



Obesity impairs general health-related quality of life (HR-QoL) in premenopausal women to a greater extent than the polycystic ovary syndrome (PCOS)

Journal:	<i>Clinical Endocrinology</i>
Manuscript ID:	CEN-2010-000337.R1
Manuscript Type/Office:	2 Original Article - Europe, excluding UK
Date Submitted by the Author:	08-Jun-2010
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Key Words:	Hirsutism < Conditions: < Ovary, Female infertility < Conditions: < Ovary, Polycystic ovary syndrome < Conditions: < Ovary

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3 1 **Title:** Obesity impairs **general** health-related quality of life (HR-QoL) in premenopausal women to a
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5 2 greater extent than the polycystic ovary syndrome (PCOS).
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10 4 **Short Title:** Obesity, PCOS and HR-QoL
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40 18 **Key words:** Quality of life, obesity, polycystic ovary syndrome.
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44 20 **Acknowledgements:** This study was supported by the Spanish Ministry of Science and Innovation,
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46 21 Instituto de Investigación Carlos III, grant FIS PI080944. CIBERDEM is also an initiative of Instituto
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48 22 de Investigación Carlos III.
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53 24 **Financial disclosure:** The Authors have nothing to disclose
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55 25

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57 26 **Word count:** 2667; **Word Count for Abstract:** 221; **Number of Tables:** 4; **Number of Figures:** 1
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3 27 **STRUCTURED SUMMARY**
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7 29 *Objective:* Obesity is frequently associated with the polycystic ovary syndrome (PCOS), and both
8 30 conditions may impact the health-related quality of life (HR-QoL) of affected patients. We aimed to
9 31 estimate the relative impact of obesity and PCOS on the general HR-QoL of premenopausal women.

10 32 *Design:* Case-control study.

11 33 *Patients:* Consecutive overweight and obese premenopausal women seeking advice for weight loss, of
12 34 whom 32 were diagnosed with PCOS and 72 had no evidence of androgen excess and were considered
13 35 controls.

14 36 *Measurements:* Spanish versions of the Short Form 36 Health Survey (SF-36) questionnaire and the
15 37 Nottingham Health Profile (NHP) were self-administered by the women.

16 38 *Results:* PCOS patients and controls had similar body mass index, yet controls were older. General
17 39 HR-QoL mean scores were similar in both groups, yet PCOS patients scored worse in the role-
18 40 emotional item of SF-36, and controls scored worse in the pain item of NHP. Increasing grades of
19 41 obesity, on the contrary, were associated with worse scores in the NHP and SF-36 items related to
20 42 general and physical aspects of HR-QoL. When compared with the standards established for the
21 43 Spanish general population, both PCOS patients and controls frequently presented with abnormal
22 44 scores, yet only increasing grades of obesity were associated with more frequent abnormal scoring.

23 45 *Conclusions:* Obesity impaired general HR-QoL to a greater extent than PCOS in overweight and
24 46 obese premenopausal women.
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47 Introduction

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49 Health-related quality of life (HR-QoL) is a multidimensional concept that comprises physical,
50 emotional and social concepts associated with a specific disease and its management.¹ The polycystic
51 ovary syndrome (PCOS) is a life-time disorder that appears in up to 6.5% of Spanish premenopausal
52 women.² The clinical signs and symptoms of PCOS, derived from the androgen excess and ovulatory
53 dysfunction that define the syndrome^{3,4} include hirsutism, acne, menstrual irregularity and infertility
54 and have a peripubertal onset. Therefore, these signs and symptoms exert a negative impact on mood
55 and psychological function of affected women for decades. Not surprisingly, depression is frequent in
56 PCOS patients and the presence of hirsutism has been described in association with anxiety and
57 psychological complaints.⁵⁻¹⁰

58 Moreover, PCOS is frequently associated with insulin resistance, obesity and related metabolic
59 disorders.¹¹ Obesity in particular is present in almost 50% of PCOS patients in clinical series¹¹ and
60 may impair by itself the HR-QoL of women.¹²⁻¹⁵ However, to date it is unclear whether PCOS by
61 itself,¹⁶ or its associations with obesity and other metabolic derangements,¹⁷⁻¹⁹ are the major
62 contributors to the impaired HR-QoL previously reported women in whom both conditions, PCOS and
63 weight excess, coexist.

64 We aimed to delineate the specific contributions of PCOS and of weight excess to the impairment
65 in the general HR-QoL of premenopausal women seeking advice for weight loss.

67 Material and Methods

69 Patients

70 The present study derived from an earlier report addressing the prevalence of PCOS among
71 otherwise healthy premenopausal women seeking medical advice for weight loss.²⁰ In brief, all the
72 premenopausal women referred by their general physicians to the Department of Endocrinology of
73 Hospital Universitario Ramón y Cajal, for weight loss from May 1, 2002, through December 31, 2005,
74 were prospectively evaluated. All the women were referred from the primary care facilities attending a

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3 75 specific suburb of Madrid which has a medium-low socio-economic status. Inclusion criteria required
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5 76 being referred exclusively for weight loss as the main complaint, having a body mass index (BMI,
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7 77 calculated as weight in kilograms divided by the square of height in meters) above 25, being younger
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9 78 than 50 years, and not having classic menopausal symptoms such as hot flushes. **Women taking**
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11 79 **medications that might interfere with hormone profiles, such as contraceptives or insulin sensitizers,**
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13 80 **were also excluded.**

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16 81 The diagnosis of PCOS used the criteria derived from the 1990 conference sponsored by the
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18 82 National Institute of Child and Human Development: clinical and/or biochemical hyperandrogenism
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20 83 together with ovulatory dysfunction, after excluding secondary aetiologies such as non-classic adrenal
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22 84 hyperplasia, hyperprolactinaemia and androgen-secreting tumours.²¹ **Having both hyperandrogenism**
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24 85 **and ovulatory dysfunction, and although an ovarian ultrasound scan was not obtained, the PCOS**
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26 86 **patients diagnosed here also fulfilled more recent definitions of PCOS.**^{3,4,22} The assays and specific
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28 87 methods used to establish these criteria have been described in detail elsewhere.^{20,23,24} The study was
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30 88 approved by the local ethics committee and all participants gave written informed consent.

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33 89 From a total of 113 consecutive women recruited, 32 had PCOS, 3 had hyperandrogenemia
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35 90 without evidence of oligoovulation, 2 had idiopathic hirsutism, 2 had isolated chronic oligomenorrhea
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37 91 without clinical or biochemical hyperandrogenism, and 2 had oligomenorrhea and hyperprolactinemia,
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39 92 precluding the diagnosis of PCOS. The remaining 72 women had no evidence of hyperandrogenism or
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41 93 reproductive abnormalities and were considered as the nonhyperandrogenic control group for further
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43 94 comparisons.²⁰ **Because none of the control women had clinical or biochemical hyperandrogenism or**
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45 95 **menstrual disturbances or ovulatory dysfunction, the presence of PCOS according to recent**
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47 96 **definitions^{3,4,22} was ruled out reliably in all of them even in the absence of an ovarian ultrasound scan.**
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49 97 The present study focuses on the comparison of **general** HR-QoL among the 32 PCOS patients with
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51 98 the 72 controls.

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57 100 *HR-QoL questionnaires*
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3 102 We measured **general** HR-QoL using the Spanish versions of the Short Form 36 Health Survey
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5 103 (SF-36) questionnaire²⁵ and the Nottingham Health Profile (NHP).²⁶
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7 104 The SF-36 questionnaire uses 36 questions to estimate HR-QoL in eight scaled scores, which are
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9 105 the weighted sums of the questions in their section. Four scores measure physical health (physical
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11 106 functioning, role-physical, bodily pain and general health) and four measure mental health (vitality,
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13 107 social functioning, role-emotional and mental health).²⁷ Each scale is directly transformed into a 0-100
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15 108 scale on the assumption that each question carries equal weight. The higher the score, the better the
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17 109 result for the particular item.
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20 110 The NHP is an auto-administered test of 45 questions distributed into two parts. Part I includes 38
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22 111 questions grouped into six sections: physical ability (8 questions), pain (8 questions), sleep (5
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24 112 questions), social isolation (5 questions), emotional reactions (9 questions), and energy level (3
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26 113 questions). Part II consists of 7 general questions that may not be applicable and is seldom used
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28 114 nowadays. Each question has to be answered as 'yes' or 'no'. Each scale is weighted, and the weights
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30 115 are transformed to yield scores from 0 (no distress) to 100 (maximum distress). Scores are obtained for
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32 116 each section and combined in order to obtain a total score.
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35 117 The SF-36 and NHP questionnaires were self-administered by the women **early in the morning and**
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37 118 **3 to 8 days after a spontaneous or progesterone-induced withdrawal menstrual bleeding.** We compared
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39 119 the results of the PCOS patients with those of the controls, and we also compared the results of both
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41 120 groups with the reference percentiles established for the Spanish general population of the same age-
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43 121 range and sex.^{28,29} Values above the 95th percentile were considered abnormal for the NHP, and values
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45 122 below the 5th percentile were considered abnormal for the SF-36.
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51 124 *Statistical analysis*

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55 126 We express results as means \pm SD unless stated otherwise. We used the Kolmogorov-Smirnov test
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57 127 to estimate the distribution of continuous variables, and we applied logarithmic or square root
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59 128 transformations as needed to ensure normality. We submitted normally distributed variables to a
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129 general linear model that included having PCOS or being a control as the independent variable, and

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3 130 included age as a covariate to correct for the difference in age among PCOS patients and controls.
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5 131 Variables that remained skewed even after mathematical transformation were submitted to Mann-
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7 132 Whitney U tests and, for variables showing statistically significant differences, the possible impact of
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9 133 the difference in age between patients and controls was explored by analyzing Spearman's correlation
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11 134 of these variables with age in the whole population.
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14 135 The impact of the grade of obesity on HR-QoL indexes was explored considering PCOS patients
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16 136 and controls as a whole. We used the Kruskal-Wallis non-parametric ANOVA and, when this test
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18 137 resulted in statistically significant differences, we identified which grades of obesity caused these
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20 138 differences by using repeated Mann-Whitney U tests in which the Bonferroni correction was applied
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22 139 to the level of significance. For nominal and ordinal variables we applied Pearson's χ^2 or Fisher's
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24 140 exact tests, as appropriate.
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27 141 We used the PASW Statistics 18 software (SPSS Inc. Chicago, Illinois) to compute statistic
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29 142 analyses. A $\alpha = 0.05$ level of significance was used for all analyses except when Bonferroni
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31 143 adjustments were needed in order to correct for multiple comparisons among subgroups of women.
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35 36 145 **Results**

37 38 146 39 40 147 *Clinical characteristics of overweight and obese premenopausal women depending on the presence or* 41 42 148 *absence of PCOS*

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44 149 The comparisons of the clinical and biochemical characteristics of PCOS patients and controls
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46 150 are included in Table 1. We introduced age as a covariate in the general linear model because
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48 151 PCOS patients were younger compared with controls. PCOS patients presented with increased
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50 152 hirsutism scores, androgen, triglycerides and luteinizing hormone concentrations, and reduced sex
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52 153 hormone-binding globulin and estradiol levels. PCOS patients were insulin resistant compared with
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54 154 the controls, and therefore had increased fasting insulin levels and homeostasis model assessment
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56 155 insulin resistance and β -cell function indexes, and reduced insulin sensitivity index as calculated from
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58 156 the results of an oral glucose tolerance test.³⁰ **The number of pregnancies and deliveries was reduced in**
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60 157 **PCOS patients when compared with the controls.**

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159 Impact of PCOS on the HR-QoL of overweight and obese premenopausal women

160 The only statistically significant difference among PCOS women and controls in the NHP
161 consisted of a reduced score in the bodily pain item of PCOS patients compared with the controls,
162 whereas no difference was observed in any other item (Figure 1). Because this variable was skewed
163 even after mathematical transformations we used nonparametric correlation to estimate a possible
164 influence of the older age of the controls in their higher bodily pain scores. These scores showed a
165 statistically significant yet **very** weak correlation with age ($r^2 = 0.065$, $P = 0.009$).

166 Similarly, PCOS was associated only with a worse score in the role-emotional item of the SF-36
167 test even after correcting for the difference in age, whereas no difference was observed in any other
168 item (Figure 1).

169 When compared with the reference values established for the Spanish population, the percentages
170 of subjects with abnormal scores in the NHP **were** not different in PCOS patients and controls, yet
171 both groups showed a large percentage of women showing abnormally increased scores in the energy
172 and mobility items and in the total score (Table 2). The percentage of women with scores abnormally
173 reduced with respect to the reference populational data was higher in PCOS patients compared with
174 the controls in the role-emotional item of SF-36, and there was a large percentage of women in both
175 groups presenting with abnormal scores in the general health, physical functioning, role-emotional and
176 social functioning items of the SF-36 test (Table 2).

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178 Impact of the grade of obesity on the HR-QoL of overweight and obese premenopausal women

179 For these analyses we considered PCOS patients and controls as a whole, and we classified them
180 according to their BMI into overweight (BMI 25.0 – 29.9 kg/m²), grade 1 obesity (BMI 30.0 – 34.9
181 kg/m²), grade 2 obesity (BMI 35.0 – 39.9 kg/m²) and grade 3 obesity (BMI equal or above 40.0 kg/m²)
182 subgroups.

183 The pain item of the NHP showed abnormally higher scores in women presenting with grade 1, 2
184 and 3 obesity compared with overweight women (Table 3), and the physical ability item was also

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3 185 worse in grade 3 obese women compared with overweight women (Table 3). No other differences
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5 186 among grades of obesity were observed in other NHP items (Table 3).

7 187 Regarding SF-36, women presenting with grade 2 and 3 obesity had abnormally reduced scores
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9 188 compared with overweight women in the physical functioning item (Table 3), and the general health
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11 189 item was also reduced in women with grade 3 obesity compared with the overweight subgroup (Table
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13 190 3).

15 191 Finally, the number of women presenting with scores above the 95th percentile of the NHP scores
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17 192 of the Spanish general population was higher for the physical ability item in obese women compared
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19 193 with overweight women (Table 4), and there was a large percentage of obese presenting with
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21 194 abnormal scores also in the energy and total score of the NHP although not showing differences
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23 195 among grades of obesity (Table 4). Similarly, the number of women presenting with scores below the
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25 196 5th percentile of the SF-36 scores of the Spanish general population was higher for the general health
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27 197 item in obese women compared with overweight women (Table 4), and there was a large percentage
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29 198 of obese presenting with abnormal scores also in the physical functioning, role-emotional and social
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31 199 functioning items, although not showing differences among grades of obesity (Table 4).

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201 Discussion

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203 Our present results suggest that, when adequately paired for weight, there are very few differences
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205 among premenopausal women with or without PCOS in their HR-QoL. Our PCOS patients showed
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207 worse results compared with the controls only for the role-emotional item of the SF-36 questionnaire.
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209 This item evaluates emotional problems that interfere with aspects pertaining to daily life and their
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211 laboral sphere. Also, PCOS patients **scored lower, and therefore better**, in the pain item of the NHP
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213 compared with the controls, yet the older age of the later might explain this particular difference
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215 because HR-QoL worsens with age.³¹

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217 In contrast with the minimal impact of PCOS on HR-QoL, obesity was associated with a broad
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219 worsening of many aspects evaluated by the HR-QoL scales used here, in conceptual agreement with
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221 previous studies in children and adults.^{32,33}

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3 213 Compared with overweightness, obesity associated in our series worse scores in the pain and
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5 214 physical ability items of the NHP and in the physical functioning and general health items of the SF-
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7 215 36. The results regarding the pain and physical ability item of NHP may be related to the well-known
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9 216 association of obesity with osteomuscular disorders and with the obvious difficulties that weight
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11 217 excess impose of mobility.³⁴ Similarly, obesity exerted a negative impact of the SF-36 items related to
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13 218 daily life activities, including mobility and personal care, influencing the general health perception of
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15 219 these women.

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18 220 Moreover, when compared with the standards derived from the general population, obese women
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20 221 frequently scored abnormally in the energy, physical ability and total score items of the NHP, and in
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22 222 the general health and physical functioning items of SF-36. Also, the frequencies of abnormal scores
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24 223 tended to be higher with increasing grades of obesity, reaching statistical significance compared with
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26 224 the overweight subgroup for the physical ability item of NHP and the general health item of SF-36.
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28 225 Although quite frequent, the abnormal scores in the role-emotional and social functioning items of SF-
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30 226 36 were similarly distributed in overweight and obese women. Considering that PCOS was equally
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32 227 prevalent in overweight and obese women in the present series of premenopausal women²⁰ this finding
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34 228 possibly reflected the specific impact of PCOS on the emotional aspects of HR-QoL.

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37 229 The negative impact of obesity may explain the worsening of **general** HR-QoL of PCOS patients
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39 230 in previous studies **by others**, considering that obesity is frequently associated with PCOS.³⁵ The
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41 231 impairment of HR-QoL, psychological well-being and sexual satisfaction in PCOS patients reported in
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43 232 an earlier **study conducted in Germany**^{36,37} might have been influenced by the fact that this series of
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45 233 **German** PCOS patients were much heavier compared with their controls and, **in sharp contrast with**
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47 234 **our present study, the German series included many PCOS patients referred for the treatment of**
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49 235 **infertility, a trait that may impair HR-QoL by itself.**

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52 236 **In conceptual agreement with our present results, previous studies showed** that the differences in
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54 237 HR-QoL among adolescents with or without PCOS disappeared when controlling for the influence of
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56 238 body mass index,³⁸ and no differences in the SF-36 questionnaire were found among PCOS patients
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58 239 and controls in adults when adjusting for weight.¹⁶ Similarly, body mass index was a significant
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60 240 modifier of the differences in the SF-36 found among Australian PCOS patient and controls,¹⁸ **and a**

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3 241 recent systematic review highlighted the importance that weight concerns plays in the impairment of
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5 242 HR-QoL in PCOS patients.³⁹ The contribution of obesity to the impairment of HR-QoL in PCOS
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7 243 patients was highlighted by the improvement observed after successful dietary restriction and life-style
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9 244 modification.⁴⁰

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11 245 However, our present results do not indicate, by any means, that PCOS does not impair HR-QoL
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13 246 by itself. This has been demonstrated in several studies^{7,16,18} by using a disease-specific HR-QoL
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15 247 instrument termed the Polycystic Ovary Syndrome Questionnaire (PCOSQ) that considered 5 domains
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17 248 related to this disorder: emotions, body hair, weight, infertility, and menstrual problems.^{41,42} Our study
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19 249 was, on the contrary, designed to estimate the impact of obesity and PCOS on general HR-QoL
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21 250 instruments, and therefore did not consider disease-specific dimensions that could not be answered by
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23 251 the controls. In fact, many PCOS patients scored abnormally in several items of the NHP and SF-36
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25 252 when compared with the standards derived from the general population.

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27 253 Moreover, the fact that the PCOS patients in our series were younger compared with the controls
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29 254 must be considered when interpreting our present results. As stated above, HR-QoL clearly worsens
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31 255 with age.³¹ Therefore, the age difference in among our PCOS patients and controls might have
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33 256 obscured any difference in general HR-QoL attributable to PCOS. Furthermore, as a whole PCOS
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35 257 patients showed a general HR-QoL similar to non-PCOS women who were several years older,
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37 258 possibility reflecting that their HR-QoL may be inadequately impaired for their younger age.

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39 259 In summary, obesity impaired general HR-QoL to a greater extent than PCOS in overweight and
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41 260 obese premenopausal women. Given the frequent association among both disorders, this finding
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43 261 should be considered when designing therapeutic strategies directed towards the improvement of the
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45 262 quality of life of these women.

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For Peer Review

Table 1. Clinical and biochemical characteristics in PCOS patients and controls

	Patients (n = 32)	Controls (n = 72)	P value
Age (yr)	26.1 ± 7.2	32.5 ± 7.9	<0.001
Body mass index (kg/m ²)	35.7 ± 8	35.3 ± 6.2	0.41
Waist-hip ratio	0.82 ± 0.09	0.80 ± 0.07	0.06
Abdominal circumference (cm)	95 ± 15	94 ± 13	0.11
Total body fat (kg)	35.7 ± 12.2	35.8 ± 11.1	0.52
Relative body fat (%)	38.2 ± 6.9	39.5 ± 5.6	0.84
Systolic blood pressure (mmHg)	116 ± 12	122 ± 19	0.26
Diastolic blood pressure (mmHg)	69 ± 8	72 ± 12	0.19
Hirsutism score	7.3 ± 5.5	1.0 ± 1.6	<0.001
Total testosterone (nmol/litre)	2.2 ± 1.0	1.4 ± 0.5	<0.001
Free testosterone (pmol/litre)	45 ± 21	24 ± 10	<0.001
Sex hormone-binding globulin (nmol/litre)	28 ± 14	37 ± 19	0.08
17-hydroxyprogesterone (nmol/litre)	3.0 ± 1.5	1.8 ± 1.2	0.007
Androstenedione (nmol/litre)	12 ± 6	8 ± 3	0.002
Dehydroepiandrosterone-sulphate (µmol/litre)	5.4 ± 2.0	4.2 ± 0.2	0.25
Luteinizing hormone (U/litre)	6.1 ± 3.7	4.4 ± 2.0	0.003
Follicle-stimulating hormone (U/litre)	5.8 ± 2.9	5.9 ± 1.8	0.74
Estradiol (pmol/litre)	169 ± 139	195 ± 143	0.27
Fasting glucose (mmol/litre)	5.1 ± 0.6	5.3 ± 0.7	0.96
Fasting insulin (pmol/litre)	104 ± 69	76 ± 49	0.02
Homeostasis model assessment-insulin resistance	3.5 ± 2.5	2.7 ± 1.8	0.04
Homeostasis model assessment-β	229 ± 192	128 ± 64	0.01
Insulin sensitivity index	3.9 ± 2.6	5.2 ± 3.4	0.03
Total cholesterol (mmol/litre)	4.7 ± 1.0	4.8 ± 1.0	0.39
High-density lipoprotein-cholesterol (mmol/litre)	1.2 ± 0.2	1.2 ± 0.3	0.41
Low-density lipoprotein-cholesterol (mmol/litre)	3.0 ± 0.8	3.0 ± 0.8	0.49
Triglycerides (mmol/litre)	1.3 ± 1.0	1.1 ± 0.6	0.011
Pregnancies (n)	0.4 ± 0.8	1.2 ± 1.4	0.001
Deliveries (n)	0.3 ± 0.5	0.9 ± 1.1	0.002
Abortions (n)	0.1 ± 0.4	0.3 ± 0.6	0.08

Data are means ± SD. Data were analysed using a general linear model in which age was introduced as a covariate to correct for the difference in age observed between patients and controls. Reproduced from Álvarez-Blasco et al.,²⁰ with permission.

Table 2. Women presenting with abnormal scores in tests of HR-QoL among PCOS patients and controls.

	PCOS patients (n = 32)	Controls (n = 72)	χ^2	P value
Nottingham Health Profile ^a				
Emotional reactions	2 (6%)	8 (11%)	0.602	0.72
Sleep	0 (0%)	1 (1%)	0.449	0.99
Energy	5 (16%)	7 (10%)	0.756	0.51
Pain	0 (0%)	0 (0%)		
Physical ability	3 (9%)	12 (17%)	0.954	0.38
Social isolation	2 (6%)	3 (4%)	0.210	0.64
Total score	3 (9%)	8 (11%)	0.071	0.99
SF-36 questionnaire ^b				
General health	6 (19%)	10 (14%)	0.402	0.56
Mental Health	2 (6%)	5 (7%)	0.017	0.99
Physical functioning	8 (26%)	15 (21%)	0.223	0.64
Role-physical	0 (0%)	3 (4%)	1.373	0.55
Role-emotional	12 (38%)	12 (17%)	5.417	0.02
Social functioning	7 (22%)	10 (14%)	1.033	0.31
Bodily pain	0 (0%)	6 (8%)	2.830	0.17
Vitality	2 (6%)	6 (8%)	0.135	0.99

^a Data are counts (percentage) of women presenting with scores above the 95th percentile of the Spanish general population.

^b Data are counts (percentage) of women presenting with scores below the 5th percentile of the Spanish general population.

Table 3. Influence of the grade of obesity on HR-QoL scores considering PCOS patients and controls as a whole.

	Overweight (25.0 – 29.9 kg/m ²) n = 25	Grade 1 obesity (30.0 – 34.9 kg/m ²) n = 35	Grade 2 obesity (35.0 – 39.9 kg/m ²) n = 30	Grade 3 obesity (> 40.0 kg/m ²) n = 23	χ^2	P value
Nottingham Health Profile						
Emotional reactions	31 ± 26	29 ± 29	24 ± 22	34 ± 30	1.490	0.69
Sleep	22 ± 31	24 ± 32	23 ± 28	20 ± 28	0.356	0.95
Energy	13 ± 25	27 ± 37	22 ± 30	39 ± 42	5.668	0.13
Pain	4 ± 8	16 ± 21 ^a	19 ± 22 ^a	26 ± 25 ^a	14.644	0.01
Physical ability	14 ± 14	28 ± 23	26 ± 25	36 ± 27 ^a	9.940	0.02
Social isolation	10 ± 17	8 ± 16	5 ± 14	11 ± 22	2.634	0.45
Total score	16 ± 15	22 ± 19	20 ± 16	28 ± 21	4.303	0.23
SF-36 questionnaire						
General health	69 ± 15	66 ± 17	56 ± 23	54 ± 21 ^a	9.947	0.02
Mental Health	66 ± 16	68 ± 17	70 ± 19	66 ± 23	0.717	0.87
Physical functioning	90 ± 15	81 ± 20	79 ± 19 ^a	71 ± 22 ^a	16.347	0.001
Role-physical	92 ± 21	88 ± 26	85 ± 27	88 ± 24	2.090	0.55
Role-emotional	65 ± 41	63 ± 46	68 ± 40	65 ± 43	0.111	0.99
Social functioning	80 ± 19	79 ± 27	80 ± 23	72 ± 31	0.876	0.69
Bodily pain	68 ± 22	64 ± 20	65 ± 26	55 ± 23	0.137	0.53
Vitality	58 ± 16	57 ± 19	60 ± 21	57 ± 23	0.558	0.91

Data are means ± SD.

^a $p < 0.05$ compared with overweight women according to Kruskal-Wallis tests, followed by repeated Mann-Whitney tests as *post hoc* analysis, applying Bonferroni correction to the level of significance.

Table 4. Women presenting with abnormal scores in tests of HR-QoL depending on their grade of obesity, considering PCOS patients and controls as a whole

	Overweight (25.0 – 29.9 kg/m ²) n = 25	Grade 1 obesity (30.0 – 34.9 kg/m ²) n = 35	Grade 2 obesity (35.0 – 39.9 kg/m ²) n = 30	Grade 3 obesity (> 40.0 kg/m ²) n = 23	χ^2 ^c	P value ^c
Nottingham Health Profile^a						
Emotional reactions	3 (13%)	4 (13%)	1 (4%)	2 (9%)	0.299	0.69
Sleep	0 (0%)	0 (0%)	1 (4%)	0 (0%)	0.303	1.00
Energy	1 (4%)	4 (12%)	1 (3%)	6 (26%)	1.661	0.29
Pain	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
Physical ability	0 (0%)	4 (13%)	4 (15%)	7 (32%)	5.258	0.02
Social isolation	1 (4%)	1 (3%)	1 (4%)	2 (9%)	0.028	1.00
Total score	1 (4%)	4 (13%)	2 (7%)	4 (18%)	1.355	0.45
SF-36 questionnaire^b						
General health	0 (0%)	3 (10%)	6 (22%)	7 (32%)	5.673	0.02
Mental Health	1 (4%)	1 (3%)	2 (7%)	3 (13%)	0.327	1.00
Physical functioning	1 (4%)	8 (26%)	6 (22%)	7 (36%)	7.327	0.06
Role-physical	0 (0%)	1 (3%)	1 (4%)	1 (5%)	0.927	1.00
Role-emotional	5 (21%)	10 (32%)	5 (19%)	4 (18%)	2.153	0.54
Social functioning	2 (8%)	5 (16%)	4 (15%)	6 (27%)	1.465	0.35
Bodily pain	2 (8%)	1 (3%)	2 (7%)	1 (5%)	0.377	0.62
Vitality	1 (4%)	2 (7%)	2 (7%)	3 (14%)	0.546	0.68

^a Data are counts (percentage) of women presenting with scores above the 95th percentile of the Spanish general population.

^b Data are counts (percentage) of women presenting with scores below the 5th percentile of the Spanish general population.

^c Data were submitted to Fisher's exact test. The grade 1, 2 and 3 obesity categories were merged into an obesity category that was compared with the overweight category because, with the exception of physical functioning and role-emotional, for all HR-QoL items there were more than 20% of cells with expected frequencies below 5 and/or cells with expected categories below 2, not matching the requirements of the χ^2 test.

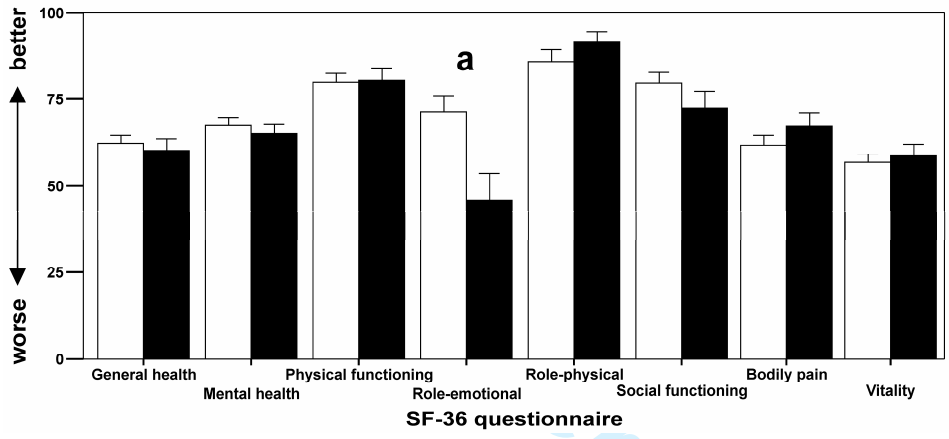
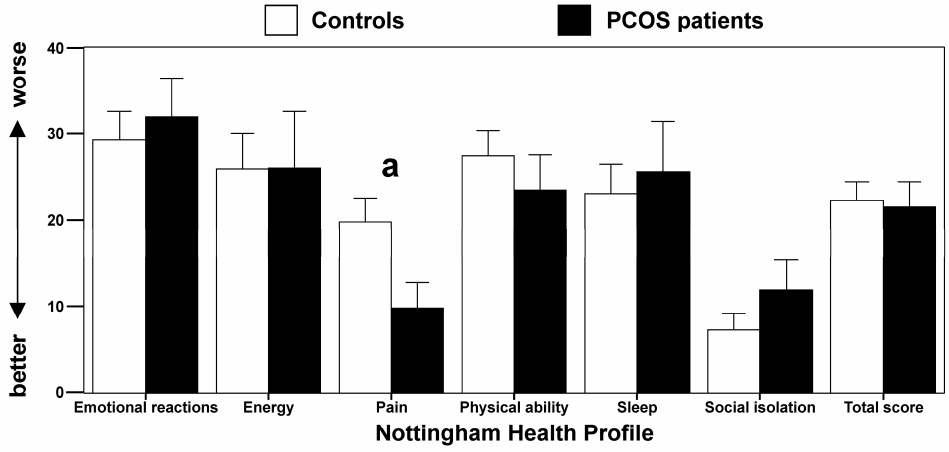
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7 **Figure 1.** Health-related quality of life scores in PCOS patients and controls. Data are means \pm SEM.

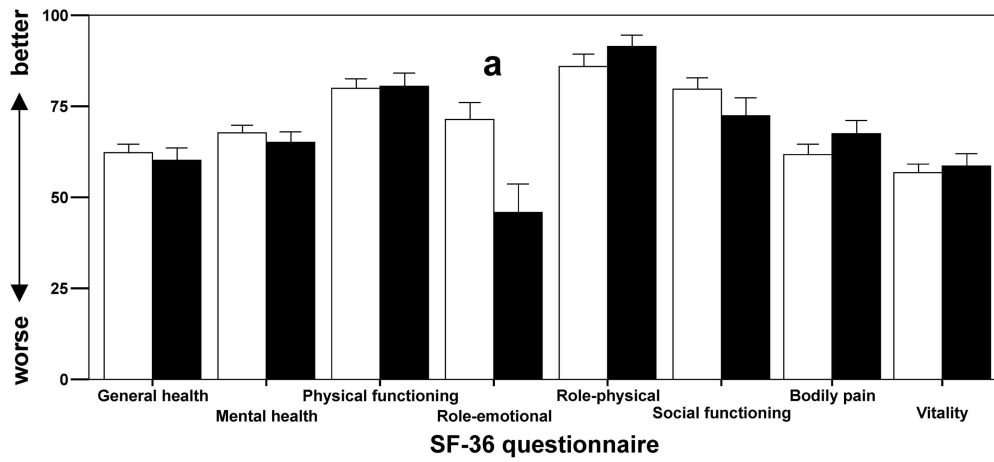
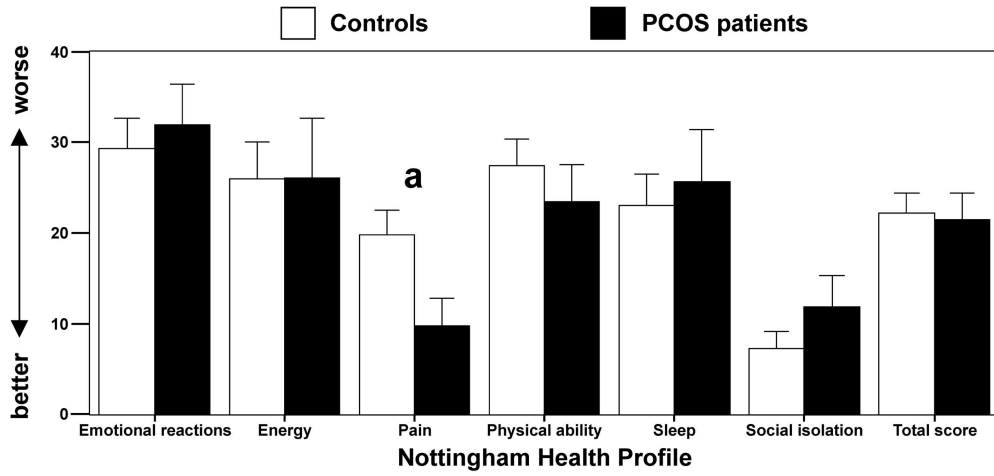
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9 ^a $p < 0.05$ for the comparison of PCOS patients and controls after controlling for a difference in age
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