibility to future complications were examined using the Polycystic Ovary Syndrome Questionnaire (PCOSQ-50). The PCOSQ-50 indicates overall health-related quality of life for the purposes of examining impact of PCOS on perceived quality of life and to determine motivational cues for symptom management (Nasiri-Amiri et al., 2016). The constructs of perceived barriers and perceived benefits were measured using the Exercise Benefits/Barriers Scale (EBBS). The EBBS helps identify beliefs about exercise that will manage symptoms or reduce risk as well as other facilitators of exercise (benefits). The EBBS also identifies tangible and psychological costs of or obstacles to exercise (barriers) (Sechrist et al., 1987). The Exercise Outcome Expectations (EOE) scale was used to measure motivation for using exercise to improve health. Depressive symptoms have a negative reciprocal relationship with the health experience. Depressive symptoms were measured using the Personal Health Questionnaire (PHQ-8). Individual characteristics (as measured by a demographic questionnaire), psychosocial determinants, and structural variables can all influence the four major constructs of the HBM (Glanz & Bishop, 2012). See Figure 3.1.

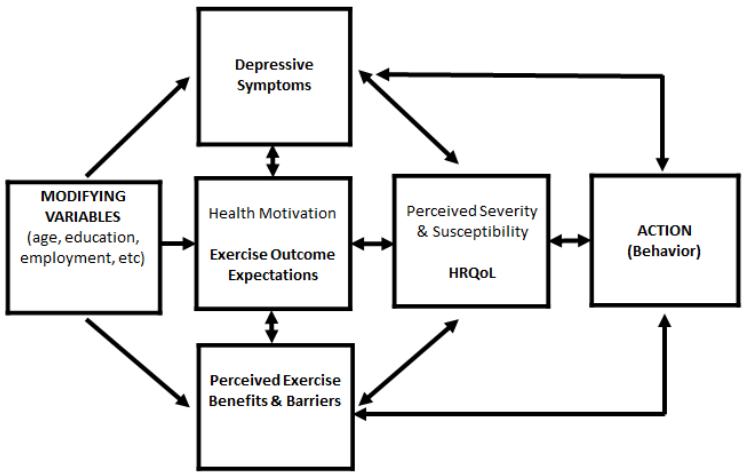

Figure 3.1

The Health Belief Model

METHODS

Study Participants

The study participants (n = 935) were recruited through two PCOS-specific Facebook groups over one week in December 2020. Inclusion criteria were women aged 18-42 with a self-report of PCOS. If eligible, women were invited to complete a cross-sectional internet-based survey to assess PCOS-specific HRQoL, exercise barriers and facilitators, exercise outcome expectations, and depressive symptoms. Participants had the option to enter a drawing to win one of eight $50 gift cards. The University of South Carolina Institutional Review Board provided an “exempt” status for the study.

Measures

Demographics

The demographic questionnaire included age, race, education, marital status, number of children, employment, insurance, geographic location, and comorbid conditions. See Table 3.1 for strata of the categorical variables.

PCOS-Specific Health-Related Quality-of-Life

The PCOSQ-50 includes 50 items in six domains: psychosocial and emotional, fertility, sexual function, obesity and menstrual disorders, hirsutism, and coping. Responses to all items are rated on a 5-point Likert scale ranging from 1 = always (worst condition) to 5 = never (best condition). Each domain score is calculated as the sum of all answered items divided by the number of answered items in that domain. The PCOSQ-50 score is calculated as the sum of all answered items divided by the number of answered items. Per the PCOSQ-50 scoring guidelines, missing items are not included when calculating the domain scores or the total PCOSQ-50 score. Lower scores indicate a lower HRQoL (Nasiri-Amiri et al., 2016). Construct validity was reported at 0.92 and test-retest reliability was reported at 0.91 (Nasiri-Amiri et al., 2018).

Depressive Symptoms

The PHQ-8 was used to assess the prevalence and severity of depressive symptoms occurring within the past two weeks. The scale consists of 8 items with a 4-point rating ranging from 0 (not at all) to 3 (nearly every day). A score of 10 or greater is considered major depression, 20 or more is severe major depression (Kroenke et al., 2009). Construct validity was reported at 0.75 and internal reliability was reported at 0.81 (Kroenke et al., 2009).

Exercise Benefits/Barriers

The EBBS uses a 4-point scale from 4 (strongly agree) to 1 (strongly disagree). The score is calculated by dividing the total mean benefit score by the total mean barrier score. The result is reported as a benefit/barrier ratio. A ratio ≥ 1 indicates that benefits are perceived greater than barriers (Lovell et al., 2010).

The benefit component comprises 29 items categorized into five subscales: life enhancement, physical performance, psychological outlook, social interaction, and preventative health. The barrier component includes 14 items categorized into four subscales: exercise milieu, time expenditure, physical exertion, and family discouragement. The reported internal consistency (alpha) for the benefits and the barriers scales were 0.95 and 0.86 respectively, while test re-test reliability was 0.89 and 0.77 respectively (Sechrist et al., 1987).

Exercise Outcome Expectations

The EOE ($\alpha = 0.75–0.87$) instrument uses a 5-point scale from 1 (strongly disagree) to 5 (strongly agree). Scores are determined by summing the ratings and dividing by the number of responses. Scores > 3 indicate a positive expectation of exercise (Resnick et al., 2000). Construct validity was reported at 0.66 and test-retest reliability was reported at 0.85 (Resnick et al., 2000).

Data Analyses

Survey data were collected in Qualtrics, transferred to IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, N.Y., USA), and then cleaned and analyzed. Descriptive statistics and frequencies or mean ± standard deviations were computed for each variable. Measures with missing data were omitted from analysis. Pearson correlations were calculated between HRQoL and all predictor variables. Linear regression analyses were used to determine the impact of the independent variables of exercise benefits, exercise barriers, exercise outcome expectations, and depressive symptoms on the outcome variable of PCOS-specific HRQoL. Backward confounder variable selection procedures were used to develop the final models. Normality, linearity, and heteroskedasticity checks performed on the data confirmed that all model assumptions were met.

RESULTS

Respondents (n=935) were 31.0± 5.8 years of age, mostly White (72%), well-educated (56% had a college degree), married (69%), and employed full-time (65%). Seventy-four percent of the sample already had one or more chronic conditions, such as high blood pressure or diabetes, in addition to PCOS. Using social media allowed participation from within and outside the US: 81% of the sample was from the US and 19% were from non-US countries. Characteristics of the sample are listed in Table 3.1. Pearson correlations revealed significant relationships between HRQoL and each predictor variable. The relationship between HRQoL and exercise barriers was of medium strength, whereas the relationship between HRQoL and depressive symptoms

Table 3.1

Descriptive statistics of study sample (n = 935)

Characteristics	Frequency
Age	31.0 ± 5.8
Race	
African American or Black	62 (7%)
American Indian or Native American	10 (1%)
Asian or Pacific Islander	54 (6%)
Hispanic, Latino/a, or Spanish Origin	77 (9%)
Middle Eastern or North African	4 (0.4%)
White	647 (72%)
Mix of Two	34 (4%)
Prefer not to answer	11 (1%)
Location	
US	761 (81%)
Non-US	173 (19%)
Educational Attainment	
Some High School	14 (1.5%)
High School or GED	69 (7.7%)
Some College	313 (34.5%)
Bachelors	312 (35%)
Masters	158 (17.6%)
Doctorate	26 (3%)
Prefer not to answer	7 (0.7%)
Employment Status	
Not Working	166 (19%)
Part Time	127 (14%)
Full Time	588 (65%)
Prefer not to answer	18 (2%)
Medical Insurance	
Yes	775 (86%)
No	109 (12%)
Prefer not to answer	16 (2%)
Marital Status	
Single	250 (28%)
Married or partnered	616 (69%)
Divorced or separated	31 (3%)
Widowed	0 (0%)
Prefer not to answer	2 (0.2%)
# of Children	
0	512 (55%)
1	160 (17%)
2	143 (15%)
3	56 (6%)
4	19 (2%)
5	4 (0.4%)
# of Chronic Diseases	

0	240 (31%)
1	254 (33%)
2	127 (16%)
3	86 (11%)
≥ 4	67 (9%)

was of large strength (see Table 3.2).

Table 3.2

Pearson correlations between HRQoL and each predictor variable

Variable	Pearson Correlation	p-value
Exercise Benefits	-0.20	$p<0.001$
Exercise Barriers	0.30	$p<0.001$
Exercise Outcome Expectations	-0.20	$p<0.001$
Depressive Symptoms	0.54	$p<0.001$

*Note: Lower scores on the PCOSQ50 indicate better HRQoL.

Depressive Symptoms

Of the 935 respondents, 893 completed the PHQ-8. The mean score for depressive symptoms was 12.5 ± 5.8, which indicated moderate depression (Table 3.3). In this study, 65% of the respondents scored ≥ 10. Overall, in this sample, seven of the depressive symptoms were experienced by participants two or more days per week. Only one symptom, (moving too slowly or feeling fidgety), was experienced one day or less per week by the respondents.

Exercise Benefits and Barriers

Of 935 respondents, 910 completed the Exercise Benefits and Barriers Scale (EBBS). For benefits, the participants agreed with most of the statements. The only exception was the category of Social Interaction (e.g., "exercising is a good way for me to meet new people"), as all the mean scores on the individual items were "disagree." For barriers, all but one of the categories were indicated as perceived barriers to exercise. Thus, this sample agreed that the exercise milieu (access, schedules, and cost), time needed to exercise, and social support specifically from family members presented the greatest barriers. Physical exertion was not scored as a barrier. As shown in Table 3.3, findings revealed that this sample of women with PCOS felt significantly higher perceived barriers (2.40 ± 0.40) than benefits (2.20 ± 0.50, $p < 0.001$) to exercise. This equated to an EBBS ratio of 0.90 ± 0.05.

Exercise Outcome Expectations

Of 935 respondents, 898 completed the Exercise Outcome Expectations (EOE) questionnaire. The mean score for EOEs was 2.4 ± 0.80 (Table 3.3). The respondents had positive exercise outcome expectations for many items (e.g., "exercise makes me feel better physically," "exercise makes my mood better in general") and "neutral" perceptions of items such as "exercise makes me feel less tired" and "exercise is an activity that I enjoy."

HRQoL

Overall, as shown in Table 3.2, the respondents (n=935) reported low HRQoL (2.68 ± 0.67), particularly in the psychosocial/emotional domain (2.40 ± 0.67) and the physical domains of obesity/menstruation (2.40 ± 0.75) and hirsutism (2.40 ± 1.36) (Table 3.3). HRQoL increased 0.32 points for every additional perceived exercise benefit and 0.61 points for every additional exercise outcome expectation (EOE). HRQoL was reduced by 1.19 points for every additional perceived exercise barrier and 2.82 points for every additional one-point increase of the depressive symptoms score (Table 3.4).

Table 3.3

Subscale and total means and standard deviations of measurements

Variable	Mean ± SD
Exercise Benefits Total (n=910)	**2.21 ± 0.72**
Life Enhancement	2.21 ± 0.72
Physical Performance	1.87 ± 0.63
Psychological Outlook	2.13 ± 0.76
Social Interaction	2.75 ± 0.82
Preventive Health	1.98 ± 0.72
Exercise Barriers Total (n=910)	**2.43 ± 0.82**
Exercise Milieu	2.82 ± 0.87
Time Expenditure	2.56 ± 0.82
Physical Exertion	1.94 ± 0.76
Family Discouragement	2.40 ± 0.82
Exercise Outcome Expectations Total (n=898)	**2.40 ± 0.80**
Depressive Symptoms Total (n=893)	**12.4 ± 5.8**
HRQoL Total (n=935)	**2.68 ± 0.63**
Psychosocial/Emotional	2.40 ± 0.67
Fertility	3.15 ± 1.10
Sexual Function	3.16 ± 1.04
Obesity/Menstrual	2.40 ± 0.75
Hirsutism	2.40 ± 1.36
Coping	2.63 ± 0.85

Table 3.4

Adjusted linear regression of exercise perceptions and depressive symptoms with HRQoL*

Independent Variables	β	95% CI
Exercise Benefits*	0.32	0.16 - 0.49
Exercise Barriers*	-1.19	-1.55 - -0.82
Exercise Outcome Expectations*	0.40	-0.12 – 0.92
Depressive Symptoms*	-2.82	-3.13 - -2.51

* Notes: Each variable was assessed for covariates and analyzed separately using linear regression. Exercise Benefits and EOE: age, education, employment, medical insurance, chronic conditions; Exercise Barriers: age, education, employment, medical insurance, # of children, chronic conditions; Depressive Symptoms: education, employment, # of children

DISCUSSION

The purpose of this descriptive, exploratory cross-sectional study was to explore the impact of perceived exercise benefits and barriers, exercise outcome expectations, and depressive symptoms among women with PCOS on HRQoL. Consistent with other studies, this sample of women with PCOS scored on the lower end of the HRQoL continuum and presented with significant depressive symptoms (Stevanovic et al., 2019; Chaudhari et al., 2018; Nasiri-Amiri et al., 2018; Nasiri-Amiri et al., 2016). Contrary to the only other known study about exercise barriers and benefits among women with PCOS, this study revealed a low benefit/barrier ratio. The prevalence of depressive symptoms among this sample was expected, as women with PCOS are eight times more likely to have depression as compared to other women (Fauser et al., 2012; Cinar et al., 2011).

HRQoL

The PCOSQ-50 was used to help quantify the effects or impact of PCOS on an individual's HRQoL. In this study, the total mean score (2.7±0.06) on the PCOSQ-50 for all participants (n=935) was comparable to the 2.94 found in a confirmatory factor analysis study involving 350 (aged 18-42) women recruited from clinics with confirmed diagnoses of PCOS (Nasiri-Amiri et al., 2018). Stevanovic et al. (2018) conducted a cross-sectional study of 76 women (aged 18-49) from medical clinics and with confirmed PCOS diagnoses to find a PCOSQ-50 mean total HRQoL score of 3.61, which, as a higher score, indicated a better HRQoL than was found in this study. The larger studies had results indicating lower HRQoL among women with PCOS. Of note, this study involved data collection during the Covid-19 pandemic, during which depressive symptoms were higher among all populations due to imposed self-isolation.

Consistent with the Nasiri-Amiri et al. (2018) study, the subcategory ratings in our study for fertility, sexual function, and coping were similar. The low rating of the coping subcategory in this study indicated issues with coping well, which was consistent with the three prior studies (Stevanovic et al., 2019; Nasiri-Amiri et al., 2018; Nasiri-Amiri et al., 2016). This study involved the largest sample size to date and yielded similar conclusions that women with PCOS have reduced HRQoL with difficulty coping with the physical and psychological sequelae of PCOS.

Depressive Symptoms

Consistent with the literature, the women who participated in this study had a high prevalence (65%) of depressive symptoms as evidenced by a score ≥10 on the PHQ-8. Direct comparisons across studies are difficult due to the different assessment tools; however, the findings across studies have been consistent. In a cross-sectional study of 70 women with PCOS, the prevalence of depressive symptoms was 26% using the Hamilton Depression Rating Scale (Chaudhari et al., 2018). In a case control study of 742 women with PCOS and 798 women without PCOS, the prevalence of depressive symptoms was 36% and 8% respectively, based on the Primary Care Evaluation of Mental Disorders Personal Health Questionnaire (Sayyah-Millini et al., 2015).

Although studies of women with PCOS show a significantly higher prevalence of depressive symptoms than studies of women without PCOS, this study revealed a higher prevalence than other PCOS studies. The higher prevalence from this study may be due to the time of data collection. Data were collected during the global pandemic of coronavirus 19 (COVID-19), a respiratory virus with potentially severe and long-term sequelae, especially among those with underlying conditions such as PCOS (Subramanian et al., 2021). Psychological distress was elevated throughout the population due to such factors as social distancing and fear (Bendau et al., 2021; Delmastro et al., 2020). In a cross-sectional study, Lesser and Nienhaus (2020) found that women were additionally affected by economic hardships and increased childcare responsibilities during the pandemic. A recent study indicated that people with depressive symptoms were more likely to experience a greater number of or more severe depressive symptoms during the pandemic (Ettman et al., 2020). Kite and colleagues (2021) conducted a cross-sectional study of women with PCOS in the United Kingdom to find that the COVID-19 lockdown had a negative impact on sleep, which was also associated with impaired QoL and higher depression/stress levels.

Depressive symptoms could have psychosocial and/or pathophysiological causes (Veltman-Verhulst et al, 2012). Physiological consequences, such as insulin resistance and hirsutism, could also overlap with the causes of depression. For example, depressive symptoms have been linked to hyperandrogenism (Fatemek et al., 2021), obesity, insulin resistance or diabetes, and low-grade inflammation (Farrell & Antoni, 2010). In this study, linear regression analysis revealed that with every one-point increase of the depressive symptom score, the PCOSQ-50 would decrease on average by 2.82 points. Specific exercise interventions have been found to be effective in reducing mild-moderate depression in the general population (Eyre et al., 2013; Carek et al., 2011).

Exercise Benefits and Barriers

Based on previous literature incorporating the EBBS in studies of women with and without PCOS, the EBBS was expected to favor benefits. In a randomized controlled trial examining the perception of exercise benefits and barriers in women with PCOS (n=43, aged 29.3 ± 0.70), the baseline data revealed an EBBS ratio of 1.33. A limitation of this study was that all participants volunteered for the exercise intervention, which may have indicated they had a positive bias toward exercise (Thomson et al., 2016). In a cross-sectional study of 400 college women without PCOS, the EBBS ratio was 1.22 (Lovell et al., 2010). While the EBBS ratio in this study indicated more barriers than benefits, the respondents agreed with most all items on the benefits subscale. However, the respondents more strongly agreed with the items on the barrier subscales. Reducing barriers is important, as our regression analysis revealed that for every added barrier, the PCOSQ-50 score would decrease on average by 1.19. This is clinically relevant as a one-point decrease on the PCOSQ-50 five-point scale indicates increased difficulty with physical and psychological functioning.

Thomson et al. (2016) reported the most common perceived barriers in their study were lack of time, fatigue, and lack of confidence. In the Gad et al.'s (2017) study, the most common perceived exercise benefit was improved self-esteem, and the most common perceived barrier was access to exercise facilities. In this study, the respondents strongly agreed that exercise facilities (access, cost, and schedules) presented the greatest barrier. Innovative approaches toward delivering exercise programs are a critical need. Self-image was the second greatest barrier in the current study, like that found by Thomson et al. (2016). Visible features, such as hirsutism and acne or potential consequences, such as infertility and obesity, are perceived as stigmatizing by many women with PCOS (Wright et al., 2020) and could cause perceived loss of femininity and increased self-consciousness about appearance in public spaces (Bazarganipour et al., 2015; Kitzinger & Willmott, 2002).

Lack of social support, specifically from family, was found to be the third greatest barrier in the current study. However, the responses to the statement, “my spouse (or significant other) does not encourage exercise,” indicated that spouse’s or significant other’s encouragement to exercise would be a possible benefit. In a content analysis of stories written by women with PCOS on a social support website, some women reported “anxiety,” “frustration,” and lower self-esteem when spouses or significant others encouraged exercise too often, as it created a sense “of not being good enough” (Wright et al., 2020). Thus, support from significant others can influence health by either promoting or undermining behavior change (Morowatisharifabad et al., 2019). Further research is needed to identify types and amount of social support that best meet the needs of women with PCOS. Programs that incorporate the spouse or significant other could hold promise.

Exercise Outcome Expectations

Outcome expectation is a multidimensional construct that includes physical (e.g., body structures and functions), social (e.g., intrapersonal relationships), and self-evaluative (e.g., emotional/affective reflections) components (Bandura, 1986). In general, outcome expectations refer to what people expect to obtain or avoid by engaging in a behavior. While no study on EOE has been done prior to this study in women with PCOS, EOE has been studied in other populations. In a randomized control trial of a physical activity intervention involving women without a chronic disease (n=118), EOEs were positive but not predictive of subsequent physical activity (Wilcox et al., 2006). However, findings from studies involving chronic diseases such as breast cancer and multiple sclerosis, revealed that positive EOEs may predict exercise participation (Hirschey et al., 2017; Morrison & Stuifbergen, 2014). Hirschey et al. (2017) further concluded that while women with chronic disease may have positive EOEs, they hold some doubt about the efficacy of exercise as treatment due to lack of awareness of these type benefits. In this study, women with PCOS had positive EOEs but with some "neutral" feelings. Weiner and colleagues (2004) reported that only 40% of women with PCOS were motivated to exercise to control a medical condition. Their findings suggest that the importance of physical activity for managing PCOS symptoms and minimizing long-term complications of PCOS may not be fully understood. More education is needed for women with PCOS that describes the benefits of exercise specific to PCOS, along with the mechanisms of action for those benefits. Health care providers can also impact knowledge by addressing exercise outcome expectations with their patients with PCOS.

STRENGTHS AND LIMITATIONS

This cross-sectional study had several strengths. The large sample size of 935 made this the largest cross-sectional study of women with PCOS to date in peer-reviewed literature. The larger sample size provides strong statistical power with a smaller margin of error and increases the external validity (Faber & Fonseca, 2014). This study is the first to consider perceived exercise outcome expectations among women with PCOS. Thus, this study adds new knowledge to the scientific literature about PCOS.

This study had several limitations. As a cross-sectional research design, the results do not indicate causality of any direction between HRQoL and perceived exercise benefits, barriers, and outcomes or depressive symptoms. This study did not require confirmation of a PCOS diagnosis, as the surveys were administered online. However, internet safeguards were added (e.g., CAPTCHA) to help prevent robotic responses. The surveys required self-reported data; thus, responses were subject to recall and social desirability biases (Althubaiti, 2016). Another limitation was the omission of a questionnaire to assess current physical activity levels. This was omitted due to potential respondent burden and will be collected in future studies. Also, weight and height were not collected due to inherent bias with self-report and the length and sensitive nature of the included surveys. The impact of body mass index on HRQoL will be assessed in future studies. The EBBS was designed for the general population and has not been validated in PCOS. Symptoms and co-morbidities associated with PCOS may present different barriers to exercise that were not identified with EBBS. Lastly, data was collected during the global COVID-19 pandemic, possibly skewing all results due to the effects of imposed self-isolation.

CONCLUSIONS

Findings revealed that this sample of women with PCOS had low HRQoL, particularly in the psychosocial/emotional domain and the physical domains of obesity, menstruation, and hirsutism. These domains were significantly associated with depressive symptoms, of which more than half the women reported. Depressive symptoms were associated with reduced HRQoL. Exercise barriers were perceived greater than exercise benefits. Barriers included facility issues, time commitment, and lack of social support. Overall, the respondents had positive to neutral exercise outcome expectations. The respondents presented with high depressive symptoms. These characteristics may interfere with exercise participation among women with PCOS. Given the crucial impact on self-management, psychological wellbeing must be considered before administering the optimal exercise intervention. Research is needed to discern effective strategies for exercise initiation and maintenance and to evaluate the effects of exercise on HRQoL and management of depressive symptoms among women with PCOS.

CHAPTER 4

PHENOTYPES AND FITNESS LEVELS AMONG A FEASIBILITY SAMPLE OF WOMEN WITH POLYCYSTIC OVARY SYNDROME[1]

[1] Wright, P. J., Wirth, M. D., Pinto, B. M., Corbet, C. L, & Dawson, R. M. 2021. To be submitted to *Clinical Endocrinology.*

ABSTRACT

Introduction: Fitness is a marker of physiological and mental health. The purpose of this exploratory, cross-sectional study was to explore the associations among anthropometrics, biomarkers, health-related quality-of-life (HRQoL), and depressive symptoms with fitness (i.e., cardiovascular capacity, muscular strength/endurance, flexibility, and self-reported physical activity levels) among women with PCOS.

Methods: A convenience sample of women with polycystic ovary syndrome (PCOS) (n=15) was recruited via flyers and snowball methods. Participants completed surveys, body measurements, a dual energy x-ray absorptiometry scan, blood work, and a fitness assessment. Data were statistically analyzed using Spearman correlations.

Results: Participants (n=15) were 25.9 (± 6.2) years of age, mostly White (80%), single (60%), and employed full-time (67%). Participants were categorized as obese (BMI 32.2 ± 8.3, percent bodyfat 41.1 ± 8.1) with ≤ 1 comorbidity. None of the women met the 2018 Physical Activity Guidelines. Participants had high free testosterone levels, high levels of high-density lipoprotein, fair cardiovascular capacity, and below average muscular strength/endurance. The following statistically significant and strong associations were found: 1) VO_2 max with percent bodyfat, sex hormone binding globulin, health-related quality of life, and depressive symptoms, 2) abdominal strength with BMI, percent bodyfat, and HDL, 3) overall physical activity level and percent bodyfat, and 4) resistance training with LDL.

Conclusion: Assessing fitness indices may help identify health risks among different PCOS phenotypes.

Keywords: polycystic ovary syndrome, phenotypes, anthropometrics, biomarkers, dyslipidemia, central adiposity, fitness testing

Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among premenopausal women with a prevalence that ranges between 15-21% (Greenwood et al., 2018; Brakta et al., 2017). Common signs and symptoms include infertility, oligomenorrhea, insulin resistance, dyslipidemia, hirsutism, acne, and lethargy. These manifestations place women with PCOS at risk for comorbid conditions such as diabetes, cardiovascular disease, certain reproductive cancers, and depression resulting in reduced health-related quality-of-life (HRQoL) (Moghadam et al., 2018). Unfortunately, a diagnosis of PCOS is often missed or delayed, as its presentation can vary widely among women (Dennet & Simon, 2015).

According to the Rotterdam criteria, PCOS is diagnosed when two of three characteristics are met: clinical or biochemical hyperandrogenism, ovulatory dysfunction, and/or ultrasound evidence of polycystic ovarian morphology. Using all possible combinations, this heterogenous condition produces four phenotypes (Table 4.1). The phenotypes not only serve as diagnostic criteria, but also as a continuum of symptom severity. The phenotypes differ in terms of anthropometric, hormonal, and metabolic indices; however, the risk for co-morbid conditions holds constant due to shared factors such as visceral adiposity and dyslipidemia (Wild et al., 2011). An estimated one in two women with PCOS presents with excess central obesity (Greenwood et al., 2018), and approximately 70% of women with PCOS have dyslipidemia (Dunaif, 2016).

Table 4.1

Characteristics of the four PCOS phenotypes

	A (~60%)	B (~8.4%)	C (~22.5%)	D (~9%)
	Classic PCOS		Ovulatory	Non-HA
Clinical or Biochemical Hyperandrogenism	+	+	+	
Ovulation Dysfunction	+	+		+
Ovarian Morphology	+		+	+

A) Hyperandrogenism + Ovulation Dysfunction + Ovarian Morphology
B) B) Hyperandrogenism + Ovulation Dysfunction
C) C) Hyperandrogenism + Ovarian Morphology
D) D) Ovulation Dysfunction + Ovarian Morphology

Phenotypic heterogeneity confounds the modification of lifestyle behavior, which is the first line treatment recommended by the Endocrine Society Clinical Practice Guidelines of PCOS (Legro et al., 2013). Whereas fitness is associated with risk reduction and improved health outcomes, less than 60% of women with PCOS engage in the recommended amount of weekly physical activity and more than 25% are sedentary (Lamb et al., 2011). Fitness (defined as the sum attributes of cardiorespiratory capacity, muscular strength and endurance, and flexibility) is a powerful marker of physical and mental health and is associated with lower mortality from any cause (Warburton & Bredin, 2016). However, fitness profiling as a predictor for health indices is unexplored among women with PCOS.

Assessing fitness indices may help identify different health risks among PCOS phenotypes and the recommended type and intensity of physical activity to mediate these risks. We performed an exploratory, cross-sectional study to identify the associations between the dependent variables of anthropometrics, hormonal and metabolic indices (i.e., PCOS biomarkers), health-related quality-of-life (HRQoL), and depressive symptoms and the independent variables of cardiovascular capacity, muscular strength/endurance, flexibility, and self-reported physical activity levels among women with PCOS.

Theoretical Model

A theoretical physiological model of PCOS based on current research guided this study (Figure 4.1). PCOS is complex and multifactorial in origin, as genetic alterations, epigenetic modifications, and environmental factors contribute to its development or the worsening of its clinical manifestations (Eiras et al., 2020). The genetic origin of PCOS is confirmed by a hereditary factor observed in first-degree relatives, as women who have mothers or sisters with PCOS are at an increased risk (35–40%) of developing the disease (Kahsar-Miller, et al., 2001). In addition to the clear genetic basis, epigenetic alterations (e.g., DNA methylation and noncoding RNA regulation) play a central role in PCOS outcomes, including heritable phenotypic difference, by controlling gene expression both dynamically and reversibly (Eiras et al., 2021). Such effects may result from environmental factors throughout development and adulthood. Environmental factors including lifestyle behaviors such as nutrition, physical activity, and smoking combined with a genetic predisposition (candidate genes) can change the epigenome landscape leading to (epi)genetic susceptibility for developing PCOS throughout life (Eiras et al., 2021).

Obesity or elevated percent body fat is a common characteristic of women with PCOS, which also affects the clinical manifestations, such as hyperandrogenism, insulin resistance, and dyslipidemia (Salehi et al., 2004). Visceral fat, the body fat located within the abdominal cavity, is a storage site for circulating androgen. Androgen also is present in the plasma as free or unbound testosterone (Legro et al., 2013). Further, hyperinsulinemia due to insulin resistance is yet another source of androgen, as hyperinsulinemia decreases the total amount of sex hormone binding globulin (SHBG) (Wallace et al., 2013), a glycoprotein that binds with androgen. Therefore, not only is excess androgen produced, but there is also less SHBG to bind and uptake the androgen, which increases free testosterone levels. In addition to the ovaries and fat cells, androgen also is produced by the adrenal glands, and is produced to excess in most women with PCOS (Legros et al.,2013). Low grade inflammation has been implicated in this process (Rudnicka et al., 2021).

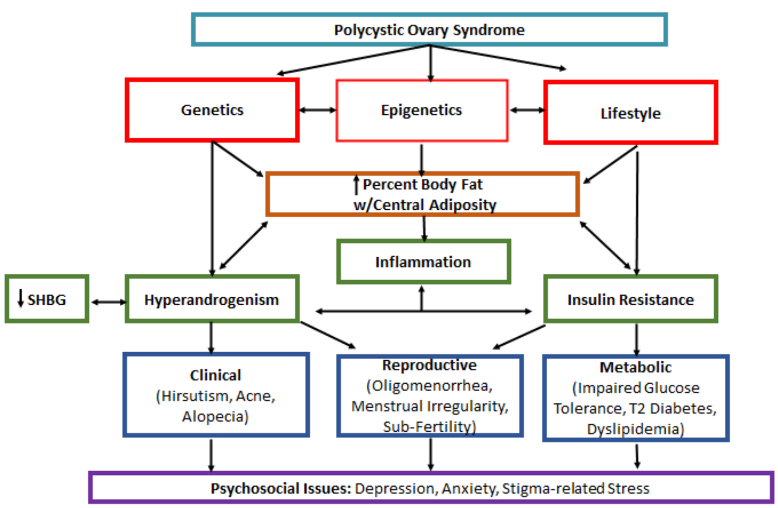

Figure 4.1

Adapted physiological model of polycystic ovary syndrome with permission (Hiam et al., 2019)

Methods

Study Overview

Participants (n=15) were recruited using flyers and the snowball method. Inclusion criteria included women aged 18-42 with a verified PCOS diagnosis. Exclusion criteria included medically induced menopause, hypertension or heart disease, orthopedic injury, and pregnancy. Potential participants were pre-screened using the Physical Activity Readiness Questionnaire to quickly identify exclusion criteria. When potential participants met requirements, they were invited to schedule an early morning fasting appointment at the Clinical Exercise Research Center (CERC) housed within the Arnold School of Public Health at the University of South Carolina (UofSC). Upon arrival, the purpose, benefits, and risks of the study were explained, and any questions or concerns were addressed. After signing the informed consent, the following measures were obtained: anthropometric measurements, venipuncture with blood draw for laboratory panel, survey completion while eating a light snack, dual energy x-ray absorptiometry (DEXA), oxygen consumption testing, and muscular fitness and flexibility testing. Participants were given a $50 gift card as an incentive. Research protocols were approved by the Institutional Review Board of the UofSC.

Anthropometrics

Anthropometric measurements included height (measured to the nearest 0.1cm using a wall-mounted stadiometer), weight (measured twice and to the nearest 0.1kg using an electronic scale), and waist and hip circumferences (measured twice and to the nearest 0.1 cm using a measuring tape). Body mass index was calculated with the formula [BMI = weight(kg) / height(m)^2)]. The waist-to-hip ratio was determined by dividing waist circumference by hip girth. Percent body fat and lean muscle mass were determined using dual energy x-ray absorptiometry (DEXA). Performed by a trained technician, DEXA uses spectral imaging, which involves less than one to two days' exposure to natural background radiation (Damilakis, et al, 2010). DEXA has shown reliability with an intraclass correlation of R = 0.99 (Kutac et al., 2019).

Laboratory-derived Data

The laboratory panel included free testosterone, SHBG, and a total lipid profile. Participants arrived to the CERC having fasted for at least eight hours. Trained personnel followed standard protocol for venipuncture to collect approximately 10mL of blood. The collected specimens were delivered to and processed at the Lexington Medical Center clinical laboratory (West Columbia, SC). Results were confidentially sent to the principal investigator at the College of Nursing. Free testosterone is used to diagnose androgen excess not due to other rare disorders (Dunaif, 2016). SHBG is also a biomarker for PCOS, as well as insulin resistance (Dunaif, 2016). A lipid profile was collected because dyslipidemia is a common metabolic abnormality in women with PCOS, with a prevalence of up to 70%. (Dunaif, 2016).

Questionnaire-derived Data

Demographics. The demographic questionnaire included age, ethnicity, educational attainment, marital status, number of children, employment, insurance, geographic residence, and comorbid conditions.

PCOS-Specific Health-Related Quality-of-Life. PCOS-specific health-related quality of life (HRQoL) was measured using the Polycystic Ovary Syndrome Questionnaire (PCOSQ-50). The PCOSQ-50 has been reported to have a construct validity of 0.92 and test-retest reliability of 0.91 (Nasiri-Amiri et al., 2018). It includes 50 items in six domains: psychosocial/emotional, fertility, sexual function, obesity/menstrual disorders, hirsutism, and coping. Answers to all items are given on a 5-point Likert scale ranging from 1 = always (worst condition) to 5 = never (best condition). A score for each domain was calculated as the sum of all answered items in the domain divided by the number of answered items. The average PCOSQ-50 score was calculated as the sum of all answered items divided by the number of answered items. Lower scores indicate a greater negative impact (Nasiri-Amiri, et al., 2016).

Physical Activity Level. The Rapid Assessment of Physical Activity (RAPA) questionnaire was used to determine the participants' level of physical activity. The RAPA includes seven yes/no questions with the sum of "yes" responses indicating the amount, frequency, and intensity of physical activity. The RAPA contains a second section asking about the inclusion of resistance training and flexibility exercise.

The RAPA has been reported to have good sensitivity (100%) and specificity (75%) for determining physical activity level (Topolski et al, 2006). Positive and negative predictive value for determining physical activity levels were 94.4% and 100% respectively (Topolski et al, 2006).

Depressive Symptoms. The Personal Health Questionnaire (PHQ-8) was used to assess the prevalence and severity of depressive symptoms occurring within the past two weeks. The scale consists of 8 items with a 4-point rating ranging from 0 (not at all) to 3 (nearly every day). A score of 10 or greater indicates major depression and 20 or more indicates severe major depression (Kroenke et al., 2009). Construct validity was reported at 0.75 and internal reliability was reported at 0.81 (Kroenke et al., 2009).

Fitness Testing

Modified Bruce Treadmill. The modified Bruce treadmill test was used to estimate maximal oxygen consumption (VO_2 max) or cardiorespiratory fitness, as this measure is related to functional capacity and serves as a strong and independent predictor of all-cause and disease-specific mortality (Strasser & Burtscher, 2018). After a prolonged warm-up phase (6 minutes), the protocol is divided into successive 3-minute stages, each with a faster speed and steeper grade. The participant's heart rate (via heart rate monitor) and perceived exertion (self-report) is monitored throughout the test. The final score is calculated using the total time spent in the working phases with the formula $(4.38 \times T) - 3.9 = VO_2$ max. The estimated VO_2 max is then compared to gender- and age-based normative data. The modified Bruce treadmill test was chosen as the safest alternative, as at least some participants were anticipated to have a sedentary lifestyle. Bruce (1971) reported a Pearson product moment correlation coefficient between predicted VO_2 max and measured VO_2 max of 0.94 for women without cardiac conditions (n = 5509). The average predicted error was -0.6 $mL*kg^{-1}*min^{-1}$ for the general equation.

Modified Push Up Test. Using the American College of Sports Medicine (ACSM) protocol, the modified push up test was used to estimate upper body muscular fitness.

The test involves performing push-ups in a modified position (knees bent with lower legs in contact with the mat). The score is the total number of modified push-ups performed with proper form in one minute. The score was compared to gender- and age-based normative data. The norm-referenced test-retest reliability estimate, using intraclass correlations from a one-way analysis of variance (ANOVA), was R = 0.99 (Benny & Mahar, 2001).

Curl-Up Test. Using the ACSM protocol, the curl-up test was used to estimate abdominal muscular fitness. Abdominal or core strength is deemed important due to the direct relationship with balance and stability (Hsu et al., 2018). In a supine position, the participant is asked to repetitively lift the upper body approximately 30 degrees (a partial sit-up) and then lower to a metronome set at 40 beats/minute. The score is the number of curl-ups performed to the beat with proper form. The score was compared to gender- and age-based normative data. Psychometric findings included high test-retest reliability (r = 0.98), moderately high inter-apparatus reliability (r = 0.71), and moderately high inter-tester reliability (r = 0.76) (Diener et al., 1995).

Sit-and-Reach Test. Using the ACSM protocol, the sit-and-reach test was used to assess hamstring flexibility. This measure was chosen because hamstring flexibility is related to low back and knee joint health (Reis & Macedo, 2015). The participants sat against a wall with their feet placed at the 15-inch mark on a measuring tape. Keeping knees straight and feet plantar flexed, the participants reached forward with both hands. The score was the farthest distance reached of three trials. The score was compared to gender-and age-based normative data. The sit-and-reach test has shown a moderate mean criterion-related validity for estimating hamstring extensibility (r = 0.46-0.67) (Mayorga-Vega et al., 2014).

Statistical Analyses

Analyses were conducted using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics (frequencies or mean ± standard deviations) were computed for each variable. Given the small sample, assumptions of normality were not met. Thus, bivariate analysis was conducted between each fitness variable (outcome measures) and each independent variable. As all variables were continuous, Spearman correlations were conducted.

Results

Participants (n=15) were 25.9 (± 6.2) years of age, mostly White (80%), well-educated (70% had a college degree), single (60%), and employed full-time (67%). Characteristics of the study sample are listed in Table 4.2.

Phenotypically, the women were obese (BMI 32.2 ± 8.3, percent body fat 41.1 ± 8.1) with high levels of free testosterone (7.6 ± 4.3). Many of the women (53%) reported being regularly active , but not meeting the recommended guidelines of 150 minutes of moderate-to-vigorous activity per week. Only 40% (n=6) reported incorporating resistance training into their physical activity regimen, whereas 60% (n=9) reported using flexibility training as part of their physical activity routine. Table 4.3 presents the clinical ranges, the mean (±SD) of the total population (i.e., reference group), a descriptor of the sample mean value for each study characteristic, and the percent of the sample at risk based on that characteristic.

Table 4.2

Descriptive statistics of study sample (n=15)

Characteristics	Frequency
Age	25.9 ± 6.2
Ethnicity	
African American or Black	0% (0)
Hispanic, Latino/a, or Spanish Origin	13.3% (2)
White	80% (12)
Mix of Two	6.7% (1)
Educational Attainment	
High School or GED	13.3% (2)
Some College	36.4% (4)
Bachelors	33.3% (5)
Masters	26.7% (4)
Employment Status	
Not Working	13.3% (2)
Part Time	20% (3)
Full Time	66.7% (10)
Medical Insurance	
Yes	100% (15)
Marital Status	
Single	60% (9)
Married or Partnership	40% (6)
# of Children	0.5 ± 1.0
# of Chronic Diseases	0.5 ± 0.6

Table 4.3

Means and standard deviations of laboratory and fitness variables compared to clinical guidelines (n=15)

Variable	Reference Values	Mean ± SD	Descriptor	Sample # at Risk
Body Mass Index (BMI)	<18.5 (underweight) 18.5–24.9 (normal) 25–29.9 (overweight) ≥ 30 (obesity)	32.2 ± 8.3	**obese**	12 (80%)
Waist-to-Hip Ratio (WtH)	≤ 0.80 (low risk) 0.81-0.84 (moderate risk) ≥ 0.85 (high risk)	0.81 ± 0.10	**moderate risk**	7 (47%)
Percent Body Fat	21 - 32%	41.1 ± 8.1	**obese**	14 (93%)
Free Testosterone	0.7-3.6 pg/mL	7.6 ± 4.3	**high**	11 (73%)
Sex Hormone Binding Globulin (SHBG)	18 - 144 nmol/L	23.0 ± 12.9	normal	6 (40%)
High Density Lipoprotein (HDL)	40-59 mg/dL	63.2 ± 12.9	**high**	3 (20%)
Low Density Lipoprotein (LDL)	< 100 mg/dL	91.0 ± 24.0	normal	5 (33%)

Triglycerides (TGs)	< 150mg/dL	93.0 ± 32.0	normal	1 (7%)
VO2 Max (mL/mg/min)	Based on age	36.8 ± 10.6	**fair**	5 (33%)
Upper Body Muscular Endurance	Based on age	15.4 ± 4.0	**below average**	7 (47%)
Abdominal Muscular Endurance	Based on age	21.3 ± 18.2	**below average**	12 (80%)
Flexibility (inches)	Based on age	18.8 ± 2.8	average	6 (40%)

Women with PCOS in this study reported a neutral total HRQoL (3.3 ± 0.7) but their scores in the obesity/menstrual and hirsutism domains were low. The overall sample mean for depressive symptoms was low, indicating fewer symptoms; but four (27%) participants scored high (≥10), indicating major depression (Kroenke et al., 2009). Table 4.4 details the means and standard deviations for the HRQoL and depressive symptoms surveys.

Table 4.4

Means and standard deviations of the HRQoL and depressive symptoms survey data (n= 15)

Variable	Mean ± SD
HRQoL Total	**3.3 ± 0.7**
Psychosocial/Emotional	3.2 ± 0.7
Fertility	3.9 ± 0.9
Sexual Function	3.3 ± 0.9
Obesity/Menstrual	3.1 ± 0.9
Hirsutism	3.1 ± 1.4
Coping	3.4 ± 0.8
Depressive Symptoms Total	**7.3 ± 5.3**

Correlational analyses yielded nine statistically significant (p<.05) associations and seven associations with large effect sizes that approached statistical significance (p=0.05-0.15). Free testosterone ($Test_F$) was the only clinical indicator that was not associated with any fitness variable among this sample of women with PCOS (Table 4.5).

Table 4.5

Bivariate analysis of anthropometrics, PCOS biomarkers, HRQoL, and depressive symptoms with fitness variables (n=15)

Variable	VO_2 Max		Strength 1 (upper)		Strength 2 (abdominal)		Flexibility		RAPA 1 (PA level)		RAPA 2 (RT)	
	R	p	R	p	R	p	R	p	R	p	R	p
BMI	**-0.49**	**0.07**	-0.29	0.29	**-0.66**	**0.01**	0.40	0.14	**-0.63**	**0.12**	-0.06	0.82
% Bodyfat	**-0.59**	**0.02**	-0.44	0.10	**-0.61**	**0.12**	0.22	0.43	**-0.72**	**0.00**	-0.09	0.74
WtH	-0.06	0.83	-0.05	0.86	-0.28	0.32	0.15	0.60	**-0.47**	**0.08**	0.25	0.36
$Test_F$	0.39	0.16	0.04	0.89	-0.23	0.39	0.07	0.82	0.02	0.95	-0.17	0.54
SHBG	**0.73**	**0.00**	0.26	0.34	0.33	0.23	-0.00	0.99	0.20	0.47	0.10	0.74
HDL	0.16	0.57	0.14	0.63	**0.59**	**0.02**	**-0.48**	**0.07**	-0.02	0.95	**-0.46**	**0.08**
LDL	-0.03	0.91	0.12	0.67	-0.20	0.49	0.08	0.77	0.33	0.23	**0.52**	**0.05**
TGs	-0.43	0.11	-0.11	0.69	-0.14	0.62	0.09	0.75	**-0.47**	**0.08**	-0.17	0.54
HRQoL	**0.72**	**0.00**	0.36	0.19	0.36	0.62	-0.42	0.12	0.28	0.32	0.13	0.66
DepSx	**-0.67**	**0.00**	-0.31	0.25	-0.20	0.48	-0.06	0.84	-0.39	0.15	**-0.49**	**0.06**

* BMI = body mass index; DepSx = depressive symptoms; HDL = high density lipoprotein; HRQoL = health-related quality of life; LDL = low density lipoprotein; PA = physical activity; RT = resistance training; $Test_F$ = free testosterone; TGs = triglycerides; VO_2 max = maximum oxygen volume; WtH = waist-to-hip ratio
RED: statistically significant associations $p < 0.05$
PURPLE: approaching statistical significance ($p = 0.06$-0.15) with large effect size

Discussion

The purpose of this exploratory, cross-sectional study was to explore the associations among anthropometrics, PCOS biomarkers, health-related quality-of-life (HRQoL), and depressive symptoms with fitness (i.e., cardiovascular capacity, muscular strength/endurance, flexibility, and self-reported physical activity levels). Strong associations will be discussed.

Obesity Indices

BMI

According to clinical guidelines, this sample was described as "obese." BMI is the recommended indicator for determining weight status and health risk (NIH, 2010). However, BMI has limits as it cannot determine body composition or predominant location of bodyfat.

Waist-to-hip Ratio

Central obesity is associated with greater metabolic disturbances, such as insulin resistance, dyslipidemia, elevated blood pressure, and certain reproductive cancers. Participants with a high waist-to-hip ratios (> 0.80) are at risk for increased morbidity and mortality compared to those with less central adiposity. The greater risk is due to storage of visceral deposits or fat storage within the abdominal cavity surrounding the organs (Hwang, et al., 2015). It has been proposed that androgens stimulate the differentiation of pre-adipocytes to adipocytes (adipose tissue dysfunction), especially in the abdomen area, facilitating the development of visceral-type obesity in women with PCOS (Rudnicka et al., 2021).

***Bodyfat Percentage*.**

Bodyfat percentage provides a more accurate indication of weight-related diseases (Mondal & Mishra, 2017). Modest weight loss of 3-5% is associated with clinically significant health improvements (Jensen et al., 2015). However, the type of weight lost (i.e., lean muscle mass versus fat mass) is most important, as the loss of fat mass is associated with improved glucose regulation, insulin sensitivity, immune function, and blood pressure regulation (Cava et al., 2017). A loss of lean mass places women at risk for osteoporosis and lowers metabolic capacity (Weiss et al., 2017).

VO_2 Max

Cardiovascular capacity, as measured by VO_2 max, is an indicator of long-term morbidity and mortality (Mandsager et al., 2018). The American Heart Association published a scientific statement in 2016 recommending that VO_2 max be regularly assessed and used as a clinical vital sign (Ross et al., 2016). The VO_2 max was characterized as "fair" among the women with PCOS in this study. This finding was alarming as VO_2 max gradually decreases 1-2% per year after the age of 25 years (Bara et al., 2019), and the mean age of this sample was 25.9 (± 6.2) years. The participants did not meet recommended physical activity guidelines, which is not different from women in general (CDC, 2020). However, the mean VO_2 max was lower than the VO_2 max reported for apparently healthy women in the same age group (Bara et al., 2019). More research is necessary to delineate factors associated with decreased VO_2 max among women with PCOS.

Consistent with other studies in other populations, VO_2 max had a strong, negative relationship with BMI ($R= -0.49$, $p=0.07$) and percent bodyfat ($R=-0.59$, $p=0.02$). Debate exists about the causal direction between VO_2 max and body composition. Findings from a cross-sectional study by Maciejczyk and colleagues (2017) suggested that high body mass, independent of cause (high lean mass or high bodyfat percentage) decreases VO_2 max relative to total body mass. Whereas a prospective randomized trial conducted by Skrypnik and colleagues (2015) concluded that exercise impacts VO_2 max, which affects body composition. These studies included obese women, but not women with PCOS.

SHBG. VO_2 max had a strong, positive association with SHBG ($R=0.73$, $p<0.001$). SHBG production is regulated by androgens (decrease), estrogens (increase), and insulin (decrease). The participants in this study presented with low levels of SHBG, which is often related to hyperandrogenism (also present in the women participants in this study) (Qu & Donnelly, 2020). The association between physical activity or cardiovascular fitness might be mediated, in part, through androgens; however, this has only been studied in men (Wolin, et al., 2007). Findings from a recent systematic review of exercise effects on hormones suggest that SHBG was largely unaffected by aerobic exercise but increased with either the isolated use of anaerobic exercise (resistance training) or the combination of aerobic and anaerobic exercise (Shele et al., 2020). In addition, women with PCOS who exercised at vigorous intensities had higher levels of SHBG than women who exercised with lower intensities (Shele et al., 2020).

HRQoL. VO_2 max had an exceptionally strong and positive relationship with HRQoL ($R=-0.72$, $p<0.01$). Several studies have shown that women with PCOS have reduced PCOS-specific HRQoL, especially in the psychosocial domain. However, only three randomized controlled exercise trials have measured this outcome, all which revealed improved physical functioning, general health, social functioning, and mental health (Kite et al., 2019). Therefore, improving VO_2 max with exercise may improve HRQoL among women with PCOS.

Depressive Symptoms. VO_2 max had a strong but negative association with depressive symptoms ($R=-0.67$, $p=0.01$). VO_2 max as a predictor of depressive symptoms has not been extensively studied among the general population and not at all among women with PCOS. In a cross-sectional study of women without PCOS (aged 26-43 years) who did not meet physical activity guidelines, VO_2 max was found to be the only physiologic characteristic (as compared to body fat percentage, autonomic indices, and physical activity levels) to independently predict depressive symptoms scores (Tonello et al., 2019). This relationship was also found in a sample of middle-aged men (Tolmunen et al., 2009).

Free Testosterone

Free testosterone is the most potent circulating androgen and the most sensitive biomarker for androgen excess in women with PCOS (Barbieri, 2021). A large percentage (73%) of this sample had high free testosterone levels, which may explain the low (i.e., poor) obesity/menstrual and hirsutism subscale scores on the PCOSQ-50, as other studies have suggested (Amiri et al., 2018; Cinar et al., 2011). Testosterone levels above normal range in women cause infrequent menstrual cycles and male-pattern hair growth (Zhang et al., 2021). A higher testosterone level in women also increases the risk of diabetes by 37% (Ruth et al., 2020). Not all women diagnosed with PCOS have androgen excess, yet they may still experience clinical signs of androgen excess such as hirsutism. Women with PCOS without excess androgen tend to have testosterone levels at the higher end of the normal range, either naturally are due to oral contraceptives (Zhang et al., 2021). However, women with PCOS are more sensitive to testosterone than women without PCOS (Paris & Bertoldo, 2019); therefore, they can still have clinical signs of hyperandrogenism.

HDL

Previous research findings indicated that approximately 70% of obese women with PCOS (Dunaif, 2016) and 36% of leaner women with PCOS have dyslipidemia (Kim & Choi, 2013). Although the mean LDL total in this study was in the normal range, 5 participants (33%) presented with dyslipidemia. Contrary to other studies, the women in this study had high levels of HDL a protective or negative risk factor. The finding of high HDL levels was counter-intuitive given the fair VO_2 max and high levels of percent bodyfat. The high HDL levels may be due to unique characteristics of this small sample. More research is needed with a larger sample.

Muscular Fitness

The women in this study had below average upper body and abdominal muscular fitness for age, a risk factor for musculoskeletal injuries and osteoarthritis (de la Motte et al., 2017) due to poor posture and instability (Hsu et al., 2018). Evidence suggests that obese individuals have reduced maximum muscle strength relative to body mass compared to non-obese persons (Abdelmoula et al., 2012). In this study, the three participants with a BMI within normal range scored average to above average on both the push-up and curl-up muscular fitness tests. The two participants with the highest BMIs and percent body fat levels were unable to perform the curl-up test and scored poorly on the push-up test. More research is necessary to determine if body fat percentage is related to muscle activation and/or muscle morphology, such as muscle volume and architecture (Tomlinson et al., 2016).

Obesity Indices. The relationship between abdominal fitness and obesity indicators among women in general is not well studied. A cross-sectional study of healthy men and women aged 18-30 found that women had lower abdominal strength due to differences in anatomical structure and higher body fat mass (Rasif & Wang, 2017). Findings from another cross-sectional study indicated that obesity has a significant negative impact on core muscular endurance among young adult men, regardless of which measure of obesity is assessed (Mayer et al., 2012). However, a prospective study comparing normal-weight women with PCOS (phenotype D) with women without PCOS and similar obesity indices revealed that the women with PCOS had lower muscle endurance than control group women. The researchers hypothesized that factors such as insulin resistance and visceral adiposity may damage muscle function in women with PCOS by slowing protein synthesis (Dogan & Caltekin, 2021).

Flexibility. Flexibility had a strong, negative relationship with HDL (R=-0.48, p=0.07). Research to date examining the metabolic impacts of yoga have revealed reduced LDL, but no significant effects on HDL (Azami et al., 2019). The positive association in this study may be due to the participants' higher HDL levels.

Physical Activity Level

Physical activity level was assessed using the 2018 Physical Activity Guidelines for Americans, which prescribes at least 150 minutes a week of moderate-to-vigorous aerobic exercise (Piercey et al., 2018). Physical activity level had strong, negative associations with BMI (R=-0.63, p=0.01), bodyfat percent (-0.72, p<0.01), waist-to-hip ratio (-0.47, p=0.08), and triglycerides (R=-0.47, p= 0.08).

Obesity Indices. The strong negative associations between physical activity level and obesity indices are consistent with the literature. Many studies reveal that performing regular aerobic exercise, especially of vigorous intensity, decreases BMI, body fat percentage, and waist-to-hip ratio over time (Cleven et al., 2020). Mario and colleagues (2017) found this to be specifically true among women with PCOS.

Triglycerides. Research findings reveal that triglycerides may decrease with physical activity, but as with body fat indicators, the physical activity must be regular and performed at higher intensities (Marandi et al., 2013).

Resistance Training Level

The performance of resistance training, as determined by RAPA, had a strong negative relationship with HDL (R=-0.46, p=0.08) and depressive symptoms (R=-0.49, 0.06) and a strong positive relationship with LDL (R=0.52, p=0.05). More research is needed because very few studies have examined the isolated use of resistance training to improve health outcomes among women with PCOS (Wright et al., 2021).

Lipid Panel. In a previous study, HDL and LDL were assessed after a three-arm parallel randomized trial comparing health outcomes after ten weeks of high intensity interval training, resistance training, or physical activity (aerobic). No significant changes were found among lipid panels from any group (Almenning, et al., 2015). These results are contrary to those found in this study; however, the women in this study who reported performing resistance training also reported performing aerobic exercise.

Depressive Symptoms. The findings from this study are consistent with a meta-analysis of 33 randomized control trials assessing the efficacy of resistance training on reducing depressive symptoms in the general population (Gordon et al., 2018). Additionally, two studies involving women with PCOS revealed significant reductions in depressive symptoms after resistance training programs lasting 8 to 32 weeks (Lara et al., 2015; Vizza et al, 2016).

In summary, assessing fitness indices has the potential to identify PCOS signs and symptoms among the PCOS phenotypes. Research evidence, although limited at this time, supports associations between fitness and health outcomes. The scientific literature includes evidence that every type of physical activity confers hormonal or metabolic benefit when performed regularly and at higher intensities. This study supports current research and adds associations between fitness parameters and health outcomes not yet explored.

This cross-sectional, exploratory study had several strengths. The participants provided confirmation of a PCOS diagnosis from a board-certified physician. Anthropometrics were precisely measured by trained professionals and body composition was determined with dual x-ray absorptiometry. The list of anthropometric, hormonal, and metabolic indices was not exhaustive, but representative and allowed exploration of the association between fitness profiles and health outcomes.

This study also had limitations. As a cross-sectional research design, the results do not indicate causality between fitness profiles and the participants' anthropometric characteristics, biomarkers, HRQoL, or depressive symptoms. The study enrolled a convenience sample and many of the participants were college students. As such, findings may not be generalizable to the PCOS population. The sample was small; however, there were several statistically significant associations between participants' fitness levels and their biopsychosocial characteristics. A glucose tolerance test was not included in this study due to cost and the well-researched and known feature of insulin resistance in most women with PCOS (Lim at al., 2018). However, SHBG levels were collected, which is a marker of insulin resistance, and consequently, a predictor of diabetes (Wallace et al., 2013). Lastly, information about medication use, specifically that of estrogen-based oral contraceptives, was not collected and may have confounded results including HDL.

Conclusion

PCOS is a chronic endocrinopathy among premenopausal women that significantly affects anthropometric, hormonal, and metabolic factors, as well as HRQoL and psychological well-being. The PCOS phenotypes confound diagnosis and treatment due to the heterogeneity of physical and biochemical presentation. However, the risk for comorbid conditions remains the same among all four phenotypes. Assessing fitness indices may help identify different health risks among PCOS phenotypes and the recommended type and intensity of physical activity to mediate these risks. Future studies should investigate the effect of different exercise approaches on fitness parameters, such as aerobic capacity and muscular endurance, and corresponding health outcomes.

CHAPTER 5

USING SELF-DETERMINATION THEORY TO EXPLORE PHYSICAL ACTIVITY MOTIVATIONAL STRATEGIES AMONG WOMEN WITH PCOS[1]

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1 Wright, P. J., Dawson, R M., Corbett, C. L., Pinto, B., & Wirth, M. D. 2021. To be submitted to *Health Education & Behavior Journal*

ABSTRACT

The first line treatment for women with polycystic ovary syndrome (PCOS) is exercise. However, evidence reveals that few practitioners advise this lifestyle behavior and fewer than 60% of women with PCOS are even regularly active. Participatory action research was employed to solicit the voices of women with PCOS regarding exercise barriers and motivational supports (people, services, technology, and/or behavioral change strategies) that may promote the initiation and maintenance of exercise in premenopausal women with PCOS. A Community Advisory Board (CAB) of seven women with PCOS was created and met virtually three times from June to July 2021 using the Zoom platform. CAB discussions were facilitated using theory-informed semi-structured focus group guides. Meeting transcripts were analyzed using low inference content analysis. Results revealed themes that aligned with the three innate psychological needs from the self-determination theory, with a fourth theme being motivational supports. The findings add new knowledge to both general and PCOS-specific barriers to exercise and community-chosen strategies that may help with the initiation and maintenance of exercise for symptom management and risk reduction of comorbid conditions.

Keywords (6): participatory action research, community advisory board, polycystic ovary syndrome, self-determination theory, motivation, physical activity

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrinological disorder among premenopausal women (Azziz, 2019). PCOS is associated with visceral adiposity, insulin resistance, dyslipidemia, and depressive symptoms, placing the women at risk for cardiovascular disease, diabetes, reproductive cancers (Meier, 2018), and depression (Cooney & Dokras, 2019). The scientific literature, both epidemiological and interventional, supports the benefits of regular physical activity, especially sustained moderate-to-vigorous intensity, to prevent or delay the onset of comorbid conditions (WHO, 2021). There is also strong evidence that regular physical activity reduces the risk of clinical depression and depressive symptoms among people without clinical depression (King et al., 2018). However, fewer than 60% of women with PCOS are regularly physically active and more than 25% are sedentary (Lamb, 2011). Hence, motivational underpinnings that facilitate adopting and sustaining the recommended physical activity to improve the health among women with PCOS are needed.

Motivation is defined as ‘a driving force(s) responsible for the initiation, persistence, direction, and vigor of goal-directed behavior’ (Oxford Dictionary of Psychology, 2014) and all aspects of intention and activation (Ryan & Deci, 2000). Motivation determines adoption and maintenance of healthy lifestyle behaviors, such as physical activity (Kwasnicka et al., 2016). Understanding PCOS-specific exercise barriers and potential motivational exercise supports is crucial toward developing relevant and sustainable interventions for women with PCOS. The purpose of this qualitative descriptive study was to explore exercise barriers and motivational supports (people, services, technology, and/or behavioral change strategies) that may hinder or promote exercise initiation and maintenance among women with PCOS.

Theoretical Framework

The science of behavior change increasingly emphasizes theory-based intervention approaches, as theories help identify underlying mechanisms of action and proximal intervention targets (i.e., mediators and moderators). Self-determination theory (SDT), introduced by Ryan and Deci (2000), is a metatheory of human motivation, personality development, and well-being. The underlying assumption is that humans are naturally inspired and self-determined but require social supports to develop and maintain their natural potential and well-being. SDT considers the intersection of personality and social context to predict the likelihood of adopting and maintaining physical activity behavior by predominantly focusing on a motivation taxonomy and three innate psychological needs.

Motivation (willingness and energy to enact a behavior) exists in three forms: 1) amotivation (relative lack of intention to engage in a behavior), 2) extrinsic motivation (external reward-driven behavior), and 3) intrinsic motivation (inherent satisfaction to perform a behavior). Extrinsic motivation comprises four categories (external regulation, introjected, identified regulation, and integrated), with each differing by type of external reward. For example, external regulation is performing a behavior to obtain an award or avoid a punishment; introjected regulation is performing a behavior to avoid a negative feeling, such as guilt. Identified regulation is performing a behavior to achieve an external outcome, such as weight loss, whereas integrated regulation is performing the behavior due to belief the behavior is helpful. The types of motivation exist on a continuum between self-determined and non-self-determined behaviors, representing the degree of internalization (Figure 5.1). “Internalization” is the process by which behaviors become more autonomously regulated over time.

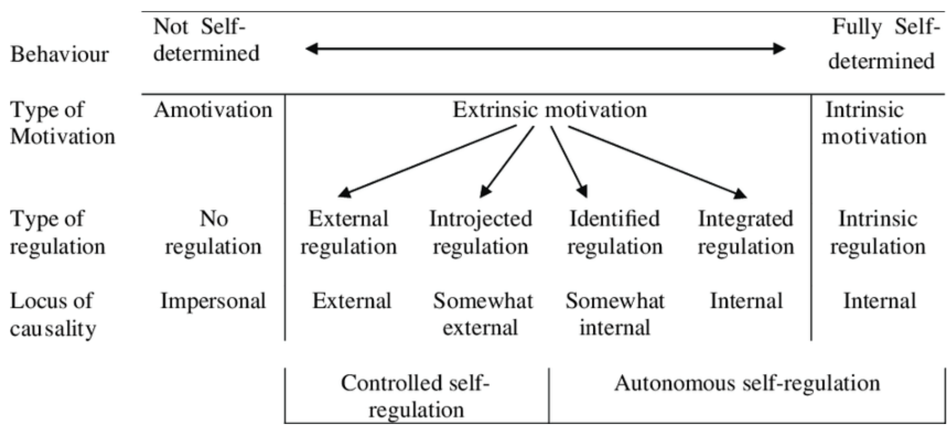

Figure 5.1

Self-determination continuum with motivational styles, loci of causality, and regulation processes as adapted from Deci and Ryan (2000) by Singer (2021)

Psychological need is an “energizing state that, if satisfied, conduces toward health and well-being but, if not satisfied, contributes to pathology and ill-being” (Deci & Ryan, 2000, p. 74). The three innate psychological needs are autonomy (freedom to choose a behavior), competence (ability to perform and master a behavior), and relatedness (sense of belonginess). According to SDT, satisfying these psychological needs leads to internalizing autonomous behaviors. Recently, researchers employing an SDT perspective found that self-determination and motivational orientation offered an appropriate framework to further understand physical activity behavior among those with a chronic condition (Fasczewski & Gill, 2018).

Materials and Methods

This study was conducted in June and July 2021 after approval by the University of South Carolina Institutional Review Board. First, a community advisory board (CAB) of women with PCOS was formed to engage members in an equitable, collaborative research process. CAB members were volunteers identified from prior PCOS studies and received a $20 gift card per meeting for their time and expertise. Meetings were conducted using SDT-informed, semi-structured focus group guides created by the first author (PJW), a master's prepared registered nurse, and the second author (RMD), a qualitative methodologist and nurse practitioner familiar with PCOS medical management. Focus group guides were specifically developed to meeting goals. For example, one goal was to identify competence with exercise by asking positive and negative exercise experience ("Tell me about a time that made you feel good about/less proficient at physical activity/exercise."). Meetings were conducted via Zoom, a cloud-based videoconferencing service offering the ability to communicate in real-time with members in different geographic locations via computer or mobile device. Zoom was chosen for its ability to securely video-record and store sessions and for security features including user-specific authentication and real-time meeting encryption. (Zoom Video Communications Inc., 2016). The CAB met three times for approximately one hour per meeting. Audio recordings were professionally transcribed and subsequently compared back to the audio to ensure that they represented the participants' discussion as accurately as possible.

Using low inference content analysis, two researchers (PJW and RMD) collaboratively reviewed the transcripts and used an iterative process of comparative analysis to reach consensus on a coding scheme. The process of data reduction used open and axial coding followed by the identification of emergent themes. Using the SDT framework, themes were categorized by the three psychological needs and motivational strategies. To strengthen rigor and attend to reflexivity, the two researchers met regularly to discuss personal experiences and knowledge of both PCOS and exercise in relation to the CAB members' statements.

Results

CAB members (n=7) were 33.9 (± 8.1) years of age, mostly White (71%), married (86%), and employed full-time (86%). Characteristics of the CAB are listed in Table 5.1.

Table 5.1

Descriptive statistics of the CAB members

Variable	Mean ± SD or Frequency (%)
Age	33.9 ± 8.1
Race	
African American/Black	14% (1)
Hispanic	14% (1)
White	71% (5)
Educational Attainment	
Some College	43% (3)
Bachelors	43% (3)
Masters	14% (1)
Employment Status	
Part-Time	14% (1)
Full-Time	86% (6)
Medical Insurance	100%
Marital Status	
Single	14% (1)
Married/Partnership	86% (6)
# Children	1.6 ± 1.6
# Comorbid Conditions	1.0 ± 1.4

Emergent themes aligned with the three innate psychological needs (i.e., autonomy, competence, and relatedness) as described by Ryan and Deci (2000) and motivational supports. Quotes illustrating the themes are presented as stated by CAB members, without any editorial changes.

Autonomy: *" … and it was something else that hindered me …."*

Autonomy is the volitional choice and control of one's behavior. Autonomy can be affected by internal and external factors. The women juggled multiple roles (e.g., spouse, mother, daughter, friend, employee, student, and patient), all which demanded daily and competing time commitments. As a result, the women felt a loss of control in their ability to schedule time for exercise: *"My barrier is time."*

"Other barriers, children, family, school, blah, blah, blah, blah get in the way."'

"… my biggest struggle is making the time and making that a priority over other things."

As women who "*struggle*" with PCOS, some women expressed being *"robbed"* of choice due to comorbid conditions, such as vitamin deficiencies, hidradenitis suppurativa (a chronic skin condition causing painful abscesses and scarring), and depression.

"…other factors that go with PCOS that impede physical activity. Hidradenitis suppurativa is one of those factors. So the sweat glands may become clogged, they break out into boils and they have to be surgically removed. So the more you sweat, the more there's pain."

"… it (PCOS) was affecting me mentally … so like depression and just like … hopelessness. Um, so, you know, I never exercised."

Androgen excess is a feature of PCOS and can result in obesity, hirsutism, and acne. Several women expressed feeling "*unattractive*" and would therefore avoid exercise in public places. The women expressed that their appearance also *"robbed"* them of choice.

"… you hate your body and you feel fat all the time …."

"The hag hairs are terrible."

A final barrier to full autonomous choice of exercise was facility costs and location.

"… and the next closest one (gym) is 30 minutes away …."

"And so there's also the monetary component to it as well."

Competence: *" … it (lack of weight loss) crushed my spirit. And, ever since then, I haven't tried to do anything."*

Competence involves the sense of mastery and self-efficacy of one's behavior, as well as the need to feel effective when performing that behavior. A person will more likely accomplish a task or meet a goal when feeling capable of successfully performing the related activities, or when the task results in the expected outcome.

"… it gave me a sense of accomplishment."

"…it's (the body) working correctly and everything's going great and you're powerful, I think that's the most rewarding thing about it."

However, when one feels ineffective, incompetent, or unable to accomplish a task or goal, the effort may seem meaningless (Steger et al., 2009).

"… so I will not do a group because I have no rhythm. I can't do anything like that."

"It's depressing when you don't see your results, you don't want to try anymore."

Relatedness: "*We are in it together.*"

Relatedness is the interpersonal dimension, reflecting the extent to which a person feels connected to others, has caring relationships, and belongs to a community. Several studies (correlational, longitudinal, and experimental) revealed a strong positive correlation between sense of belonging and meaningfulness (Lambert et al., 2013). The CAB members agreed.

"… and I can't do it on my own."

"… just like family in general or anyone who will just go on that journey with you …."

"… just someone who understands what you're going through and who is someone who is also knowledgeable about PCOS."

Motivational Supports: *"I've, like everybody, tried all kinds of different things and I've liked some and I've not liked some."*

The CAB members listed supports (people, services, technology, and behavioral change strategies) with potential to promote and sustain exercise as a healthy lifestyle behavior. CAB members presented advantages and disadvantages of each in relation to general and PCOS-specific exercise barriers (Table 5.2).

Discussion

All CAB members described exercise motivation by extrinsic factors. No member represented extremes on the continuum, neither amotivation nor fully self-determined intrinsic motivation. According to SDT, different forms of regulation can coexist for the same behavior and may vacillate over time and across contexts (Ryan & Deci, 2000). A strength of SDT is the inclusion of motivational forces within a socioenvironmental

Table 5.2

Motivation support types, strategies, advantages, and disadvantages as discussed by the CAB

MOTIVATIONAL SUPPORT TYPE	STRATEGY	ADVANTAGES	DISADVANTAGES	EXEMPLAR QUOTE
People	"Accountability Buddy"	Personal connection Fun	Availability	"…someone to guide you through, to say don't give up, don't sit on that couch."
	Coach	Personal connection Performance-based feedback Progression Tailored programs	Mismatch of personalities Cookie cutter programs Lack of PCOS knowledge	"A coach keeps me accountable."
	Community Support Group	Empathy Knowledge Ideas	Difficult to find	"…I'm learning new things about PCOS from other people across the world who have found things that work for them …."
	Family	Promotes health for all Fun	Not interested Different schedules	"And if you get the family into it, I mean, of course our kids, it's fun and they see us and it's a family activity …."
Services	Group Training	Fun Competition	Lost in crowd Not tailored to ability Self-conscious Self-efficacy	" … no, I do not have the self-confidence to be able to do a (aerobics) group like that."
	Personal Training	Personal connection Tailored program	Cost Lack of PCOS knowledge	"…finding trainers who understand and will be your companion during it, be a teammate with you while you're going through your journey …."

	Physician Guidance & Support	Trust	Sole focus on weight loss	"So, I will definitely go to the doctor first."
Technology	Digital Products • Applications • Videos • Podcasts • Websites	Convenient Leveled Educational	Easy to ignore Cost Eventual boredom Technology upgrades	"I started using (an app)… for free. And I found a coach which is like a counselor too and another group of people who we bounce ideas off each other and support each other."
	Wearables • Pedometer • Watches	Competition with self & others Can be more holistically health-focused	"Obsession with numbers" Promote "guilt"	"… athletic watches, whether you're trying to fill a ring or keep track of the amount of steps you're taking, can really be a useful tool."
Behavioral Change Strategies	Goal Setting	Provides reason Provides focus Measurable	Setting wrong goal Unrealistic expectations	"I think it can be very hard to keep striving for the extra goals and to keep setting goals."
	Incentives	Fun	Short-lived	"So, at some point, I'd probably be like, 'Okay, I don't care anymore.'"
	Motivational Pictures	Inspirational	Unrealistic	"…because when you look at magazines, they're going to show you the skinny models, not what real people look like …."
	Environmental Change	Flexible Tailor to comorbid conditions	Weather Access	"… I can hike down here in the fall and wintertime and not be as miserable sweaty …."

context. Ryan and Deci (2000) further explained that social-contextual conditions can facilitate ("help flourish") or forestall ("thwart") natural processes of self-motivation and healthy psychological development. Examples mentioned by CAB members included the birth of a long-awaited baby and a shift change at work, both which altered the value placed on exercise, thus shifting self-regulation of that behavior.

Intrinsically motivated behaviors, the prototype of self-determined actions, stem from the self. However, SDT recognizes that extrinsically motivated actions can become self-determined as individuals identify with and fully assimilate their regulation. It is through internalization that individuals can be extrinsically motivated and still be committed. Barriers to healthy lifestyle behaviors, such as physical activity, have been cited to undermine or cause failure of internalization of autonomous self-regulation (Ryan & Deci, 2000). Accumulated research now suggests that internalization and commitment to long-term self-regulation is most likely evident when individuals experience supports for competence, autonomy, and relatedness (Kim et al., 2017; Tiexeria et al., 2012; Ryan & Deci, 2000).

Autonomy

All CAB members acknowledged the multiple health benefits of physical activity. However, all members reported being insufficiently active. Members expressed that volitional choice to exercise *"takes a backseat"* to other priorities, as *"life just got in the way."* The concept of little to no discretionary time to participate in activities that build social and human capital is referred to as time poverty (Whillans, 2020). Ironically, time poverty forces individuals to compromise by encouraging unhealthy behaviors, (e.g., buying fast food) which creates a cyclic pattern of defeat or learned helplessness (Odabasi, 2013). Whillans (2020) debates that time poverty is not necessarily a mismatch between responsibilities and available hours, but a mental outlook on the value of those hours; time poverty is both psychological and structural. Whillans (2020) expounds by providing creative ways to "fund time." Each strategy involves changing perspective of the value of time; give time a financial equivalent and then budget time and money together.

These women described responsibilities beyond the traditional definition of paid employment. These women detailed activities of childrearing, caregiving for aging parents, and other family obligations in addition to traditional paid employment. Women in developed and developing nations spend an average of 2 and 3.4 times more hours per day as men on unpaid work respectively, shouldering the heaviest burden of cooking, cleaning, and caring for children and the elderly (Division UNS, 2015). This inequitable gender-based allocation of unpaid domestic work, representing "double-duty" for women who enter the workforce, often limits discretionary time for women (Hyde et al., 2020) and promotes self-neglect (Ranji et al., 2018). This finding is not unique to women with PCOS; however, previous qualitative work found that women with PCOS more strongly adhere to cultural female gender roles to reclaim a feminine identity (Nasiri-Amiri et al., 2014; Kitzinger & Willmott, 2002).

The systemic oppression of women via gender inequality is accompanied by restrictive gender norms dictating societal female expectations (Hyde et al., 2020). This includes the gender-specific ideals permeated about a woman's presentation (Messias et al., 1997) and gender performativity (Butler, 1988). The CAB frequently mentioned hirsutism and obesity and placed emphasis on being "*hairless*" and "*skinny*," as several compared themselves to *"normal"* women. Pfister and Romer (2017) found similar results when they interviewed Danish women with PCOS, all who perceived their bodies as different from femininity norms. Negative self-evaluation of bodyweight and shape can lead to low self-esteem, depressive symptoms, and social phobia (Weinberger et al, 2016). In an observational study by More and Phillips (2019), body dissatisfaction led to less autonomous regulation among women, which led to less frequent physical activity.

Lastly, several of the women reported lack of autonomy due to physical and mental limitations imposed by PCOS. Physical limitations included common sequelae among some women with PCOS. However, some conditions could be circumvented by choosing alternate forms of exercise. For example, one member was prone to hidradenitis suppurativa (inflamed and infected sweat glands), necessitating avoidance of hot environments and excessive perspiration. An alternative form of exercise could be swimming or water aerobics.

Depression was cited several times as an exercise barrier, which research has revealed as a prevalent exercise barrier (Firth et al., 2016). Although recent meta-analyses indicate that exercise can significantly improve psychological well-being among people with depression (Rosenbaum et al., 2014), the women lacked energy to initiate exercise. Screening for depressive symptoms and providing resources may be an essential first step before prescribing exercise as therapeutic management. Longitudinal studies assessing physical activity and subjective well-being have shown that greater well-being predicts maintained or increased activity over time (Kim et al., 2017), and that changes in leisure-time physical activity predict changes in happiness (Wang et al., 2014).

Competence

CAB members cited weight loss as the most salient reason to both start and stop an exercise regimen. Weight loss was prioritized based on body dissatisfaction and physician advice. Studies do reveal that losing 5% to 10% of body weight improves metabolic health and substantially reduces the risks of cardiovascular disease, diabetes, and cancer (Jensen et al., 2015). However, accurate information about the role of physical activity for weight loss and emphasis on the right kind of weight (i.e., fat weight versus lean muscle weight) are often missing from clinical guidance. Physical activity alone will not produce quick weight loss (Haskell et al., 2007). Physical activity enhances the ability to lose weight over time, but mostly confers metabolic benefits (McPherron et al., 2013; Fuzeki et al., 2017).

CAB members relayed clinical encounters and public health messaging that issued absent or confusing directives for weight loss. Accurate and specific guidance about realistic goal expectations increases knowledge and builds self-efficacy. Proper goal setting and positive experiences are essential toward facilitating perceived competence. Reframing goal expectations can promote physical activity participation and maintenance, as the women can seek and measure different health outcomes, such as improved endurance, increased strength, additional energy, and sense of accomplishment.

Patients rely on physicians to provide appropriate information and competent care. An effective strategy to increase physical activity among patients could be an exercise prescription issued by the practitioner (Garret et al., 2011). The "Exercise is Medicine" initiative was launched by the American College of Sports Medicine in 2007 to encourage primary care practitioners to prescribe exercise as part of the treatment plan (Lobelo et al., 2014). However, physicians report barriers to implementing exercise prescriptions as lack of clinical time, limited education about exercise dosing (Gagliardi et al., 2015), and the absence of a counseling protocol (O'Brien et al., 2016).

Positive and informative feedback increases perceived competence (Ryan & Deci, 2000). Practitioners are in a unique position to foster competence by recognizing and reinforcing healthy behaviors and related health outcomes, such as an optimal blood pressure. The "Exercise is Medicine" initiative has proposed using physical activity level as a vital sign (Bowen et al., 2019). Assessing physical activity at clinic visits reframes its value to practitioners, encourages physical activity counseling and discussion of positive exercise outcome expectations, and confirms the patients' knowledge and efforts.

Relatedness

Humans are social beings and strive for connectedness with others. A social support system helps individuals feel understood and accepted. CAB members emphasized the need to "*be understood*" in the context of the "*struggle*" with PCOS. The social support network could be one or many people, known or unknown. Consistent with a series of experiments designed to examine types of social connection, people are motivated to perform a task based on “being understood” or “mere belonging,” which is independent of casual acquaintance versus longstanding relationships with family or friends (Walton et al., 2012). As CAB members discussed, a motivational support could be anyone or group if PCOS was either understood or experiential.

Motivational Supports

According to SDT, motivational supports include conditions that nurture versus inhibit internalization (Ryan & Deci, 2000). As barriers challenge levels of motivation, different forms of regulation must coexist for the same health behavior; these may vacillate over time and across contexts (Ryan & Deci, 2000). Keeping with the ancient Greek inscription, “know thyself,” self-awareness is critical while traversing the dynamic life course. Behavioral self-regulation is the capacity to assess cognitive, affective, and/or behavioral responses to daily life in context of a larger goal and adapt (Weidner et al., 2016). Thus, motivational strategies may need to change or be used in combination to match life demands. The capacity to self-regulate and appropriately choose alternative motivational strategies are skills that could be taught to help promote and maintain physical activity.

SDT posits that people experience more self-determined motivation types when activities make them feel autonomous, competent, and related. Self-determined motivation types are preferred given the association with more positive experiences and behavior maintenance. Findings from this study supported SDT and emphasized that social context can serve to nurture or undermine human behavior. As such, assessing and serving individual needs while addressing the social environment is necessary before initiating a physical activity intervention. For example, as women with PCOS are eight times more likely to have depression than women without PCOS (Fauser et al., 2011), a pre-exercise screening to address depressive symptoms may be beneficial. Clinical encounters could offer this assessment and promote psychological autonomous motivation via brief physical activity counseling. More in-depth discussions and additional resources may be provided by other clinical team members. During follow-up visits, the clinical team could incorporate the physical activity vital sign as instructional feedback and reinforcement.

The women with PCOS detailed many competing time commitments. Although this is probably true for many people, these women desired strategies to best incorporate physical activity given both life-demands (e.g., family) and PCOS-specific needs (e.g., grooming rituals, physical comorbidities). An efficacious intervention could include education and skill-building for choosing alternative physical activity types and settings that circumvent exercise barriers.

Lastly, CAB members strongly emphasized the need to "*be understood*." The women stated that any motivational strategy should include someone or a group that either possessed a formal education of PCOS or experiential knowledge of PCOS. Motivational supports could include a peer coach and/or a community support group to provide accountability, encouragement, and/or coping strategies and suggestions.

Strengths and Limitations

This study offered several strengths. As participatory action research, the study included the voice of women with PCOS throughout the research process. The approach was especially appropriate as the study was informed by SDT and specifically addressed the psychological needs of autonomy, competence, and relatedness.

Due to COVID-19, CAB meetings were held virtually. This was a strength as women from different geographic locations participated. The virtual platform was convenient and cost-effective, while providing an easier and more secure way to record and transcribe sessions. However, one meeting was interrupted with technical challenges of a dropped call and pauses due to poor connectivity.

PCOS is a chronic health condition that requires life-long symptom management. Physical activity, a first-line treatment, requires motivation for behavioral self-regulation. The purpose of this qualitative study was to discuss exercise barriers and identify motivational supports (people, services, technology, and/or behavioral change strategies) that may promote the initiation and maintenance of exercise among women with PCOS. As informed by SDT, a participatory action research approach was chosen to promote autonomy among the members, capitalize on their experiential competence, and foster a sense of relatedness within the group. Additionally, SDT was the lens through which discussions were created and data analyzed. Internalization of self-determined motivation should be approached by considering each of the three innate psychological needs (Ryan & Deci, 2000). A physical activity intervention for women with PCOS must offer choice (autonomy) by eliciting perspectives and providing a menu of options tailored to the individual’s ability (competence) and empathetically (relatedness) delivered with positive and informative feedback. This approach requires that women with PCOS possess self-awareness and the knowledge and skill necessary to adapt accordingly. Further research is necessary to use these PCOS-specific and theory-informed findings to develop efficacious, easily disseminated, and innovative physical activity interventions.

CHAPTER 6

CONCLUSIONS AND RECOMMENDATIONS

Polycystic ovary syndrome (PCOS) is the most common endocrinopathy among premenopausal women with an estimated prevalence of 15-21% (Greenwood et al., 2018; Blagojevic et al., 2017; Brakta et al., 2017). PCOS signs and symptoms can include infertility, oligomenorrhea, hirsutism, acne, and fatigue, placing women with PCOS at increased risk for cardiovascular disease, diabetes, certain reproductive cancers, and depression (Legro et al., 2013; Cooney et al., 2017). Current Endocrine Society Clinical Practice Guidelines recommend exercise as first-line treatment for premenopausal women with PCOS given the known benefits of exercise, such as improved insulin sensitivity. However, less than 60% of all women with PCOS are physically active and more than 25% are sedentary (Lamb, 2011).

Initiating and sustaining behavior change, such as adding regular physical activity or exercise, is challenging and requires more research. Understanding exercise outcome expectations and perceived exercise barriers and facilitators may provide insight into mechanisms that affect behavior change. In addition, PCOS-specific factors may necessitate a different approach to behavior change as compared to approaches used with the general population. Thus, the overall objective of this dissertation was to gain knowledge to begin developing exercise interventions for women with PCOS. Multiple methods were used to investigate three specific aims: 1) Explore the relationships among biopsychosocial characteristics, self-reported exercise, exercise outcome expectations, and potential barriers and facilitators to exercise among premenopausal women with PCOS; 2) Explore the relationships among hormonal concentrations, lipid profiles, anthropometric attributes, and fitness levels of premenopausal women with PCOS; and 3) Identify supports (people, services, technology, and/or behavioral change strategies) that may promote initiation and maintenance of exercise in premenopausal women with PCOS.

CONCLUSIONS

Aim 1

Aim 1 involved an online survey of several questionnaires. The findings revealed that respondents (n = 935) reported low health-related quality-of-life (HRQoL), greater exercise barriers than benefits, neutral exercise outcome expectations, and high depressive symptoms. Statistically significant predictive relationships were found between each variable and HRQoL, with depressive symptoms having the strongest influence on HRQoL. Results indicated that women with PCOS and high depressive symptoms scores were three times more likely to have reduced HRQoL than women with PCOS and low depressive symptoms scores.

Aim 2

Aim 2 included assessments for anthropometric data (height, weight, and body composition), laboratory values (free and total testosterone, sex hormone binding globulin, and lipid panel), and fitness (aerobic capacity, muscular endurance, and flexibility). The following statistically significant and strong associations were found: 1)

VO_2 max with percent bodyfat, sex hormone binding globulin, health-related quality of life, and depressive symptoms, 2) abdominal strength with BMI, percent bodyfat, and HDL, 3) overall physical activity level and percent bodyfat, and 4) resistance training with LDL. The results indicated that fitness indices are linked to health indicators among women with PCOS.

Aim 3

Aim 3 involved a community advisory board of seven women with PCOS who met on 3 occasions to discuss exercise barriers and motivational supports (people, services, technology, and/or behavioral change strategies) that may promote exercise initiation and maintenance. The findings revealed themes that aligned with the innate psychological needs described in the self-determination theory (SDT) (autonomy, competence, and relatedness) and motivational strategies based on motivation types. However, barriers such as stigma-related stress, low self-esteem, depression, lack of social support, daily competing time demands, and a dynamic socioenvironmental context challenged internalization of self-regulation. Lastly, the women reported a need to be understood given the unique challenges they encounter due to PCOS.

IMPLICATIONS

Aim 1 results suggest that promoting exercise outcome expectations and benefits, overcoming exercise barriers, and managing depressive symptoms are important foci in future efforts to improve HRQoL among women with PCOS and to promote physical activity behavior. Given the crucial impact of depressive symptoms on self-management, psychological wellbeing must be considered before and during an exercise intervention. Thus, depressive screening needs to precede an exercise intervention to identify those who may have depression and address this concern by providing the appropriate resources.

Healthcare providers, physicians and nurses, are in position to promote positive exercise outcome expectations among their patients with PCOS by educating them about the many physical and biochemical benefits associated with types and dose of exercise. Healthcare providers are a trusted source of information, and patients may respond to their guidance (Lobelo & de Quevedo, 2013). One barrier to this practice is low level of knowledge on basic physical activity guidelines for health and the lack of training on simple exercise prescriptions among healthcare providers (Lobelo & de Quevedo, 2013). Thus, healthcare providers need more education about the role of exercise as therapeutic management.

Aim 2 findings provide preliminary evidence that fitness profiling may help identify individual health risks among the four phenotypes of PCOS. The PCOS phenotypes exist due to the various combinations of the diagnostic criteria, which specify that women must have two or three of the following: hyperandrogenism, menstrual irregularities, and/or polycystic ovaries. Therefore, phenotypes present differently such that one woman may have high testosterone levels and another woman diagnosed with PCOS may not.

Aim 3 results suggests that motivational exercise supports can be determined after consideration of general (e.g., time commitment) and PCOS-specific (e.g., grooming rituals and stigma-related stress) barriers, psychological needs, and an individual's socioenvironmental context. This study lends evidence that an exercise intervention for women with PCOS must offer choice (autonomy) by eliciting perspectives and providing a menu of options tailored to the individual's ability (competence). The findings also revealed that exercise interventions must be empathetically (relatedness) delivered with positive and informative feedback. A structured support system may be necessary as women with PCOS expressed need to connect with others that understand PCOS experientially or by formal education. The women expressed that a knowledgeable support system offered encouragement and accountability.

Implications from these studies indicate that women with PCOS would benefit from a multidisciplinary team approach, as healthcare providers (practitioners and nurses), public health professionals, and counselors to facilitate exercise as a therapeutic management strategy. However, more awareness of and knowledge about PCOS and exercise as therapeutic management is needed among healthcare professionals to accomplish: 1) quicker diagnosis and more effective treatment, 2) promotion of and education about exercise, 3) clinical follow-up that reinforces the importance of exercise, and 4) appropriate referrals to other team members and to community-based exercise programs as appropriate. Healthcare practitioners could prescribe exercise as a component of the treatment plan and incorporate the "physical activity as a vital sign" formula to reassess the patient and reinforce the physical activity behavior each visit. These tools were included in the "Exercise is Medicine" initiative launched by the American College of Sports Medicine in 2007 (Lobelo et al., 2014).

FUTURE RESEARCH

The knowledge gained from the studies in this dissertation will inform future studies and interventions. Research is needed to test theory-informed exercise interventions to evaluate the effects of exercise on HRQoL, manage depressive symptoms among women with PCOS, and discern effective motivational strategies for exercise initiation and maintenance.

Although PCOS represents four different phenotypes, the risk for other co-morbid conditions, such as cardiovascular disease and diabetes, remains constant. Research with larger sample sizes is necessary to determine if fitness profiling can identify individual health risks across the PCOS phenotypes and be used to tailor exercise interventions that improve PCOS-specific health outcomes.

Further research is also needed to identify the optimal type of exercise for therapeutic management, which may also provide insight about the pathophysiology of PCOS. However, ultimately, the type of exercise will depend on individual preference. Therefore, further research is critical toward identifying the minimum dose of the different types of exercise to attain symptom management among women with PCOS.

Lastly, research is necessary to test the feasibility of incorporating physical activity prescriptions and physical activity as a clinical vital sign into healthcare delivery. If feasible, research will be needed to test the effectiveness of this strategy toward promoting the initiation and maintenance of physical activity.

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