

Sleep disruption and depression, stress and anxiety levels in women with polycystic ovary syndrome (PCOS) during the lockdown measures for COVID-19 in the UK

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32 **Abstract**

33 **Background:** Lockdown measures have been enforced globally in response to the COVID-19
34 pandemic. Given the comorbidity burden in women with polycystic ovary syndrome (PCOS), these
35 lockdown measures may have a particularly negative impact on sleep health, quality of life (QoL), and
36 depression/stress levels in this population. The aim of this study was to explore whether such potential
37 problems were present in women with PCOS during the COVID-19 lockdown in the UK.

38 **Methods:** UK women with PCOS were recruited through social media into a cross-sectional study
39 during the COVID-19 lockdown. The study survey was delivered online, and included demographic
40 and COVID-19 relevant questions, as well as validated questionnaires/scales, namely the Insomnia
41 Severity Index (ISI), Depression Anxiety and Stress Scale (DASS-21), and PCOSQOL questionnaire.

42 **Results:** 333 women with PCOS [median age: 30.0 (9.0) years] were recruited. Participants were
43 dichotomized based on responses regarding the impact of COVID-19 restrictions on their sleep
44 [negative (N=242) versus no/positive (N=91) impact]. No differences were noted between groups
45 regarding age, time since PCOS diagnosis, body mass index, or number of comorbidities. Based on the
46 ISI, 44.2% of participants reporting a negative impact on sleep exhibited at least moderately severe
47 clinical insomnia. Compared to those who reported no/positive effect on sleep, the participants
48 reporting a negative impact on sleep also reported poorer QoL, based on the total PCOSQOL score,
49 with a greater impact of PCOS and poorer mood in the corresponding PCOSQOL domains. Based on
50 the DASS-21, the latter also had statistically higher depression and stress levels compared to the
51 former. Finally, for this cohort significant inverse correlations were noted between the ISI and
52 PCOSQOL scores (total and domain scores), whilst the DASS-21 and ISI scores were positively
53 correlated (all p -values $<.001$).

54 **Conclusion:** The majority of recruited UK women with PCOS reported that the COVID-19 lockdown
55 had a negative impact on their sleep, which was also associated with impaired QoL and higher
56 depression/stress levels. Whilst further research is required, women with PCOS should be considered

57 a vulnerable population that may experience an adverse impact on sleep, QoL and mental health
58 wellbeing due to lockdown measures during the COVID-19 pandemic.

59

60 **Keywords:** Polycystic ovary syndrome (PCOS), COVID-19, lockdown, sleep, anxiety, depression,
61 stress, quality of life

62

63 **1 Introduction**

64 Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus-
65 2 (SARS-CoV-2), usually manifests as a respiratory tract infection with mild symptomatology
66 (asymptomatic in many cases) (1-3). However, COVID-19 can also lead to severe manifestations in a
67 proportion of high-risk individuals with respiratory and/or extra-pulmonary symptoms/complications
68 requiring hospitalization (1-3). As the latter may require intensive care unit (ICU) support and may
69 even be fatal, the COVID-19 pandemic has resulted in enforcement of varying degrees of nationwide
70 lockdown, quarantine and self-isolation measures in many countries worldwide (4, 5). These measures
71 aim to reduce SARS-CoV-2 transmission in the general population, and thus the risk of severe COVID-
72 19 in vulnerable groups (*e.g.*, older individuals and patients with certain respiratory and cardio-
73 metabolic diseases) (6-12). Indeed, compelling evidence strongly indicates that certain chronic cardio-
74 metabolic diseases, including diabetes and obesity, constitute key risk factors predisposing to severe
75 COVID-19 (6-12). Notably, although severe COVID-19 is more common in men (13, 14), the
76 aforementioned cardio-metabolic comorbidities, which significantly increase the risk of adverse
77 COVID-19 related clinical outcomes, are also markedly prevalent in women with polycystic ovary
78 syndrome (PCOS) (15-17).

79 PCOS is the most common endocrine disorder in reproductive-aged women, affecting up to 15-20%
80 of this female population depending on the studied population and the applied diagnostic definition
81 (18, 19). After excluding other endocrinopathies with similar symptomatology (19, 20), PCOS is
82 typically diagnosed based on the presence of at least two out of three diagnostic criteria, namely
83 ovulatory dysfunction, hyperandrogenism (clinical and/or biochemical) and polycystic ovaries (PCO)
84 as identified by ultrasound (21). In addition, women with PCOS are also at a high risk of cardio-
85 metabolic complications, particularly obesity, insulin resistance, type 2 diabetes (T2DM),
86 hypertension, non-alcoholic fatty liver disease (NAFLD) and obstructive sleep apnoea (OSA) (22-27).

87 Furthermore, women with PCOS often exhibit psychological comorbidity, with higher prevalence of
88 coexisting anxiety and/or depression (28-31), which also tends to impair their overall quality of life
89 (QoL) compared to women without PCOS (32, 33). Given this increased comorbidity burden, women
90 with PCOS may experience a particularly negative impact from the lockdown/quarantine and self-
91 isolation measures imposed against the transmission of SARS-CoV-2 and may also be at increased risk
92 of severe COVID-19 (16).

93 Overall, global measures to control the COVID-19 pandemic are expected to inevitably have a negative
94 psychological effect upon the general population (34) due to various factors, including the enforced
95 quarantine measures (35) and their socio-economic impact (36), as well as the concern about COVID-
96 19 (34). This has been previously reported in relation to SARS, which was shown to promote increased
97 stress, anxiety and depression in the general population (37). Such findings are increasingly reported
98 during the current COVID-19 pandemic, with an observed increase in self-reported symptoms of
99 anxiety, depression and stress (38). Moreover, these negative psychological effects are likely linked to
100 disrupted sleep quality (39). In previous longitudinal studies, new onset mental health issues have been
101 linked to increased sleep disruption (40-42), whilst disturbed sleep is also considered to be a
102 contributing factor to the development of new mental health disorders (43). Of note, irrespective of the
103 COVID-19 pandemic, sleep disturbances are more prevalent in women with PCOS than in the general
104 population (44, 45), potentially due to coexisting OSA, particularly in women with poorer metabolic
105 profiles (26), and/or depression which is also a major predictor of poor sleep quality (46). Furthermore,
106 reduced self-esteem and body satisfaction, which are both frequently associated with PCOS, have also
107 been demonstrated to contribute towards disrupted sleep (44).

108 In this context, it is likely that a two-fold effect of increased psychological distress due to the COVID-
109 19 pandemic alongside the established disease-related burden of PCOS may further contribute to
110 impaired sleep quality and QoL, linked also to increased anxiety, depression and stress levels (47). To

111 date, there have been no published studies exploring these issues in women with PCOS during the
112 COVID-19 pandemic. Therefore, the aim of the current study was to determine whether the COVID-
113 19 pandemic has had a negative effect upon the sleep quality of women with PCOS in the United
114 Kingdom (UK), and whether any such impairment was associated with reduced QoL and increased
115 stress, anxiety or depression in this female population.

116 **2 Methods**

117 For the purposes of this study, we conducted a cross-sectional study based on a web-based survey
118 between 2nd June and 17th August 2020. Ethical approval was granted by the ethics committee of
119 Coventry University (application number: P106195) in May 2020. Recruitment was conducted through
120 social media and with the support of Verity (the UK PCOS charity) and PCOS support groups on
121 Facebook. Participant eligibility criteria included female sex with a previous medical diagnosis of
122 PCOS, age from 18 to 45 years, and UK residency.

123 A range of structured and validated questionnaires were used to collect the study data; questionnaires
124 were completed online using the survey software, Qualtrics[®] XM (Qualtrics XM, Provo, Utah, USA).
125 Where participants expressed an interest in participation, a study URL link to the survey was emailed
126 to them directly. Alternatively, participants could access the questionnaires directly via the same study
127 URL posted on social media channels. The study URL link contained an initial participant information
128 sheet, as well as provision of informed consent. Where participants failed to complete the provided
129 online survey, this was translated as withdrawal from the study and all data for these participants were
130 excluded from the final analyses.

131 To capture relevant participant characteristics, a demographics questionnaire was created for this
132 survey. This included self-reported information about time since PCOS diagnosis and diagnosed PCOS
133 phenotype, height, weight, age, questions relating to sleep affected by COVID-19 restrictions (*i.e.* ‘to

134 *what extent do you believe that quarantine measures due to COVID-19 have affected your sleep*
135 *pattern?*”), presence of comorbidities and typical sociodemographic questions. In the context of this
136 study, the PCOSQOL was utilized as a validated measure of QoL (48). The PCOSQOL is a disease-
137 specific questionnaire which was developed and validated to measure QoL in UK women with PCOS,
138 and is also the first PCOS-specific measurement tool to encompass all phenotypic subgroups according
139 to the most recent diagnostic criteria (48). Briefly, this questionnaire incorporates 35 Likert-based
140 questions allowing participants to report the impact of various PCOS-related symptoms upon their day-
141 to-day life, with subscales which allow reporting of the impact of PCOS, infertility, hirsutism and mood
142 upon QoL (49-51). Total scores are summated with lower scores indicative of poorer QoL.

143 Information about the mental health wellbeing of each participant was also captured using the
144 Depression, Anxiety and Stress Scale (DASS-21) (52). The DASS-21 includes 21 questions, seven
145 relating to each domain for depression, anxiety and stress, and requires respondents to rate their level
146 of agreement (0-3) to a series of statements. Each domain score is calculated by summing the responses
147 and multiplying by two, whilst normative and cut-points for depression, anxiety and stress are
148 provided. Finally, the Insomnia Severity Index (ISI) was applied to measure participants’ self-
149 perceived insomnia (53), as a validated and reliable tool for the assessment of insomnia severity (54,
150 55). The ISI targets the subjective symptoms and consequences of insomnia, as well as the degree of
151 concerns or distress caused by those difficulties. The ISI is composed of seven items that, respectively,
152 evaluate the severity of sleep-onset (initial), sleep maintenance (middle), early morning awakening
153 problems (terminal), satisfaction with current sleep pattern, interference with daily functioning,
154 noticeability of impairment attributed to the sleep problem, and level of distress caused by the sleep
155 problem. Each of these items is rated on a five-point Likert scale and the time interval is “*in the last 2*
156 *weeks*”. Total ISI scores range from 0-28, with higher scores indicating greater insomnia severity.

157 ***Statistical Analysis***

158 Statistical analysis was completed in IBM SPSS Statistics for Windows (Version 26.0, IBM Corp;
159 Armonk, NY) and in R statistical software (R Core Team (2018). *R: A Language and environment for*
160 *statistical computing*. [Computer software]. Retrieved from <https://cran.r-project.org/>), using the *car*:
161 and *MASS*: packages) (56, 57), and statistical significance was set at $p < 0.05$. Descriptive characteristic
162 reports were generated and Shapiro-Wilk tests of normality were completed. Accordingly, a non-
163 parametric approach was adopted for subsequent analysis, as appropriate. Responses to the question
164 ‘*to what extent do you believe that quarantine measures due to COVID-19 have affected your sleep*
165 *pattern?*’ were split into a dichotomous response – namely, into negative effects or no effect/positive
166 effects – which was used as a categorical variable. Independent samples Mann-Whitney U tests were
167 completed to evaluate the between group differences. Spearman’s correlations between the ISI and
168 other questionnaires (*i.e.* PCOSQOL total and domain scores, and the DASS-21) were also completed
169 for the entire study cohort and also within each group.

170 Given the Likert scale nature of the data in this study, where Likert scales are a special case of ordinal
171 data, we utilized an ordinal logistic regression (OLR) approach. The OLR approach is comparable to
172 a conventional multiple regression approach, where there may be one dependent variable and one or
173 more independent variables. It does however differ from ordinary least squares multiple regression, by
174 treating the dependent variable as an ordered categorical variable, based upon the principle of
175 cumulative-odds (58). The coefficient of determination, R^2 , summarizes the proportion of variance in
176 the dependent variable associated with the independent variables, with larger R^2 values indicating that
177 more of the variation is explained by the model, to a maximum of 1. However, in non-parametric
178 regression, it is not possible to compute a traditional R^2 , and a pseudo R^2 is computed instead. In this
179 study, we opted to report Nagelkerke’s R^2 (R^2_N), which is an adjusted version of the Cox & Snell R^2
180 that adjusts the scale of the statistic to cover the full range from 0 to 1 (59, 60). To test the statistical

181 significance of each model coefficient (β), we used the Wald test to compute a Wald statistic with a
182 chi-square distribution. All participant background characteristics were adjusted for in the OLR.

183

184 **3 Results**

185 In total, 333 participants met the eligibility criteria and consented to participate in the present study,
186 completing the online survey. Pertinent demographics/characteristics for the recruited study cohort are
187 presented in Table 1. The vast majority of the study participants (92.5%) were of White ethnic
188 background. Of the recruited cohort, 40% were married and a further 40% were single, with the
189 remaining 20% being in other non-married relationships, divorced, separated or widowed.
190 Approximately 73% of participants stated that they have no children. Moreover, the majority (63.1%)
191 of the study participants were in full-time employment, 40.2% were educated to at least degree level,
192 and 51.1% had the lowest household income (\leq £39,999). Finally, participants were asked to self-report
193 their diagnosed PCOS phenotype; 46.5% indicated that they had all three PCOS diagnostic
194 characteristics (*i.e.* hyperandrogenism, menstrual disruption, and PCO), 13.5% PCO and menstrual
195 disruption, 9.6% PCO and hyperandrogenism, 6.9% hyperandrogenism and menstrual disruption, and
196 the remaining 23.1% were unsure of the PCOS phenotype with which they had been diagnosed.

197 *****Insert Table 1 here*****

198 When participants' responses to the question about the impact of COVID-19 restrictions on their sleep
199 were dichotomized into negative and no/positive responses, 242 participants reported that they had
200 experienced either a significant or small negative effect upon their sleep, whilst the remaining 91
201 reported either no such effect, or at least a small positive effect upon their sleep. Using the ISI scoring
202 guidelines, 44.2% of those reporting negative effects met the scoring threshold (>14) for a diagnosis

203 of at least moderately severe clinical insomnia. Key outcomes of interest were compared between these
204 two study groups and these findings are summarized in Table 2.

205 *****Insert Table 2 here*****

206 Overall, there were no differences between the study groups regarding age, weight, body mass index
207 (BMI), time since PCOS diagnosis, or number of comorbidities. As expected, the self-reported
208 insomnia severity assessed by the ISI was significantly higher in those who reported a negative effect
209 of COVID-19 on their sleep quality compared to those who reported no such effect or a relevant
210 positive effect (Table 2). Furthermore, the former also reported poorer QoL, as measured by the total
211 PCOSQOL score, whilst they also reported a greater impact of PCOS and poorer mood in the
212 corresponding PCOSQOL domains. Finally, based on the corresponding DASS-21 scale scores, those
213 reporting a negative effect of COVID-19 on their sleep quality also had statistically higher depression
214 and stress levels, but not anxiety, compared to those who reported no such effect (Table 2).

215 For the entire study cohort, Spearman's correlation tests showed an inverse correlation between the ISI
216 and PCOSQOL total score ($r_s = -.384, p < .001$), and domain scores for Impact of PCOS ($r_s = -.379, p$
217 $< .001$), Infertility ($r_s = -.225, p < .001$), Hirsutism ($r_s = -.205, p < .001$), and Mood ($r_s = -.405, p < .001$).
218 Furthermore, significant positive correlations were also noted between the ISI and the DASS-21
219 Depression ($r_s = .377, p < .001$), Anxiety ($r_s = .410, p < .001$), and Stress ($r_s = .467, p < .001$) scores.
220 These correlations between the ISI and the total PCOSQOL score, all PCOSQOL domains apart from
221 Hirsutism, and DASS-21 scores also remained statistically significant within each of the two groups
222 (data not shown).

223 Results of the OLR indicated that Stress, Anxiety, and Depression, as measured by the DASS-21,
224 alongside PCOSQOL domain scores for Mood, Hirsutism, Infertility, and Impact of PCOS were
225 significant predictors of ISI score (all p values $< .01$; Table 3). Furthermore, we found that the DASS-

226 21 variables were the greatest predictors of ISI score, accounting for the largest proportion of variance
227 in the dependent variable (Stress: Wald χ^2 : 87.23, OR: 1.23 (1.18, 1.29), R^2_N : 0.05, $p < .001$; Anxiety:
228 Wald χ^2 : 64.06, OR: 1.19 (1.14, 1.25), R^2_N : 0.03, $p < .001$; Depression: Wald χ^2 : 55.5, OR: 1.15 (1.11,
229 1.20), R^2_N : 0.03, $p < .001$). Finally, no participant characteristic significantly influenced the direction
230 or magnitude of the OLR (all p values $> .2$).

231 ***Insert Table 3 here***

232 4 Discussion

233 To our knowledge, this is the first study to assess the self-reported sleep quality of women with PCOS
234 in the UK during the lockdown/quarantine measures imposed in response to the COVID-19 pandemic,
235 and explore potential corresponding associations with QoL and depression, anxiety, and stress levels
236 in this female population. Of note, according to the findings of the present study approximately 73%
237 of the study participants reported that their sleep quality had worsened since COVID-19 restrictions
238 were imposed. Interestingly, when compared to data from a study in the general population during
239 COVID-19 lockdown measures (61), the prevalence of clinical insomnia based upon the ISI among the
240 women with PCOS of the present study was markedly greater (~35% vs ~10%). Our findings are in
241 accord with data reported from a web-based study in the Greek general population during the national
242 lockdown due to COVID-19, where 37.6% of participants (particularly women) scored above the
243 threshold for insomnia based on a relevant validated questionnaire (62). Prior to the COVID-19
244 pandemic, global estimates for the prevalence of insomnia ranged between 3.9% to 22% (63), thus
245 these findings suggest that there has been an exacerbation of sleep disturbances (*e.g.*, insomnia) during
246 this pandemic.

247 The present findings showing that the majority of women with PCOS self-report negative effects upon
248 their sleep during the COVID-19 restrictions highlight insomnia and poor sleep health as a significant

249 problem in this female population. However, it should be noted that it is difficult to determine the
250 magnitude of this problem/change without having relevant baseline assessments before this pandemic.
251 Indeed, due to practical difficulties in studying women with PCOS in representative population-based
252 samples, there is an overall paucity of data on the prevalence of sleep disturbances in this population
253 to allow precise comparisons (64). Notably, one common known sleep disorder in women with PCOS
254 is OSA, with a recent meta-analysis reporting that OSA prevalence in women with PCOS is 35% (95%
255 confidence interval: 22.2 to 48.9%) which is further increased in the presence of overweight/obesity
256 (45). Nevertheless, OSA does not appear to be a defining factor for the findings of the present study,
257 since only 1.2% of participants indicated that they had received a medical diagnosis of OSA, and there
258 were no between group differences for BMI or additional comorbidities (*e.g.*, T2DM) that are often
259 associated with PCOS and OSA (26). Undiagnosed OSA is common in this female population (26),
260 and may also be present among the participants of this cohort, but whether this could be an underlying
261 factor contributing to the present findings requires further and more targeted research.

262 Another mechanism contributing to sleep disturbances in this study may relate to increased depression,
263 anxiety and stress levels. Indeed, depression, anxiety and stress yield the largest beta coefficients and
264 account for the largest amount of variance to ISI scores in the results of the ordinal logistic regression
265 in the present study. Of interest, when the whole study cohort was considered, 51.5% reported that they
266 had previously received a medical diagnosis of anxiety and/or stress. Whilst it was unclear whether
267 these diagnoses were made prior to, or during the COVID-19 pandemic, additional insight can be
268 gained from the self-reported DASS-21 scores. Based on this validated questionnaire, the prevalence
269 rates of at least mild depression, anxiety, and stress in the study cohort were 80.5%, 70.6% and 64.6%,
270 respectively, which are higher than the reported corresponding medical diagnoses. Notably, these are
271 also higher than those reported by a meta-analysis for depression (33.7%; 95% CI: 27.5 to 40.6),
272 anxiety (31.9%; 95% CI: 27.5 to 36.7), and stress (29.6%; 95% CI: 24.3 to 35.4) in the general

273 population during the COVID-19 pandemic (65). Collectively, these data suggest that during the
274 current pandemic, women with PCOS are experiencing a greater psychological burden than the general
275 population, with a markedly higher prevalence. This is in accord with the latest international evidence-
276 based guidance on PCOS, which highlights that, irrespective of a global pandemic, women with PCOS
277 are more likely to experience depression and anxiety (66).

278 Other reported risk factors for decreased sleep quality during the COVID-19 pandemic are changes to
279 sleep patterns (61), worries about health (67), financial consequences (68), social interactions (69),
280 reduced physical activity (62), and gender with women being reportedly 56% more likely than men to
281 experience sleep disruption during this pandemic (70). As such, it is plausible that such factors further
282 contribute to a potential multifactorial effect upon an already ‘at risk’ population (71), which clearly
283 exacerbates sleep disruption and may result in reduced QoL. Indeed, the results of the present study
284 support this notion, since women with PCOS who reported negative sleep effects during the COVID-
285 19 pandemic also exhibited reduced QoL (as measured by the PCOSQOL) compared to those without
286 any, or with positive effects on sleep. Based on the corresponding PCOSQOL domains, this association
287 was apparently burdened by the impact of PCOS and affected mood in the study participants. However,
288 what cannot be determined by the present findings is the directional role of sleep disruption in the
289 aforementioned milieu for which further studies are clearly needed.

290 Interestingly, longitudinal studies have previously reported associations between sleep disorders,
291 anxiety, and depression (72, 73), which are known to independently impair QoL (74). Moreover, it has
292 been purported that there is a bidirectional relationship between sleep quality and mental wellbeing
293 (75), with sleep quality independently predicting the prevalence of anxiety and/or depression, whilst
294 anxiety and depression are also predictors for reduced sleep quality (42, 76). Due to the nature of our
295 analysis, the current study is unable to determine the causal direction between sleep and mental
296 wellbeing. However, it is likely that the COVID-19 pandemic has created an overarching environment

297 which further exacerbates this relationship with the net result being further impairments of mental
298 health and sleep quality leading to reduced QoL. As prior to the COVID-19 pandemic, women with
299 PCOS were already recognized as a patient population at an increased risk of anxiety/stress, depression,
300 sleep disorders and impaired QoL (18, 19); the disrupting circumstances of this pandemic mean then
301 that there should be a renewed and heightened focus from healthcare professionals to ensure that
302 adequate support and treatment provision is available to reduce and, where possible, prevent further
303 comorbidity and impaired QoL in these women (16).

304 *Study Limitations*

305 There are certain limitations which should be acknowledged in the present study. This study relied
306 upon participant self-report which can lead to a degree of decreased clarity/accuracy in the provided
307 answers, thus inevitably introducing a degree of information bias to the study findings. For example,
308 it is known that individuals tend to over-report their height and under-report their weight (77), an effect
309 which appears to be further exaggerated in individuals with overweight/obesity (78). This may lead to
310 discrepancies in self-reported anthropometric data which, given the key role of metabolic health in
311 PCOS severity/comorbidity (79) and sleep quality (26) may impact to some degree on the study
312 findings. However, this methodology is frequently employed in studies of this nature, whilst validated
313 instruments/questionnaires were utilized to capture key study data of interest. Another study limitation
314 is the lack of comparative baseline data for the study cohort for a period prior to the COVID-19
315 pandemic. The study survey questions asked about changes in sleep quality due to COVID-19
316 restriction measures, but without validated baseline measurements, it is not possible to quantify the
317 exact extent to which the corresponding outcomes have been affected. This issue could be addressed
318 to some degree at a follow-up time point when current restrictions have been eased/lifted. To this aim,
319 the relevant prospective follow-up of this study cohort has been planned. Furthermore, although the
320 large sample size in the present study is a distinct strength, it is accompanied by some inherent

321 limitations. For instance, OLR yielded significant R^2_N for all variables, yet most were of little practical
322 significance; thus, in interpreting these results, the potential fallacy of large sample sizes must be
323 considered (80). Finally, as this is a cross-sectional study, the present findings cannot be used to infer
324 conclusions regarding the temporal/causal relationship between the noted negative impact on sleep and
325 reported levels of depression/stress.

326 **5 Conclusion**

327 The present study offers a novel insight regarding the self-reported sleep quality of women with PCOS
328 during the COVID-19 pandemic lockdown, and how this is associated with QoL and depression,
329 anxiety, and stress levels in this population. Based on our present findings, it is evident that the majority
330 of UK women with PCOS in this study cohort feel that the applied measures imposed in response to
331 the COVID-19 pandemic had a negative impact on the quality of their sleep, with high prevalence of
332 insomnia. There is also evidence that those women with PCOS and impaired sleep have greater levels
333 of psychological morbidity (*e.g.*, depression/stress) and reduced QoL. Whilst it appears that the
334 restrictive measures due to COVID-19 have increased this comorbidity burden in these women with
335 PCOS, the exact magnitude of the impact of this global pandemic upon these parameters and the
336 underlying temporal/causal relationship is less clear. Nevertheless, it has previously been reported that
337 during such disease outbreaks, the number of individuals whose mental health is negatively affected
338 can be greater than the number affected by the infection (81), and that the mental health implications
339 and their prevalence can be even more significant than the epidemic itself (82). Another key message
340 to consider based on the present study is that there are certain groups that may remain relatively
341 overlooked despite being particularly vulnerable during this pandemic. Women with PCOS should be
342 considered within these parameters, since they are at increased risk of cardio-metabolic complications
343 which, in turn, may increase the risk of severe COVID-19, whilst they are also susceptible to significant
344 psychological comorbidity which, regardless of COVID-19, may impair their overall wellbeing.

345

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557

558 **7 Conflict of Interest**

559 *The authors declare that the research was conducted in the absence of any commercial or financial*
560 *relationships that could be construed as a potential conflict of interest.*

561 **8 Author Contributions**

562 CK, LA, GM, JEB, IK, HSR developed the study protocol. CK drafted the initial manuscript. CK and
563 CCTC performed the statistical analyses. CK, CCTC, LA, GM, JEB, IK, HSR contributed to the
564 literature search and drafted and/or revised sections of this manuscript. IK and HSR supervised the
565 study, combined, edited and revised all drafts of this manuscript. All authors approved the final
566 manuscript.

567

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570

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576

577

578 **Table 1.** Breakdown of socioeconomic and ethnicity characteristics of interest for the study cohort of UK women
 579 with polycystic ovary syndrome [PCOS; N = 333; median age (interquartile range) = 30.0 (9.0) years].

Variable	N (%)
Ethnicity	
White	308 (92.5)
Mixed background	9 (2.7)
Asian or Asian British	8 (2.4)
Black or Black British	4 (1.2)
Other ethnic background	3 (0.9)
Declined to indicate	1 (0.3)
Relationship status	
Single	134 (40.2)
Married	132 (39.6)
Co-habiting	22 (6.6)
Long-term relationship	19 (5.7)
Civil-partnership	12 (3.6)
Engaged	8 (2.4)
Divorced	3 (0.9)
Separated	2 (0.6)
Widowed	1 (0.3)
Children	
No	242 (72.7)
Yes	91 (27.3)
Education	
Undergraduate	135 (40.2)
College	107 (32.1)
Postgraduate	60 (18.0)
Secondary	26 (7.8)
Doctorate	5 (1.5)
Employment	
Full-time employment	210 (63.1)
Part-time employment	47 (14.1)
Student	27 (8.1)
House person	19 (5.7)
Unemployed	21 (6.3)
Self-employed	9 (2.7)
Household income	
≤ £39,999	170 (51.1)
£40,000-£79,999	137 (41.1)
≥ £80,000	26 (7.8)

All percentage data has been rounded to one decimal place.

580

581 **Table 2.** Key outcomes of interest for the study cohort of UK women with polycystic ovary syndrome
 582 (PCOS) when split into a dichotomous response regarding the impact of the lockdown measures due
 583 to COVID-19 on sleep (reported negative effects versus no or positive effect).

Study Variables/Outcomes	Full study cohort of women with PCOS (N = 333)	Negative impact on sleep (N = 242)	No/Positive impact on sleep (N = 91)	<i>P</i>
Age (years)	30.0 (9.0)	29.0 (9.0)	30.0 (10.3)	.426
Years Since PCOS Diagnosis	8.0 (9.9)	7.3 (9.8)	8.2 (12.0)	.336
Weight (kg)	93.9 (37.9)	93.9 (37.2)	91.2 (37.5)	.290
BMI (kg/m ²)	34.8 (13.6)	35.0 (13.1)	34.0 (14.7)	.322
PCOSQOL				
Total Score	101.0 (60.5)	97.0 (59.0)	114.0 (65.8)	.003
Impact of PCOS	40.0 (28.5)	38.0 (26.0)	50.5 (30.5)	.001
Infertility	24.0 (27.0)	23.0 (27.0)	30.5 (26.5)	.077
Hirsutism	16.0 (18.0)	16.0 (17.0)	17.5 (20.3)	.348
Mood	17.0 (10.0)	16.0 (9.0)	21.0 (11.0)	.001
DASS-21				
Depression	18.0 (17.0)	18.0 (16.0)	13.0 (16.0)	.014
Anxiety	10.0 (12.0)	12.0 (12.0)	10.0 (11.0)	.094
Stress	18.0 (14.0)	18.0 (12.0)	15.0 (14.5)	.007
Insomnia Severity	12.0 (9.5)	14.0 (8.0)	7.0 (8.0)	<.001
Comorbidities	1.0 (2.0)	1.0 (2.0)	1.0 (3.0)	.737

Data are presented as median (interquartile range). Between group comparisons performed by independent samples Mann-Whitney U tests. Insomnia severity as assessed by the validated Insomnia Severity Index (ISI). Significance was set at $p < 0.05$. BMI: body mass index; PCOSQOL: Polycystic ovary syndrome quality of life questionnaire; DASS-21: Depression, Anxiety and Stress Scale; *P*: asymptotic two-sided significance.

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585

586

587 **Table 3.** Results from the ordinal logistic regression (OLR) for the study cohort of UK women with polycystic ovary syndrome (PCOS).

Predictor	β	95% CI		SE	Z	OR	95% CI		Wald χ^2	R ² _N	p
		Lower	Upper				Lower	Upper			
DASS-21 Stress	0.21	0.17	0.25	0.02	9.055	1.23	1.18	1.29	87.23	0.05	< .0001
DASS-21 Anxiety	0.17	0.13	0.22	0.02	7.793	1.19	1.14	1.25	64.06	0.03	< .0001
DASS-21 Depression	0.14	0.11	0.18	0.01	7.314	1.15	1.11	1.20	55.5	0.03	< .0001
PCOSQOL Mood	-0.12	-0.1	-0.08	0.01	-7.692	0.88	0.86	0.91	62.49	0.02	< .0001
PCOSQOL Hirsutism	-0.03	-0.05	-0.01	0.008	-3.288	0.97	0.95	0.99	10.98	0.005	.001
PCOSQOL Infertility	-0.03	-0.04	-0.01	0.006	-3.942	0.97	0.96	0.98	15.79	0.008	< .0001
PCOSQOL Impact of PCOS	-0.03	-0.04	-0.02	0.005	-6.771	0.96	0.95	0.97	48.01	0.02	< .0001

CI: Confidence Interval, β : beta-coefficient, SE: Standard Error, OR: Odds ratio, R²_N: Nagelkerke's pseudo-R²

PCOSQOL: Polycystic ovary syndrome quality of life questionnaire; DASS-21: Depression, Anxiety and Stress Scale (21 item)