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# The Influence of Polycystic Ovary Syndrome (PCOS) and Other Related Factors upon Health-Related Quality of Life in Women of Reproductive Age: A Case-Control Study

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#### ABSTRACT

This study aimed to assess the impact of a polycystic ovary syndrome (PCOS) diagnosis and other factors on health-related quality of life (HRQoL) in women of reproductive age. Online questionnaires were completed and study groups compared. Potential causal relationships were evaluated using path analysis. Analyses revealed that a PCOS diagnosis alongside BMI had the largest effect on HRQoL. Higher levels of physical activity (PA) were not associated with greater HRQoL, and PA was not directly affected by any other outcome. However, reduced selfesteem was identified as a key factor in the promotion of physical and mental health.

**ARTICLE HISTORY** 

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#### **KEYWORDS**

Physical activity; women's health; mental health; physical health; path analysis; self-esteem; polycystic ovary syndrome; PCOS

## Introduction

Polycystic ovary syndrome (PCOS) is the most frequent endocrine disorder in women of reproductive age (ESHRE & ASRM Group, 2004), affecting up to 21% of this population depending on the applied diagnostic criteria and the studied cohort (Boyle et al., 2012). Women with PCOS typically have hyperandrogenaemia, menstrual irregularity, and/or polycystic ovaries (PCO) (Kyritsi et al., 2017; Lizneva et al., 2016). Furthermore, most

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women with PCOS exhibit metabolic (e.g., overweight/obesity, or insulin resistance) (Hutchison et al., 2011; Li et al., 2019; Lim et al., 2012; Shirazi et al., 2021) and/or psychological (e.g., anxiety and depression) (Karjula et al., 2017; Tay et al., 2019) comorbidities. Overall, the health burden of PCOS impacts adversely upon health-related quality of life (HRQoL) (Moghadam et al., 2018), an important outcome in the context of chronic disease treatment and management (Dokras et al., 2018), relating to patient-reported physical, social, and emotional well-being (Colwell et al., 2010). Indeed, consistently lower HRQoL has been noted in women with PCOS when compared with data from healthy populations (Asdaq et al., 2020; Panico et al., 2017; Sánchez-Ferrer et al., 2020), or those with other chronic diseases (Coffey et al., 2006; Naumova et al., 2021).

The physical benefits of increasing physical activity (PA) levels have been widely reported across a range of populations (Warburton & Bredin, 2017), including PCOS (Kite et al., 2019, 2022). Moreover, increased PA or engagement with exercise regimes may also improve HRQoL, particularly in those with chronic diseases, such as cancer (Fuller et al., 2018), chronic respiratory conditions (Eichenberger et al., 2013), and rheumatoid arthritis or osteoarthritis (Kelley et al., 2015). Interestingly, most of the studies that have compared the PA levels of women with PCOS against healthy controls reported that despite poorer physical and mental health in women with PCOS, there were no statistical differences in energy expenditure between these groups (Mario et al., 2012; Rodino et al., 2016; Wang et al., 2021). However, despite the high prevalence of PCOS, there is still limited evidence about the potential mediating role of PA in the physical and psychological manifestations of PCOS.

Accordingly, the objectives of the current study were to identify whether there are differences in HRQoL between women with PCOS and a healthy control group, and to explore whether higher levels of PA facilitate improved HRQoL. Furthermore, this study aimed to estimate any potential simultaneous impact of not only a PCOS diagnosis but also of other predictive factors (i.e., PA and its determinants, body mass index [BMI], self-esteem) upon the mental and physical domains of HRQoL.

#### **Material and Methods**

Ethical approval was granted by the Aston University Ethics Committee (project number: 1442). Recruitment of reproductive-aged (18–45 years) women with PCOS (selfreported diagnosis) and controls (self-reported being free from any chronic condition) took place between January 9 and May 9, 2019, via advertisements on social media, through PCOS support groups, and in online forums hosted by Verity, the UK-based PCOS charity. Using snowball sampling, potential respondents were encouraged to share the study advert within their networks to anyone they thought may be eligible/ interested to participate.

#### **Study Questionnaires**

A range of questionnaires were used to collect the study data. All study questionnaires were completed online using the survey software, Qualtrics<sup>®</sup> XM (Qualtrics XM, Provo, Utah, USA) which was accessed through a study URL link.

Each participant completed a study-specific questionnaire to ascertain sociodemographic and anthropometric data, including self-reported age, height (m) and weight (kg), BMI (kg/m<sup>2</sup>), and waist circumference (cm). Furthermore, participants were asked if they had ever been diagnosed with PCOS; if they responded affirmatively, they were asked to specify the time since diagnosis and to identify the specific PCOS phenotype associated with their diagnosis (PCO, menstrual disruption, and excess androgens; PCO and menstrual disruption; PCO and excess androgens; or menstrual disruption and excess androgens; or alternatively answer as "do not know"). Questions about participant ethnicity, marital status, occupational status, education level, whether they have children, and their approximate household income were also included.

HRQoL was assessed by the validated 12-item Short Form (SF-12v2) Health Survey (Ware et al., 1996) which provides eight health scales (physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health), as well as physical and mental component summary scores. Values for each scale are calculated by transforming raw scores into norm-based scores (Gandek et al., 1998). For the path analysis performed for this study, the raw individual mental and physical health scores were combined to give an overall composite score for quality of life (Ware et al., 1994). Whilst not commonplace, this approach was taken due to a high degree of correlation between domain and composite scores (Table A1) and for simplification of the path analysis model.

Participants in the PCOS study group were also given a PCOS-specific questionnaire, i.e., the PCOS-Q. The PCOS-Q is a 26-item questionnaire that was developed to assess the impact of PCOS symptoms, and their associated treatments, across five domains, each related to a common symptom of PCOS (Cronin et al., 1998), i.e., emotions, body hair, body weight, infertility, and menstrual problems. Participants respond to each of the 26 items on the PCOS-Q by selecting an answer on a 1–7 scale; seven is representative of optimal function and one the poorest function. Each item is weighted equally when scored, meaning that each domain is presented as a score out of seven regardless of the number of items.

Self-reported PA was assessed via the International Physical Activity Questionnaire Long Form (IPAQ-LF) (Hagströmer et al., 2006), which asks participants to recall their last seven days of PA and is widely used in clinical settings and PA research. Summation of self-reported PA duration, multiplied by weekly frequency and normative Metabolic Equivalent of Task (MET) data (Ainsworth et al., 2011) provides continuous data reported as MET-min/wk and categorical data based upon low, moderate, or high levels of PA.

The Self-Efficacy for Exercise Scale, a 9-item questionnaire, was used to measure selfefficacy barriers to exercise (Resnick & Jenkins, 2000) and to assess perceived motivational barriers to completion of PA. For this scale, participants are tasked with scoring from 0 to 10 (*not confident*: 0; *very confident*: 10) how confident they are that they could exercise for 20 minutes, three times per week, given a variety of situations. The total score of this scale is calculated by summing the responses to each question (possible scoring range: 0–90), with a higher score indicating higher self-efficacy for exercise.

In addition, the Exercise Benefits/Barriers Scale was used to broadly measure participants' perceived benefits and barriers to participation in exercise (Sechrist et al., 1987). This scale requires respondents to rate their agreement with 43 statements (benefit items: 29; barrier items: 14) using a 4-point Likert scale. Answers are scored from 1 to 4 👄 C. KITE ET AL.

4 (*strongly disagree*: 1; *strongly agree*: 4), with the 14 barrier items being reverse scored. Total scores range from 43 to 172, with a lower score indicative of fewer perceived benefits and greater perceived barriers.

Finally, self-esteem was measured using the Rosenberg Self-Esteem Scale (Rosenberg, 1965), which utilizes a 4-point Likert scale allowing participants to respond to 10 statements about themselves (a higher score indicates a greater level of self-esteem).

### **Statistical Analysis**

All study questionnaires were scored according to their individual criteria, and data were collated in Excel (Microsoft Excel v16.04849.1000; Microsoft Corporation, Washington, USA). Statistical analysis was completed in jamovi (the jamovi project, v.1.6) and in IBM SPSS Amos (IBM SPSS Amos, v.25.0.0, Amos Development Corporation, PA, USA).

Due to the sample size ( $\geq 20$ ), the Shapiro-Wilk test of normality was completed on each variable, separated by group, and Q-Q plots were visually inspected; where data were non-normally distributed, median and interquartile range (IQR) were reported and Mann-Whitney U tests were completed to highlight between-group differences. Between group median difference, effect size (Cohen's *d*), 95% confidence intervals (CIs) and statistical significance values (*p*) were reported for all non-parametric outcomes. Where data were normally distributed, mean ± standard deviation (SD) were reported, and Welch's *t*-test was used (Delacre et al., 2017). In these analyses, pairwise exclusion was used to deal with missing values.

Due to the prevalence of nonparametric variables, Kendall's rank correlation  $(\tau_b)$  was chosen to measure the strength of association between two variables. Where variables were highly correlated and deemed to be reporting similar effects (e.g., body mass, BMI, and waist circumference), the variable with the largest sample size was retained. Where these variables were domains from a questionnaire (e.g., mental and physical domains of the SF-12v2), the aggregated score was used as the variable in the regression.

A separate analysis was completed on the domain scores from the PCOS-Q. Because these data were nonparametric, median difference (MD) and IQR were calculated between domains and a Durbin-Conover pairwise comparison was used to identify statistical differences.

In order to generate a complete data set for the path analysis of this study, full information maximum likelihood (FIML) regression imputation was used to account for missing data. Although pairwise or listwise deletion are commonly used, FIML was regarded as more favorable to preserve the sample size, whilst FIML also provides data estimates that are unbiased and more efficient than other methods (Enders & Bandalos, 2001). Moreover, the composite HRQoL score was used as the endogenous variable and the remaining variables were arranged into a path model to indicate causal relationships between the exogenous (diagnosis of PCOS, and BMI), mediating (self-efficacy for exercise, self-esteem, perceived benefits/barriers of exercise, and MET-min/wk) and endogenous variables. The decision to use the composite HRQoL score was taken since the effect of the exogenous and mediating variables upon HRQoL varied little when individual domain scores, or indeed the composite score, were inputted into the path model. Collapsing the two domain scores into a single measure for HRQoL simplified the path model whilst retaining meaning.

#### Results

#### **Participant Characteristics**

In total, 194 participants accessed the online surveys and consented to participate (Figure 1). Based upon the exclusion criteria, 40 participants were deemed ineligible due to reporting one or more chronic conditions other than PCOS. Of the remaining 154 participants, 24 were deemed to have provided insufficient data to warrant inclusion in the analysis. As such, 130 eligible participants were included in the two study groups (PCOS: 64; controls: 66). Regarding the self-reported phenotype of the women with PCOS, the majority (52%) self-reported as having excess androgens, menstrual dysfunction, and PCO, whilst 17% were unsure of the phenotype for their PCOS diagnosis.

Certain demographic differences exist between the groups, with  $\sim$ 63% of women with children being in the control group (Table 1). Women in the control group also tended to be educated to a higher level and have a greater household income than their counterparts. Furthermore, a larger number of women in the control group selfreported that they were currently a student. Whilst there were no statistically significant

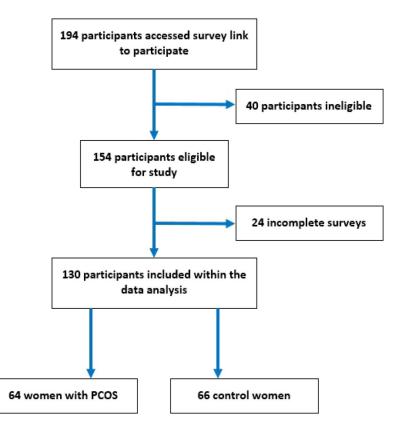


Figure 1. Flow diagram for the recruitment of women of reproductive age into the study group with polycystic ovary syndrome (PCOS) and the one without (control).

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Variable	Total ( <i>n</i> = 130)	$\begin{array}{c} PCOS \\ (n = 64) \end{array}$	Control ( <i>n</i> = 66)
Age range (years)	19–45	21–45	19–45
Ethnicity		21 13	19 15
White	108 (83.1%)	57 (89.1%)	51 (77.3%)
Asian or Asian British	13 (10%)	2 (3.1%)	11 (16.6%)
Black or Black British	3 (2.3%)		3 (4.5%)
Chinese	1 (0.8%)	1 (1.6%)	-
Gypsy or Traveler	1 (0.8%)	1 (1.6%)	_
Other mixed background	3 (2.3%)	3 (4.7%)	_
Declined to specify	1 (0.8%)	5 (4.776)	1 (1.5%)
Marital Status	1 (0.070)		1 (1.370)
Single	52 (40%)	23 (35.9%)	29 (43.9%)
Married	52 (40%)	22 (34.4%)	30 (45.5%)
Divorced	6 (4.6%)	5 (7.8%)	1 (1.5%)
Widowed	1 (0.8%)	1 (1.6%)	1 (1.5%)
Civil partnership	3 (2.3%)	1 (1.6%)	2 (3.0%)
Other	16 (12.3%)	12 (18.8%)	2 (3.0%) 4 (6.1%)
Children	10 (12.5%)	12 (18.870)	4 (0.1%)
Yes	38 (29.2%)	14 (21.9%)	24 (36.4%)
No	. ,	. ,	· · ·
Occupation	92 (70.8%)	50 (78.1%)	42 (63.6%)
•	(2 (40 50/)	24 (52 10/)	20 (42 00/)
Full-time employed	63 (48.5%)	34 (53.1%)	29 (43.9%)
Part-time-employed	16 (12.3%)	10 (15.6%)	6 (9.1%)
Student	35 (26.9%)	10 (15.6%)	25 (37.9%)
House person	5 (3.8%)	5 (7.8%)	-
Unemployed	2 (1.5%)	1 (1.6%)	1 (1.5%)
Other	9 (6.9%)	4 (6.3%)	5 (7.6%)
Education	- /	- /	
Secondary	6 (4.6%)	6 (9.4%)	_
College	28 (21.5%)	15 (23.4%)	13 (19.7%)
Undergraduate	50 (38.5%)	26 (40.6%)	24 (36.4%)
Postgraduate	32 (24.6%)	14 (21.9%)	18 (27.3%)
Doctorate	14 (10.8%)	3 (4.7%)	11 (16.7%)
Household Income			
$\leq$ £39,999	77 (59.2%)	43 (67.3%)	34 (51.5%)
£40,000-£79,999	42 (32.3%)	16 (25%)	26 (39.4%)
$\geq$ £80,000	11 (8.4%)	5 (7.8%)	6 (9.1%)

Table 1. Key sociodemographic	characteristic	of the	study	participants	with	polycystic	ovary	syn-
drome (PCOS) and without (contr	ol).							

Note: All percentage data rounded to one decimal place.

differences between the age and height of the two groups, women with PCOS had higher body weight, BMI, and waist circumference than the control group (Table 2). Moreover, women with PCOS reported lower scores in all domains of the SF-12v2, which is indicative of overall poorer HRQoL.

Results from the PCOS-Q are presented in Table 3. When domain scores were compared, there were statistical differences between five domains; the weight domain was statistically lower than emotions (MD = -1.15, p < .001), menstrual problems (MD = -1.10, p < .001), body hair (MD = -0.70, p = .004), and infertility (MD = -0.60, p =.025), whilst infertility was also lower than emotions (MD = -0.55, p = .043). It is evident that concerns about body weight and infertility are the most prevalent in this sample.

With regard to other measures, women with PCOS had statistically lower self-esteem than the controls, whilst also perceiving fewer benefits and greater barriers to exercise (Table 2). When the highest and lowest perceived benefits/barriers to exercise were split by study group and scored, there were similarities between the top scoring results, and Table 2. Comparison of self-reported variables between women with polycystic ovary syndrome (PCOS) and the control group.

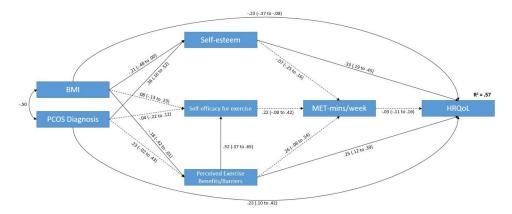
				Gilicelini	INCURI				
				PCOS/	or mean				
	Total ( <i>n</i> = 130)	PCOS ( $n = 64$ )	Control $(n = 66)$	CON	diff	Lower	Upper	Cohen's d	<i>p</i> value
Age (years)	31 (11.25)	30 (9.75)	32 (13.50)	0/0	-2.00	-4.00	1.00	-0.192	0.297
Height (cm)	165.1 (10.00)	165.1 (8.06)	164.5 (9.25)	0/0	0.60	-1.40	2.80	0.107	0.349
Weight (kg)	65.16 (38.27)	91.30 (45.31)	63.00 (18.30)	0/0	28.30	12.77	33.00	1.121	< 0.001
BMI (kg/m <sup>2</sup> )	24.51 (13.29)	32.91 (16.60)	23.28 (5.25)	0/0	9.63	4.65	11.59	1.129	< 0.001
WC (cm)	81.28 (31.60)	101.60 (40.62)	74.00 (16.66)	11/8	27.60	15.24	32.50	1.315	< 0.001
Self-esteem scale	16.86 (5.68)	14.00 (5.21)	19.34 (5.20)	5/1	-5.32	-7.18	-3.47	-1.020	< 0.001
Self-efficacy/exercise	42.40 (17.77)	40.44 (21.35)	43.64 (15.95)	2/0	-3.20	9.83	3.43	-0.170	0.341
				3					
Physical functioning	56.5 (8.59)	56.5 (5.59)	56.5 (0.00)	5/2	0.00	-0.00	-0.00	-0.606	.001
Role physical	57.2 (13.80)	48.0 (18.40)	57.2 (9.21)	5/2	-4.61	-9.21	-0.00	-0.710	<.001
Bodily pain	57.4 (10.20)	47.3 (20.40)	57.4 (10.20)	5/2	-10.19	-10.19	-0.00	-0.742	<.001
General health	44.7 (10.80)	44.7 (15.10)	55.5 (10.80)	5/2	-10.78	-10.78	-0.00	-0.768	<.001
Vitality	47.7 (10.10)	37.7 (20.10)	47.7 (12.60)	5/2	-10.06	-10.06	-10.06	-0.955	<.001
Social functioning	46.5 (20.20)	36.4 (10.10)	46.5 (10.10)	5/2	-10.10	-10.10	-10.09	-0.946	<.001
Role emotional	44.9 (19.60)	33.7 (16.80)	50.5 (16.80)	5/2	-11.18	-16.77	-5.59	-0.934	<.001
Mental health	40.2 (12.20)	34.1 (12.20)	46.3 (12.20)	5/2	-12.19	-12.19	-6.10	-1.082	<.001
SF-12 physical	55.6 (11.00)	53.3 (12.40)	57.0 (7.19)	5/2	-3.51	-6.29	-0.83	-1.159	<.001
SF-12 mental	37.8 (11.20)	31.9 (10.70)	43.2 (8.76)	5/	-11.28	-14.79	-7.77	-1.155	<.001
IPAQ-LF									
MET-min/wk	3478.5 (3257.9)	3447.0 (3648.0)	3010.5 (3295.5)	5/5	436.50	-385.00	1278.00	0.158	0.280
Sitting-min/wk EBBS	2370.0 (1515.0)	2460.0 (1665.0)	2340.0 (1830.0)	1/0	120.00	-300.00	540.00	0.060	0.603
Benefits	88.50 (18.00)	84.0 (14.75)	93.5 (17.0)	4/0	-9.50	-12.00	-4.00	-0.595	0.001
Barriers	39.00 (8.25)	38.0 (9.25)	41.5 (8.25)	4/0	-3.50	-6.00	-1.00	-0.482	0.003
Total▲	128.85 (25.00)	122.78 (18.92)	133.47 (20.50)	4/0	-10.69	-16.59	-4.78	-0.639	0.001
<i>Note:</i> Unless otherwise CON: Control group; CI: Physical Activity Questic	indicated, data are pre- confidence interval; ME	sented as median (IQF D: median/mean differ -min/wk <sup>-</sup> Metabolic eo	Note: Unless otherwise indicated, data are presented as median (IQR) and Mann-Witney U tests performed; A Parametric data reported as mean (SD), and Welch's <i>t</i> -test performed; CON: Control group; CI: confidence interval; MD: median/mean difference; BMI: body mass index; WC: waist circumference; HROOL: health-related quality of life; IPAQ-LF: International Physical Activity Onectionnaire Long Form: MFI-min/we: Metabolic equivalent of task minutes ner week as measured by the IPAO-LF: FIRS: Exercise Renefits/Barriers Scale: <i>n</i> value: sign	ests performed dex; WC: waist ner week as m	;      Parametric d, circumference;      circumference;	ata reported as HRQoL: health-re PAO-I F· FRRS· F›	mean ( <i>SD</i> ), an lated quality o cercise Benefits	ld Welch's <i>t</i> -test f life; IPAQ-LF: In s'Barriers Scale: <i>n</i>	performed; ternational value: sin-
Physical Activity Questionnaire Long	onnaire Long Form; MEI	-min/wk: Metabolic eq	Physical Activity Questionnaire Long Form; MET-min/wk: Metabolic equivalent of task minutes per week as measured by the IPAQ-LF; EBBS: Exercise Benefits/Barriers Scale; p value: sig-	per week as m	neasured by the I	PAQ-LF; EBBS: E>	kercise Benetits	;/Barriers Scale; <i>p</i>	value

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PCOS-Q Domain	Median Score	Interquartile Range
Emotions	3.05	1.57
Body hair	2.60	3.30
Weight	1.90	2.75
Infertility	2.50	3.81
Menstrual problems	3.00	2.25

Table 3. Domain-specific	scores of the health-related quality-of-life questionnaire for won	nen with
polycystic ovary syndrome	e (PCOS-Q) reported from the study participants with PCOS.	



**Figure 2.** Schematic presentation of the path analysis model based on the findings of the present study. Bidirectional arrows are indicative of correlation between exogenous variables. Single directional arrows indicate significant standardized path coefficients and bias-corrected 95% confidence intervals for direct effects. A dashed arrow indicates nonsignificant direct effects. All values rounded to two decimal places (PCOS: diagnosed with polycystic ovary syndrome; BMI: body mass index (self-reported); HRQoL: health-related quality of life as measured by aggregate SF-12 score; MET-min/wk: metabolic equivalent of task minutes per week as measured by the IPAQ-LF).

some disparity with the lowest scoring (Table A2). The highest scoring benefits in both groups were similar and generally related to physical health and well-being; by contrast, the lowest scoring benefits tended to be linked to social well-being. There were also similar findings for the highest scoring barriers; both groups scored "exercise tires me," "exercise is hard work for me," and "I am fatigued by exercise" in their top three, whereas there was a marked difference in the lowest perceived barriers.

In contrast to the Exercise Benefits/Barriers Scale, there were no statistically significant between-group differences in self-efficacy for exercise. In addition, when data from the IPAQ was analyzed, there were no between-group statistical differences in either MET-min/wk or sitting time.

### **Path Analysis**

Within our path model (Figure 2), both a diagnosis of PCOS and BMI had direct effects on HRQoL (standardized  $\beta = 0.230$ , and  $\beta = 0.234$ , respectively) and self-esteem ( $\beta = 0.364$  and  $\beta = -0.213$ , respectively). Furthermore, PCOS also had the largest indirect ( $\beta = 0.177$ ) and total effect ( $\beta = 0.407$ ) upon HRQoL. PCOS diagnosis was closely followed by BMI (indirect  $\beta = -0.116$ ; total  $\beta = -0.351$ , respectively), which in addition had a direct effect on the Exercise Benefits/Barriers Scale score ( $\beta = -0.180$ ). The Self-Esteem ( $\beta = 0.326$ ) and Exercise Benefits/Barriers Scale ( $\beta = 0.254$ ) scores also demonstrated a direct effect upon HRQoL and, although they had no statistically significant indirect effects (via PA as a mediator), both demonstrated a total effect upon HRQoL in this model ( $\beta = 0.324$  and  $\beta = 0.265$ , respectively). The Exercise Benefits/Barriers Scale score also had a statistically significant total effect on weekly PA ( $\beta = 0.376$ ). Self-efficacy for exercise and weekly PA had no effect (either direct or indirect) on any other variable in the model (Table 4).

#### Discussion

#### **Between-Group Differences**

The existing evidence consistently highlights impaired HRQoL in women with PCOS (Amiri et al., 2019; Naz et al., 2020; Yoldemir et al., 2017), that is also markedly lower than in women without PCOS (Asdaq et al., 2020; Benetti-Pinto et al., 2015; Drosdzol et al., 2007;

**Table 4.** Direct, indirect, and total effects of variables in the Health-Related Quality of Life (HRQoL) causal model.

		95% C	I for $\beta$	
	Standardized Coefficient	Lower	Upper	p value
Direct Effects				
$PCOS \rightarrow HRQoL$	0.230	0.099	0.420	0.004
$PCOS \rightarrow Self-esteem^{\dagger}$	0.364	0.163	0.517	0.021
$PCOS \rightarrow SEE^{\dagger}$	-0.039	-0.220	0.116	0.517
$PCOS \rightarrow EBBS^{\dagger}$	0.225	-0.022	0.426	0.068
$BMI \to HRQoL$	-0.234	-0.368	-0.076	0.007
$BMI  ightarrow Self\operatorname{-esteem}^\dagger$	-0.213	-0.478	0.000	0.050
$BMI \to SEE^\dagger$	0.082	-0.134	0.233	0.460
$BMI \to EBBS^\dagger$	-0.180	-0.415	-0.009	0.038
Self-esteem $\rightarrow$ HRQoL	0.326	0.185	0.445	0.018
$Self-esteem \to MET-min/wk^\dagger$	-0.069	-0.252	0.162	0.612
$SEE \rightarrow MET-min/wk^{\dagger}$	0.224	-0.078	0.419	0.118
$EBBS \to MET\text{-}min/wk$	0.260	-0.055	0.542	0.119
$EBBS \to HRQoL$	0.254	0.124	0.391	0.010
$EBBS \to SEE^\dagger$	0.520	0.368	0.654	0.006
$MET\text{-}min/wk \to HRQoL^\dagger$	0.029	-0.113	0.164	0.740
Indirect Effects				
$PCOS \rightarrow HRQoL$	0.177	0.072	0.283	0.018
$PCOS \rightarrow MET-min/wk^{T}$	0.051	-0.057	0.177	0.305
$BMI \to HRQoL$	-0.116	-0.266	-0.018	0.023
$BMI \to MET\text{-}min/wk^{\dagger}$	-0.035	-0.154	0.059	0.519
Self-esteem $\rightarrow$ HRQoL	-0.002	-0.035	0.008	0.626
$SEE \rightarrow HRQoL^{\dagger}$	-0.006	-0.026	0.038	0.411
$EBBS \to MET\text{-}min/wk$	0.117	-0.006	0.285	0.066
$EBBS \to HRQoL$	0.011	-0.038	0.093	0.684
Total Effects				
$PCOS \rightarrow HRQoL$	0.407	0.255	0.571	0.011
$BMI \to HRQoL$	-0.351	-0.507	-0.194	0.005
$Self-esteem\toHRQoL$	0.324	0.196	0.446	0.012
$EBBS \to HRQoL$	0.265	0.127	0.407	0.012
$EBBS \to MET\text{-}min/wk$	0.376	0.130	0.586	0.015

PCOS: Diagnosed with polycystic ovary syndrome; BMI: Body Mass Index; HRQoL: Health-related Quality of Life as measured by total SF-12 score; SEE: self-efficacy for exercise; EBBS: Exercise Benefits/Barriers Scale; MET-min/wk: Metabolic equivalent of task minutes per week as measured by the International Physical Activity Questionnaire Long Form (IPAQ-LF); 95% CI: Bias corrected 95% confidence interval;  $\rightarrow$  denotes causal direction of path.

<sup>†</sup>Data reported are equal to Total Effects for path.

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Sánchez-Ferrer et al., 2020; Shishehgar et al., 2016). The present findings agree with this, showing statistically worse values across all eight summary health scores and both the physical and mental component scores of the SF-12v2. Studies utilizing the SF-12v2 to assess HRQoL in women with PCOS are scarce, meaning there are limited data for comparison. However, a recent case-control study found women with PCOS had poorer physical component scores compared to controls, and our findings agree with this (Sánchez-Ferrer et al., 2020). When the mental component score was considered, we reported a statistical difference favoring the control group, but Sánchez-Ferrer et al. (2020) reported no such difference. Notably, the norm-based score for women with PCOS in our study was markedly lower than that reported by Sánchez-Ferrer et al. (mean 44.2, 95% CI: 42.4 to 46.1). Interestingly, another previous study that used only the raw scores (0–100) from the Bodily Pain subscale to compare women with PCOS to controls reported statistically higher bodily pain severity in women with PCOS. However, the magnitude of difference is greater, and mean scores lower, in the current study compared to those previously reported (Morán-Sánchez et al., 2021).

The paucity of previous studies using the SF-12v2 makes it difficult to infer clinical relevance from our findings. However, a previous study reported change scores for each domain of the SF-36 before and after an aerobic exercise intervention (Costa et al., 2018), identifying thresholds for clinical significance. Although these scores cannot be compared directly, the effect size (*d*) of key domains can be compared. In the present study, the between-group effect sizes for the role emotional and mental health summary scores were greater than the change from baseline effect sizes (d = 0.8, 95% CI: 0.0 to 1.6; and d = 1.0, 95% CI: 0.0 to 2.0, respectively) reported in Costa et al. (2018), suggesting clinical importance in the current study. We also reported a statistically significant difference between mental and physical summary scores (mean difference = 19.2, 95% CI: 15.7 to 22.6) in women with PCOS, suggesting that PCOS has a greater psychological impact than it does physical, which agrees with findings reported by a previous study (Bazarganipour et al., 2013).

Since the PCOS-Q is specific to people living with PCOS, this validated PCOS-specific questionnaire was not administered to women in the control group. For those living with PCOS, statistically lower scores were reported for weight compared to other domains. This is in accord with other studies using the PCOS-Q (Barnard et al., 2007; Coffey et al., 2006, Thomson et al., 2010; Jones et al., 2004; McCook et al., 2005), or other HRQoL measurement tools (Kerchner et al., 2009), which have also reported that excess body weight has the greatest detrimental effect upon HRQoL in those with PCOS. For infertility, we found that this was the second lowest domain affecting HRQoL, and this is also in agreement with findings from Jones et al. (2004) and Coffey et al. (2006).

These findings should be further explored by future research focusing on identifying HRQoL thresholds for clinically important changes/differences in women with PCOS, and by incorporating assessments of psychological well-being and appropriate treatment/management strategies during the management of PCOS. Moreover, there is a need to standardize the version of the tool used, whilst ensuring it is robust and valid for use in a range of different cultural/social settings (Taghavi et al., 2015).

As commonly reported in the relevant literature, women with PCOS in our study also reported higher body weight, BMI, and waist circumference than the control group. The association between obesity and PCOS has been widely reported, with available older data indicating that the obesity prevalence in UK women with PCOS was 35–38% (Balen, 1995; Kiddy et al., 1990). Given the increasing obesity prevalence rates in the general population over the past few decades (Moody & Neave, 2016), it is a reasonable assumption that a similar growth may have been observed in women with PCOS. A previous study in the United States (Yildiz et al., 2008) reported temporal trends of obesity prevalence in local women with PCOS reflecting the increases in obesity prevalence in the general population, which is in concordance with the findings of this study.

Furthermore, we found no statistically significant differences in the amount of selfreported PA or sitting time between women with PCOS and the control group. Previous research also supports this, with data from a large cohort study showing no differences in total PA levels between women with PCOS and controls (Moran et al., 2013), which is also supported elsewhere (Álvarez-Blasco et al., 2011; Cutler et al., 2019; Douglas et al., 2006; Lin et al., 2019; Wright et al., 2004). The lack of significant differences in sitting time between women with PCOS and controls in the present study is also in accord with most of the evidence from the existing relevant literature (Ahmadi et al., 2013; Álvarez-Blasco et al., 2011; Lin et al., 2019; Wright et al., 2004). Indeed, to our knowledge, only one study has reported increased sitting time in women with PCOS compared to a control group ( $6.3 \pm 2.8 \ vs \ 5.8 \pm 2.9 \ h/day$ , respectively; p = 0.008) (Moran et al., 2013).

The current study also revealed lower self-esteem in women with PCOS than in the control group, which contrasts with a previous study which reported no statistical differences (Annagür et al., 2014); this may be attributed to the BMI of study groups being lower than in the current study. Indeed, previous studies have reported significantly lower self-esteem across subsets of women with PCOS (i.e., subgroups with hirsutism, infertility, and obesity) compared to healthy controls, but it was those with obesity and PCOS who were far more likely to have the lowest self-esteem (Açmaz et al., 2013; Tay et al., 2019). The relationship between a higher BMI and lower self-esteem has previously been reported in the general population (Biro et al., 2006; Hesketh et al., 2004; Strauss, 2000), and the direct effect of BMI upon self-esteem in the current study tends to support this, although there is a paucity of literature on this topic in women with PCOS.

Interestingly, despite the absence of significant differences in self-reported PA between our two study groups, women with PCOS perceived both fewer benefits and a greater number of barriers to participation in exercise. Whilst greater perceived benefits have been associated with increased exercise participation (Bonheur & Young, 1991; Grubbs & Carter, 2002; Jones & Nies, 1996), it is the perceived barriers that are the most powerful predictor of a health behavior (Janz & Becker, 1984). Although there is mixed evidence as to whether women with PCOS are less active than their non-PCOS counterparts, few studies have investigated the relationship between barrier/benefit perception and PCOS. One such study compared women with PCOS to controls and, as in the current study, found many similarities in barrier/benefit perception (Banting et al., 2014). A more recent study of women with PCOS reported that the most common perceived barriers to PA were those related to physical exertion (i.e., exercise is tiring, hard work, and fatiguing) (Thomson et al., 2016), and these findings exactly match the top-cited barriers identified in this study. Notably, Thomson et al. (2016) further stated that

exposure to a lifestyle intervention may improve these perceptions, particularly those relating to barriers, and this should be a focus for future research.

#### **Path Analysis**

The path analysis model showed little evidence that PA had influenced HRQoL; no single outcome had a direct effect on the amount of self-reported PA, and similarly PA did not have a direct effect on HRQoL scores. A statistical total effect of perceived exercise benefits/barriers on MET-min/wk is reported, but this is likely due to the strength of the direct effect of Exercise Benefits/Barriers Scale scores on self-efficacy for exercise (as a mediating variable). This relationship was the only instance where an outcome was deemed to have any effect upon PA levels.

Although there may be no true relationship between PA and HRQoL in this group, it should be highlighted that there are notable limitations with self-reported data, particularly for PA (Prince et al., 2008). In this context, it is of note that the self-reported PA data in this study is higher than the most active female group from normative UK population data (Love-Koh & Taylor, 2018). It is possible that the participants within the current study are indeed highly physically active (e.g., due to motivation or medical advice relating to controlling PCOS as a chronic medical condition), but it is also likely that social desirability bias and/or the healthy volunteer effect (Froom et al., 1999; Grimm, 2010; Prince et al., 2020) may have influenced these results.

In the present study, when direct and indirect effects were summed, our model identified a diagnosis of PCOS as having the largest total effect on participant's HRQoL. When only direct effects were considered, the effect of PCOS upon HRQoL was comparable to the effect of self-reported BMI. A diagnosis of PCOS had a greater direct effect on self-esteem than did BMI, but both were statistically significant. Self-esteem had the largest direct effect upon HRQoL. In fact, self-esteem emerged as a key mediator between the exogenous variables and HRQoL. It is therefore likely that women with PCOS have a two-fold effect upon their self-esteem, namely managing a chronic disease and its associated symptoms promotes lower self-esteem but so too does increased BMI (Chu et al., 2019). Another key consideration is the bidirectional effect of self-esteem, where chronic disease reduces an individual's self-esteem, and vice versa, since previous studies have identified that low self-esteem is associated with physical dysregulation (in the context of stress) (Liu et al., 2014), and physical health complications (Cott et al., 1999). Of note, the Rosenberg Self-Esteem Scale has been used in studies in women with PCOS. Similarly, self-esteem was shown to play an important role, as a mediating factor, in the HRQoL of these women (Bazarganipour et al., 2013, 2014).

### **Study Limitations**

Certain potential limitations should be acknowledged in the context of the present study. Since the study was promoted mainly via internal university systems, calling for volunteers with or without PCOS, it is possible that a higher proportion of the control group may have originated from the local university population, as is implied by the higher number of participants in the control group who were students, and those with a doctorate-level qualification at the time of survey. The degree to which this may have influenced the results is difficult to assess.

Based on the eligibility criteria, participants had to be free from any other chronic condition which may impact on their ability to perform PA. The objective behind this decision was to isolate the impact of a PCOS diagnosis rather than any other comorbidity. However, it is widely reported that women with PCOS are more susceptible to a range of physical and psychological conditions; excluding these women means that the extent to which the present findings can be generalized for women with PCOS, and other chronic conditions may be limited.

Moreover, self-reported data always present a methodological concern, particularly regarding reporting PA (Prince et al., 2008) and sedentary behaviors (Prince et al., 2020). Such response bias for these outcomes may be a contributing factor to the absence of impact on the variance in HRQoL. It should also be noted that whilst the IPAQ has been previously validated, Lee et al. (2011) report that correlations between the IPAQ and objective measures are lower than the acceptable standard, and that the IPAQ overreports PA behaviors by as much as 84%. This phenomenon is perhaps further compounded by the fact that the IPAQ has not been validated for use specifically in women with PCOS, which reduces confidence in the true effect of PA in this study.

Similar issues around reporting also apply to the self-reporting of anthropometric measures (e.g., overreporting height or underreporting body weight) (Gorber et al., 2007), with the greatest degree of inaccuracy tending to present in women and/or in those with a higher BMI (Bigaard et al., 2005). However, a previous study of mid-aged women reported substantial agreement between self-reported and measured height/ weight data (Burton et al., 2010), and whilst this bias may typically be expected in this type of research, the online nature of the study, which offered complete anonymity, may have reduced the degree of such validity issues (Larson, 2019). Finally, the presence or absence of a PCOS diagnosis was also self-reported by the study participants; this may be regarded as a study limitation regarding the true categorization of study groups with and without PCOS. However, only 17% could not (or opted not to) report the exact phenotype for their PCOS diagnosis, meaning risk of misclassification may have been low.

## Implications for Practice and/or Policy

Given that the United Nations' Sustainable Development Goals (UN General Assembly, 2015) highlight the need to reduce health inequalities and to specifically prioritize women's health, it is perhaps no surprise that the Department of Health and Social Care's Women's Health Strategy for England (2022) was produced. This policy, which aims to reform healthcare to reduce health inequalities for women, identifies PCOS as a priority condition; the links between PCOS and impaired cardiovascular health are stated and so, too, is the need to increase awareness of PCOS amongst women and girls so that they know when, and indeed where, to seek health-care support. Furthermore, women should have access to high-quality, personalized care, which includes access to contraception for the management of menstrual problems and gynecological conditions. In this context, the present findings that identify reduced self-esteem as a key factor in the promotion of physical and mental health in women with PCOS highlight selfesteem as an additional aspect which should not be overlooked in interventions/policies on women's health. Moreover, given that women with PCOS report impaired HRQoL compared to women without, HRQoL assessment should also not be omitted by healthcare practitioners in order to facilitate a more personalized/holistic management plan according to the needs of the patient. Indeed, it is likely that greater support for mental well-being is required for women with PCOS, with a potential emphasis on improving self-esteem which is currently lacking from PCOS management pathways/approaches. Accordingly, future research should also focus on identifying clinical thresholds so that HRQoL can be monitored more effectively in these women. In addition, behavior change techniques are likely to further support women with PCOS both to improve health literacy on the benefits of PA and with barrier identification and removal.

The evidence around the effectiveness of PA in mitigating the manifestations of PCOS is mixed. Given that PA (as part of broader lifestyle changes) is now included in the international evidence-based guideline for the assessment and management of PCOS (Teede et al., 2023), it is imperative that its true effectiveness is better studied so that it can be used effectively in this population. Accordingly, PA/lifestyle measures which are specifically designed (and validated) for those living with PCOS are needed. Whilst there is a need for rigorously designed and well-reported trials in women with PCOS (Kite et al., 2019), studies should also utilize device-measurement of PA and sedentary behavior to strengthen the certainty of the evidence.

#### Conclusions

Overall, the present study shows that poorer HRQoL is reported by women with PCOS and highlights self-esteem as a key factor in the promotion of health in this patient population. A PCOS diagnosis was also noted to have a greater impact upon mental health than on physical health, with both domains being impaired in women with PCOS. Whilst previous studies suggest that increasing PA has a key role at improving health in a range of populations, the link here was not apparent. This further highlights a need for future studies, preferably using device-measured PA methods, to better understand the health-related impact of PA as well as the potential role of PA in the promotion of self-esteem in women with PCOS.

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No potential conflict of interest was reported by the author(s).

#### **Declaration of Interest Statement**

The authors have no competing interests to declare that are relevant to the content of this article.

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#### **Data Availability Statement**

The data that support the findings of this study are available from the corresponding author [CK] upon reasonable request.

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	4	Age Weight	ght BMI	MC	SEE	Benefit	Barrier	EBBS	SES	SF12 Phys	SF12 Mental	SF12 Total	MET-min/wk	Sitting
Age	μd													
Weight	н. Н	<b>062</b>												
RMI	د . د	.305 039 802	T											
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MC	τ													
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SEE	т <b>1</b>		36 –.078											
	Р.													
Benefit	τ.			9 –.218	.305									
	Ρ.				< .001									
Barrier	т. Т				.319	.411								
	۰. ۲				< .001	< .001								
EBBS	τ.				.340	.819	.611							
	Ρ.			v	< .001	< .001	< .001							
SES	т. Т				.095	.234	.229	.270						
	م				.130	< .001	< .001	<ul><li>.001</li></ul>						
SF12 Phys	т. т.				.063	.338	.236	.347	.299					
	م				.331	< .001	< .001	<ul><li>.001</li></ul>	< .001					
SF12 Mental	τ.				.112	.267	.308	.313	.535	.543				
	P.		v	v	.077	< .001	< .001	<ul><li>.001</li></ul>	< .001	< .001				
SF12 Total	τ.				.083	.303	.305	.339	.463	.737	.844			
	م	v	v	v	.184	< .001	< .001	<ul><li>.001</li></ul>	< .001	< .001	< .001			
MET-min/wk	т. т.				.212	.155	.152	.175	.058	.057	.015	.037		
	٩.				< .001	.014	.018	900.	.369	.395	.815	.573		
Sitting	1 1				167	600.	051	015	042	000.	039	020	161	
	Д				900.	.879	.406	.800	.498	.996	.534	.748	.010	

BMI: body mass index; WC: waist circumference; MET-min/wk: metabolic equivalent of task minutes per week as measured by the International Physical Activity Questionnaire Long Form; SES: self-esteem scale; EBBS: Exercise Benefits/Barriers Scale; SEE: self-efficacy for exercise; SF12: 12-item short form health survey. -.161 .010

	PCOS Group ( $n = 64$ )	Control Group ( $n = 66$ )
Number	Top three benefits	
1.	Exercising increases my level of physical fitness	Exercising increases my level of physical fitness
2.	Exercise improves my flexibility	Exercising increases my level of physical fitness
3.	Exercising improves functioning of my cardiovascular system Bottom three benefits	Exercise gives me a sense of personal accomplishment
27.	Exercising is a good way for me to meet new people	Exercising lets me have contact with friends and persons I enjoy
28.	Exercise is good entertainment for me	Exercising is a good way for me to meet new people
29.	Exercising lets me have contact with friends and persons I enjoy Top three barriers	Exercising increases my acceptance by others
1.	Exercise tires me	Exercise tires me
2.	Exercise is hard work for me	Exercise is hard work for me
3.	I am fatigued by exercise	I am fatigued by exercise / exercising takes too much of my time
	Bottom three barriers	,
12.	There are too few places for me to exercise	My spouse (or significant other) does not encourage exercising
13.	Places for me to exercise are too far away	I am too embarrassed to exercise
14.	I think people in exercise clothes look funny	I think people in exercise clothes look funny

Table A2. Highest and lowest scoring items from the Exercise Benefits/Barriers Scale separated by study group (women with PCOS vs. women without PCOS [control] group).