



Psychological and cognitive factors implicated in pain experience in women with endometriosis

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Pain, mental health, and beliefs in endometriosis

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3 1 **PSYCHOLOGICAL AND COGNITIVE FACTORS IMPLICATED IN PAIN**
4 2 **EXPERIENCE IN WOMEN WITH ENDOMETRIOSIS**
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8 4 **Abstract**
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10 5 Sixty women with a diagnosis of endometriosis (30 with low pain severity - LP; 30 with high
11 6 pain severity - HP) were evaluated at study entry (T0) and after three months (T1). At T0 they
12 7 were compared for different psychological dimensions to sixty-two age-paired healthy women
13 8 (CG). HP group had significantly higher scores on depressive symptomatology, sexual distress,
14 9 and catastrophizing than CG, and higher scores on worry traits than LP. Metacognitive beliefs
15 10 predicted sexual distress at T1, over and above pain severity. Pain affects different domains of
16 11 mental health in this population. Coping strategies, metacognitive beliefs, and worry traits may
17 12 modulate pain experience and psychological distress.
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25 13 **Keywords**
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27 14 Pain, metacognitive beliefs, coping, endometriosis, mental health, sexual distress
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Pain, mental health, and beliefs in endometriosis

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3 15 Pain severely impacts quality of life and mental health of women with endometriosis. However,
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5 16 few is still known about relationships between pain severity and quality of life, mental health,
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7 17 and beliefs. Furthermore, few studies have investigated the predictive value of metacognitive
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9 18 beliefs to subsequent quality of life and mental health among this population. In this manuscript,
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11 19 we discussed main outcomes of a prospective case-control study on women with a diagnosis of
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13 20 endometriosis. Women with endometriosis were assessed two times (T0 and T1, three months
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15 21 follow-up) and compared to a control group (CG). Quality of life, worry trait, depression, sexual
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17 22 distress, pain, coping strategies and metacognitive beliefs were assessed by means of validated
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19 23 questionnaires.
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25 **BACKGROUND**

26 Worldwide, 150 million women suffer from endometriosis. Endometriosis is a gynecological
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28 27 chronic condition, defined as the presence of endometrial-like tissue outside the uterus, which
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30 28 induces a chronic and inflammatory reaction (G.A. Dunselman et al., 2014; Kennedy et al.,
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32 29 2005). The disorder is known to lead to painful symptomatology (i.e. chronic pelvic pain,
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34 30 dyspareunia, dyschesia, low back pain, and dysmenorrhea; Vigano et al., 2004), low quality of
35
36 31 life and severe psychological disturbances (Culley et al., 2013; Pope et al., 2015). According to
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38 32 a range of studies, women with endometriosis show significantly higher levels of depression,
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40 33 somatization, sensitivity, and anxiety when compared to controls (Gambadauro et al., 2019;
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42 34 Laganà et al., 2015; Vitale, La Rosa, Rapisarda, & Lagana, 2017). The impact of pain is so
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44 35 noticeable that several authors have suggested that the pain severity is the major responsible of
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46 36 the psychological distress on this population (Cavaggioni et al., 2014; Culley et al., 2013; De
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48 37 Graaff et al., 2013; G. A. Dunselman et al., 2014; Facchin et al., 2015; Gambadauro et al., 2019;
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50 38 Lagana et al., 2015; Lagana et al., 2017; Lorencatto et al., 2006; Moradi et al., 2014; Pope et
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52 39 al., 2015; Sepulcri & Do Amaral, 2009; Souza et al., 2011). Recent literature evidenced that
53
54 40 psychological and cognitive factors may influence pain experience of women with
55
56 41 endometriosis (Zarbo et al., 2017), highlighting that women with chronic pelvic pain related-
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58 42 endometriosis are more likely to repress emotions than the control group (i.e. healthy women).
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60 43 In addition, some coping strategies (i.e. suppression of emotions, pain catastrophizing and
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45 44 passive coping style) are related to higher self-reported pain. Furthermore, some coping
46
47 45 strategies (i.e. focused on emotions, detached and rational) seem to be related to better mental
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49 46 health, while other (i.e. emotional and avoidance coping styles) to poorer mental status (Donatti
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51 47 et al., 2017; Zarbo et al., 2017).

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3 48 In addition, the recent mixed-method study of Zarbo et al. (2019) delineated a model of onset
4 49 and maintenance of acute pain experience in women with endometriosis in which personality
5 50 traits and coping strategies play a key role . According to the model, psychological distress may
6 51 be both cause (possibly due to neurophysiological or attentional mechanisms) and consequence
7 52 of acute pain in this population. The onset of acute pain is related to automatic ruminative, self-
8 53 blaming and catastrophizing thoughts and to the need to control it which, in turn, bring the
9 54 woman to engage in a range of unsuccessful coping strategies, leading to the onset of a vicious
10 55 circle characterized by negative feelings and emotions (i.e. powerlessness), attempt to control
11 56 the thoughts (i.e. trying suppressing them) and psychological distress (Zarbo et al., 2019).
12 57 In this context, the metacognitive model of Wells & Simons (2009) could provide an efficient
13 58 framework for improving the knowledge of the effects of pain on women's lives and mental
14 59 disturbances in this population. Indeed, cognitions and beliefs about worries about pain (i.e.
15 60 metacognitive beliefs) could impact the way the woman copes with the stressor (i.e. the pain)
16 61 and affect, indirectly, quality of life and mental health. Metacognitive beliefs are defined as
17 62 "stable knowledge or beliefs about one's cognitive system, and knowledge about factors that
18 63 affect the functioning of the system" (Wells, 1995). To the best of our knowledge, to date, only
19 64 one (cross-sectional) study focused on metacognitive beliefs in this population. The study found
20 65 that negative beliefs about worries affect sexual distress over and above dyspareunia and
21 66 chronic pain (Zarbo et al., 2018).
22 67 Concluding, in order to overcome existing limitations of literature, the main aims of this
23 68 research study were: a) to assess differences in quality of life, mental health (i.e. trait worry,
24 69 depressive symptomatology , sexual distress), coping strategies and metacognitive beliefs
25 70 between women with low-pain endometriosis, women with high-pain endometriosis, and
26 71 healthy women; b) to assess the predictive role of metacognitive beliefs on mental quality of
27 72 life, depression and sexual distress outcomes after 3 months.

74 MATERIAL AND METHODS

75 Participants and procedure

76 From December 2016 to April 2018, women with a diagnosis of endometriosis were recruited
77 from a hospital in north Italy to take part to this prospective case-control study. We included
78 women with a diagnosis of endometriosis, without past or concurrent neurological and
79 psychiatric disorders or severe medical conditions, and able to write and read in Italian
80 language. A total of sixty-eight women that met inclusion criteria were approached to take part
81 to the study in the department of obstetrics and gynecology or outpatient clinics in an Hospital

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3 82 in North Italy. Eight of them refused (12%), while sixty (88%) were enrolled in the study.
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5 83 During the enrolment phase (T0), participants completed a range of self-report questionnaires,
6
7 84 and had a clinical interview with a trained psychologist and a gynaecologist. Psychologist did
8
9 85 a structural interview to collect sociodemographic information and data related to current and
10
11 86 past psychiatric or neurological disorders, as well as assisted participants during the compilation
12
13 87 of questionnaires. Gynaecologist was responsible for the gynaecological examination and for
14
15 88 collecting information about the disorder (i.e. symptomatology, previous treatments,
16
17 89 localization, etc.).

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19 90 After three months (T1), women with endometriosis were contacted to complete a part of
20
21 91 questionnaires. Twenty-five women accepted to participate to the second evaluation. Basing on
22
23 92 their clinical history and gynecological examinations, from T0 to T1, women with
24
25 93 endometriosis received specific treatments. In particular, 10 (40%) of them received only
26
27 94 hormonal treatment, 3 (12%) of them did only surgical treatment, 10 (40%) of them received
28
29 95 both hormonal and surgical treatments, and 2 (8%) of them received no treatment.

30
31 96 At T0, the group of women with endometriosis was compared to a control group of sixty-two
32
33 97 healthy women recruited from general population (e.g. non-medical staff of the hospital, friends
34
35 98 or relatives) by e-mail or direct approach. We enrolled women that met the following inclusion
36
37 99 criteria: having not a chronic gynaecological disorder, not reporting past or concurrent
38
39 100 neurological and psychiatric disorders or severe medical conditions, and being able to write and
40
41 101 read in Italian language. Inclusion criteria were listed in informed consent and eligibility of
42
43 102 participants was assessed by self-reported answers to a questionnaire developed ad hoc. Control
44
45 103 group was matched for age with the group of women with endometriosis.

46
47 104 A priori power analysis has been calculated to determine an adequate sample size for the study.
48
49 105 The study was conducted in accordance with APA (1992) ethical standards for the treatment of
50
51 106 human experimental volunteers; each participant provided consent in compliance with the
52
53 107 Declaration of Helsinki (2013). Informed consent was read and signed by all participants. The
54
55 108 study was accepted by the Ethical Committee of Papa Giovanni XXIII Hospital in Bergamo
56
57 109 (Italy).

51 110 **Instruments**

52
53 111 Sociodemographic and clinical information (about endometriosis or other medical conditions)
54
55 112 were collected by means of a structured interview by a gynecologist and a psychologist. Quality
56
57 113 of life, mental health, coping strategies, metacognitive beliefs, and pain symptomatology were
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59 114 collected by means of the following validated self-report questionnaires.
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3 115 **SF-12 Health Survey** (Gandek et al., 1998; Kodraliu et al., 2001) is a 12 item self-report
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5 116 questionnaire that allows the evaluation of the quality of life in several domains. Physical
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7 117 Component Scale (PCS) and Mental Component Scale (MCS) are the two main scales that
8
9 118 assess, respectively, the physical and mental domain of quality of life. Both original and Italian
10
11 119 versions of the scale showed good validity. In this study, it was administered to endometriosis
12
120 group and control group at T0, and to endometriosis group at T1.

13
14 121 **Short-Form McGill Pain Questionnaire** (SF-MPQ; Melzack, 1987) is a self-report scale for
15
16 122 the evaluation of pain severity that includes 15 items and two subscales: Affective subscale and
17
18 123 Somatic subscale. Moreover, a total score can be obtained summing all items. Pain intensity for
19
20 124 each adjective related to pain experience is assessed in a scale from 0 (none) to 3 (severe). The
21
22 125 scale, in this study, was completed by women with endometriosis at both T0 and T1.

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24 126 **Patient Health Questionnaire 9 items** (PHQ9; Mazzotti et al., 2003; Spitzer et al., 1999) is a
25
26 127 brief self-report questionnaire for the evaluation of major depressive symptoms basing on
27
28 128 DSM-IV criteria. Cut-off points allow discriminating stage of depressive symptomatology (i.e
29
30 129 minimal, minor, moderately severe, and severe depression). High sensitivity and specificity
31
32 130 (88%) for major depression has been found in the original version of the scale. In this study,
33
34 131 women with endometriosis completed PHQ9 at both T0 and T1, while the control group
35
36 132 completed it only at T0.

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38 133 **Penn State Worry Questionnaire** (PSWQ; Meyer et al., 1990; Morani et al., 1999) is a self-
39
40 134 report questionnaire including 16 items that allows the assessment of worry traits.. The PSWQ
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42 135 is a trait measure that concerns the habit of worrying in general regardless of moments in time,
43
44 136 regardless of the circumstances. Both the original version and the Italian validation showed
45
46 137 good internal consistency (Meyer et al., 1990; Morani et al., 1999). In this study, both women
47
48 138 with endometriosis and healthy ones completed PSWQ at T0.

49
50 139 **Female Sexual Distress Scale-R** (FSDS-r; Derogatis et al., 2008) is a 13-item self-report
51
52 140 questionnaire that assesses distress related to sexuality over the previous 7 days. Sexual distress
53
54 141 can be diagnosed when the FSDS-R total score is higher than 11. The scale demonstrated a high
55
56 142 degree of internal consistency, as well as good discriminant validity and test-retest reliability
57
58 143 (Derogatis et al., 2008). In this study, women with endometriosis completed FSDS-r at both T0
59
60 144 and T1, while the control group completed it only at T0.

61
62 145 **Cognitive Emotion Regulation Questionnaire – Short Version** (CERQ-short; Garnefski &
63
64 146 Kraaij, 2006) is a self-report multidimensional scale that includes 18 items that assesses
65
66 147 coping strategies in term of individuals' thoughts after having experienced a negative event.
67
68 148 Cognitive coping strategies refer to rather stable styles of dealing with negative life events. The

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149 scale includes nine subscales, which are self-blame, acceptance, rumination, positive
150 refocusing, refocus on planning, positive reappraisal, putting into perspective, catastrophizing,
151 and other-blame. The scale has demonstrated good reliability and validity (Garnefski & Kraaij,
152 2006). In this study, both women with endometriosis and healthy ones completed the scale at
153 T0.

154 **Meta-Cognitions Questionnaire** (MCQ-30; Cartwright-Hatton & Wells, 1997; Quattropiani et
155 al., 2014) is a 30-item self-report scale for the assessment of metacognitive beliefs. The scale
156 is divided into five subscales, which are the “positive beliefs” about worry, “negative beliefs”
157 about the uncontrollability of thoughts and corresponding danger, the “cognitive confidence”,
158 the “Need to control thoughts”, and the “cognitive self-consciousness”. The Italian version of
159 the MCQ-30 (Quattropiani et al., 2014) demonstrated good psychometric properties, satisfactory
160 internal consistency, and convergent validity, as well as a good test-retest reliability. In this
161 study, both women with endometriosis and healthy women completed MCQ30 at T0.

162 **Statistical Analyses**

163 Preliminary analyses were performed to ensure no violation of the assumption of normality. In
164 order to reach our first aim (i.e. assessing differences in quality of life, mental health, coping
165 strategies and metacognitive beliefs between women with low-pain endometriosis, women with
166 high-pain endometriosis, and healthy women) we performed one-way between-groups
167 multivariate analyses of variance (MANOVAs). Low and high pain groups were shaped based
168 on the median score on MPQ-SF total score. The dependent variable was the group: women
169 with low pain endometriosis (LP), women with high pain endometriosis (HP), control group
170 (CG). Independent variables were psychological and cognitive scores. Effect sizes were
171 evaluated using Partial η^2 and interpreted according to the guidelines (small > 0.01; medium >
172 0.06; large > 0.14; Leech et al., 2005). Tukey HSD was applied for post-hoc group comparisons.
173 In addition, in order to assess our second aim regarding the predictive role of MCQ30 at T0 to
174 subsequent (after three months) mental quality of life, depressive symptomatology and sexual
175 distress in women with endometriosis, we performed hierarchical multiple regressions.
176 Therefore, we inserted – respectively- T1_MCS, T1_PHQ9, T1_FSDS as dependent variables.
177 T0_MPQ and - respectively - T0_MCS, T0_PHQ9, T0_FSDS were inserted in Block 1 to be
178 controlled. T0_MCQ30 was inserted at block 2 as predictor.

179 Confounding variables were identified basing on previous literature, conceptual framework and
180 knowledge on the topic. Preliminary regression models were performed in order to investigate
181 the separate and joint effects of variables. R-squared, Adjusted R-squared and F-test were used
182 for assessing fit of multivariable models.

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183 All statistical analyses were performed using the Statistical Package for the Social Sciences
184 (SPSS) version 23.0 and STATISTICA. All statistical tests were two-sided; a p -value $\leq .05$ was
185 considered significant.

186 RESULTS

187 Standardized scores and box plots were used to identify univariate outliers. Variables with
188 values ± 3.29 SD from the mean were considered outliers. Outlier values were brought into
189 range according to Tabachnick and Fidell (2007). Normality of each group was assessed for
190 each variable by examining box-plots, stem and leaf plots, histograms, and skewness and
191 kurtosis values. Results revealed no issues with normality. Missing data were not imputed and
192 were treated as missing. Sociodemographic and clinical information of women with
193 endometriosis ($N=60$) and control group ($N=62$) at T0 are shown in Table 1.

194 << Table 1 >>

195 One-way between-groups multivariate analyses of variance (MANOVAs) were performed to
196 investigate differences in quality of life, mental health, coping strategies and metacognitive
197 beliefs in three groups (i.e. LP; HP; CG). Analyses revealed significant effect of group for PCS,
198 PHQ9, PSWQ, FSDS-r, Refocus planning, Positive reappraisal, and Catastrophizing. Tukey
199 HSD post-hoc comparisons evidenced that HP group had significantly: a) lower scores on PCS
200 than both LP group and CG; b) higher scores on PHQ9, FSDS-r, and Catastrophizing than CG.
201 LP group had significantly: a) lower scores on PCS, PSWQ, Positive reappraisal, and Refocus
202 planning than CG; b) lower scores on PSWQ than HP group. No significant differences among
203 groups were found for MCS, Self-blame, Acceptance, Rumination, Positive Refocusing,
204 Putting Perspective, Other blame, MCQ30_POS, MCQ30_NEG, MCQ30_CC, MCQ30_CSC,
205 and MCQ30 total score. All means, standard errors, F values, Partial η^2 and significance levels
206 are reported in Table 2.

207 <<Table 2>>

208 Then, Hierarchical multiple regressions were used to assess the ability of MCQ30 at T0 to
209 predict levels of subsequent PHQ9, FSDS-r, MCS at T1, controlling for T0_MPQ-SF and –
210 respectively - for T0_PHQ9, T0_FSDS-r, T0_MCS (See Table 3). Our results showed no
211 significant effect of MCQ30 in the prediction of PHQ9 and MCS, while a significant effect has
212 been found for FSDS-r. Indeed, results showed that T0_FSDS-r and T0_MPQ inserted at block
213 1 explained 55% of the variance in T1_FSDS-r. After entry T0_MCQ30 at block 2, the total
214 variance explained by the model as a whole was 64%, $F(3, 20) = 11.58, p < .000$. Therefore,
215 T0_MCQ30 explained an additional 8% of the variance in sexual distress, after controlling for
216 FSDS-r and pain severity at T0, R^2 change = .088, F change (1, 20) = 4.83, $p .04$. In the whole

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217 model, both T0_FSDS-r ($beta = .755, p < .001$) and T0_MCQ30 ($beta = .380, p .040$)
218 significantly predicted subsequent sexual distress severity at T1. Conversely, in the full model,
219 pain severity did not predict FSDS-r at T1.

220 <<Table 3>>

221 **DISCUSSION**

222 We suggest that pain plays an important role in affecting different domains of quality of life
223 and mental health in women with endometriosis and that a strict relationship between pain
224 severity and worry trait/coping strategies seems to exist. Furthermore, we showed that
225 metacognitive beliefs are significant predictors of subsequent sexual distress, over and above
226 previous pain severity and sexual distress score. These findings confirm previous literature and
227 add significant novelty to current research on this population and lead to important clinical
228 implications.

229 ***Pain severity matters: the impact of pain on quality of life, sexual distress and depression***

230 We found that women with high-pain endometriosis had the lowest physical quality of life when
231 compared to low-pain endometriosis and control group. Similarly, women with low-pain
232 endometriosis showed lower physical quality of life than healthy women. Moreover, sexual
233 distress and depressive symptomatology were higher in women with high-pain endometriosis
234 than in the control group. Therefore, pain symptomatology is associated with worse physical
235 quality of life and higher levels of sexual distress and depressive symptomatology. Differences
236 found between the three groups confirmed previous studies of Cavaggioni et al. (2014),
237 Lorencatto et al. (2006), Souza et al. (2011) and Facchin et al. (2015). Indeed, in previous
238 studies, pain has been suggested to play an important role in affecting quality of life and mental
239 health (e.g. depression, anxiety) of women with endometriosis.

240 Moreover, even if the quality of life and depression have been widely investigated in women
241 with endometriosis - as well as in relation to pain and compared to healthy population - sexual
242 distress in this population has been insufficiently studied. Indeed, few studies have focused on
243 the concept of “sexual distress” in this population. The study of Fritzer et al. (2013) found
244 correlations between sexual dysfunctions and sexual distress, while the study of Zarbo et al.
245 (2018) found no association between sexual distress and dyspareunia or chronic pain intensity.
246 In this study, we found that women with high level of pain have higher sexual distress and
247 depressive symptomatology than healthy participants. Interestingly, these differences were not
248 found between women with low-pain and healthy ones, as well as between high-pain and low-
249 pain women with endometriosis. Indeed, healthy women and women with low-pain
250 endometriosis seem to have similar levels of sexual distress and depressive symptomatology.

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251 Our findings lead us to hypothesize that is the severity of pain, and not the presence of
252 endometriosis itself, could play a key role in affecting sexual distress and depressive
253 symptomatology.

254 ***Worry trait is related to the experience of pain***

255 Interestingly, we found higher levels of worry traits in women with high pain endometriosis
256 than in those with low pain. Personality traits (and their relationship with painful symptoms) in
257 women with endometriosis have been few investigated previously (Facchin et al., 2016;
258 Gomibuchi et al., 1993; Sepulcri & Do Amaral, 2009; Zarbo et al., 2019). The studies of
259 Sepulcri and Do Amaral (2009) and Zarbo et al. (2019) found a strict relationship between
260 anxious/worry trait and pain-intensity. Moreover, women without dysmenorrhea seem to be
261 less assertive compared with women who complained of dysmenorrhea and healthy women
262 (Gomibuchi et al., 1993). Similarly, women with painful endometriosis show lower novelty
263 seeking, exploratory excitability, and responsibility as well as higher harm avoidance and
264 fatigability when compared to control group or pain-free endometriosis group (Facchin et al.,
265 2016).

266 Our findings lead us to suggest a key role of worry traits in affecting the experience of pain in
267 women with endometriosis. In the last decades, different hypotheses (cognitive and
268 neurophysiological) have been advanced about the link between anxiety and pain experience.
269 According to the biopsychosocial model of chronic pain and disability, the experience of pain
270 is the result of a dynamic interaction between physiological, psychological, and social factors.
271 Personality traits contribute to the process of pain chronification by making people more
272 vulnerable to respond to pain in an anxious and avoidant style (Peters & Vancleef, 2008).
273 Moreover, neurophysiological mechanisms including the role of periaqueductal grey,
274 amygdala, anterior cingulate cortex (ACC) and anterior insula could play a role in mediating
275 this relationship (Wiech & Tracey, 2009).

276 ***The relationship between pain experience and coping strategies***

277 Our results showed noteworthy differences between groups for some coping strategies. In
278 particular, women with high-pain endometriosis showed higher catastrophizing than the control
279 group. Moreover, women with low-pain endometriosis showed lower scores on positive
280 reappraisal and refocus planning than the control group.

281 Previous findings have suggested that suppression of emotions, pain catastrophizing and
282 passive coping style seem to be related to higher self-reported pain in endometriosis population
283 (Zarbo et al., 2017). Martin et al. (2011), Carey et al. (2014), Zarbo et al. (2019), and McPeak

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284 et al. (2018) have previously highlighted the role of catastrophizing in affecting pain experience
285 in both cross-sectional and longitudinal studies.

286 Moreover, the link between catastrophizing and pain experience has been emphasized in
287 previous studies on different population and settings. On this regard, former studies have
288 suggested that catastrophizing might have a significant impact on pain perception via a specific
289 negative appraisal to stimuli. According to the schema-activation model (Sullivan et al., 2001),
290 individuals who exaggerate the threat value of pain stimuli or pain sensations will likely
291 increase their attentional focus on the pain. Indeed, catastrophizers tend to process preferentially
292 pain-related information and interpret even ambiguous sensations as painful.

293 Furthermore, this is the first study that assessed a wide range of coping strategies on women
294 with endometriosis in relation to pain severity and in comparison with healthy women.
295 Interestingly, we found a deficit in positive cognitive coping strategies (i.e. refocus planning
296 and positive reappraisal) in women with low-pain endometriosis than in healthy participants.
297 However, this difference seems to be statistically low.

298 ***Metacognitive beliefs predict sexual distress after three months, over and above pain severity***

299 Our findings showed that, controlling for pain and sexual distress scores at baseline,
300 metacognitive beliefs significantly predicted sexual distress severity after 3 months. Therefore,
301 results suggested that cognitions and beliefs about own worries play the most important role in
302 predict subsequent sexual distress, over and above pain severity. Our results are similar to those
303 found by a previous cross-sectional study of Zarbo et al. (2018), which found that negative
304 metacognitive beliefs were associated to sexual distress severity, over and above dyspareunia
305 and chronic pain (Zarbo et al., 2018). According to the model of Wells & Simons (2009), we
306 can suggest that metacognitive beliefs about own worries affect sexual distress passing through
307 the influence on coping strategies. In other words, beliefs about own worries may lead to a
308 dysfunctional way to cope with stressors (i.e. catastrophizing, ruminating about own problems)
309 and, indirectly, to the onset and maintenance of distress.

310

311 **CONCLUSIONS**

312 Concluding, to the best of our knowledge, this is the first case-control longitudinal study
313 assessing a wide range of psychological and cognitive conditions in women with diagnosis of
314 endometriosis. Limitations of this study include small sample size at follow-up, short-term
315 follow-up (i.e. after 3 months) and lack of control for specific medical conditions (i.e. surgery,
316 medication, stage) occurring at T0 and between T0 and T1. These conditions have been assessed
317 and reported, but their control was not possible due to the high heterogeneity of the sample and

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3 318 the complexity of endometriosis. Endometriosis represents a complex condition, in which
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5 319 control of each of such medical categories would request a bigger sample size and a forced-
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7 320 categorization of a series of variables. Furthermore, it should be highlighted that the participants
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9 321 were enrolled from a single institution, and this might reduce generalizability of our findings.
10 322 Despite these limitations, findings of this study lead us to arise significant conclusions and
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12 323 clinical implications about the role of pain, worry traits, coping strategies and metacognitive
13
14 324 beliefs in women with endometriosis. Indeed, despite literature is full of studies about the
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16 325 importance of pain in affecting the quality of life and mental health of women with
17
18 326 endometriosis, this study adds significant conclusions. We can argument that the role of pain
19
20 327 in affecting quality of life and mental health is surely significant and requests a specific
21
22 328 attention from the medical team. However, we suggest that coping strategies (in particular,
23
24 329 catastrophizing) and worry traits could affect the way women experience pain. Therefore,
25
26 330 women who usually catastrophize or show worry traits are more likely to experience higher
27
28 331 pain. Furthermore, longitudinally, metacognitive beliefs predict sexual distress over and above
29
30 332 pain. Moreover, it should be highlighted that psychological or sexual distress and sexual
31
32 333 functioning may be impaired by endometriosis-associated infertility (Laganà et al., 2016;
33
34 334 Vitale, La Rosa, Rapisarda, & Lagana, 2017; Vitale, La Rosa, Rapisarda, & Laganà, 2017), a
35
36 335 condition not specifically investigated in this study that needs specific attention.
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38 336 Important clinical implications for the medical team arise from our study. The findings of this
39
40 337 study are of particular importance if we consider the role of the psychologist in the
41
42 338 multidisciplinary team for the treatment of endometriosis. Endometriosis is a chronic and
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44 339 treatment-resistant condition that is usually disabling for the woman. A better understanding of
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46 340 the most critical psychological domains and the cognitive processes that may modulate the
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48 341 impact of this disorder is crucial. Therefore, in addition to pain assessment and treatment, the
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50 342 multidisciplinary team should keep into account and work on personality traits, reinforce
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52 343 positive coping strategies as well as reduce negative coping strategies (i.e. catastrophizing) and
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54 344 metacognitive beliefs. Cognitive-Behavioral support treatments are suggested to improve the
55
56 345 quality of life and mental health of women with pain-related endometriosis.
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COMPLIANCE WITH ETHICAL STANDARDS

347
348 The authors declare that they have no conflicts of interest. All procedures performed in studies
349
350 involving human participants were in accordance with the ethical standards of the institutional
and/or national research committee and with the 1964 Helsinki declaration and its later

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351 amendments or comparable ethical standards. Informed consent was obtained from all
352 individual participants included in the study.

353

354 **AUTHOR CONTRIBUTIONS**

355 All authors contributed to the study conception and design. Material preparation, data collection
356 and analysis were performed by CZ, AB, IC, RS, and CM. The first draft of the manuscript was
357 written by CZ and all authors commented on previous versions of the manuscript. All authors
358 read and approved the final manuscript.

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Sociodemographic Information	Endometriosis group	Control group
Age: mean (<i>SD</i>)	36.98 (8.32)	33.92 (9.4)
range	21 – 53	24-54
Education: <i>n</i>		
Middle Schools	18	4
High Schools	30	22
Bachelor's Degree	8	10
Master's Degree	2	23
Postgraduate/PhD Degree	1	2
Other	1	1
Marital Status: <i>n</i>		
Engaged	7	17
Married	31	17
Common Law	8	11
Single	12	12
Separated	2	1
Divorced	0	3
Widow	0	1
Profession: <i>n</i>		
Student	2	11
Employed full-time	27	23
Employed part-time	15	11
Self-employed	5	12
Unemployed	11	5
Child: <i>n</i>		
No	36	41
Smoke: <i>n</i>		
No	45	43
Clinical information		
Endometriosis type: <i>n</i>		
Superficial endometriosis	30	
Deep endometriosis	12	
Both superficial and deep endometriosis	13	
Adenomyosis involvement	5	
Pelvic pain*: <i>n</i>		
No	23	
Dysmenorrhea*: <i>n</i>		
No	17	
Not having menstruation	8	
Dyspareunia*: <i>n</i>		
No	29	
Not having sex intercourse	4	
Evacuation pain*: <i>n</i>		
No	42	
Urination pain*: <i>n</i>		
No	49	
Backache*: <i>n</i>		
No	26	
Time spent since diagnosis [^] : mean (<i>SD</i>)	51.45 (73.46)	
Time spent since symptoms onset [^] : mean (<i>SD</i>)	66.83 (87.39) ^a	
Past Treatment for Endometriosis: <i>n</i>		
Medical Treatments	20	
Surgical Treatments	6	
Both Medical and Surgical Treatments	24	
None	10	
Hormonal treatment*: <i>n</i>		

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Table 1. Sociodemographic and clinical characteristics of women with endometriosis (N=60) and control group (N=62) at T0

* in the last 3 months

^ in months

^a 54 cases

^b 56 cases

For Peer Review Only

Variables	Low Pain (N = 30)	High Pain (N = 30)	Control Group (N = 62)	F value	p value	Partial η^2	
T0_PCS	47.74 (9.85)	41.79 (9.02)	53.84 (4.69)	27.787	< .001*	.32	<i>a. b. c</i>
T0_MCS	44.09 (11.08)	40.34 (9.79)	45.51 (9.12)	2.826	.063	.05	
T0_PH9	5.5 (4.45)	7.1 (4.24)	4.27 (3.38)	5.422	.006*	.08	<i>c</i>
T0_PSWQ	42.57 (11.83)	48.87 (10.88)	49.13 (7.81)	5.043	.008*	.08	<i>a. b</i>
T0_FSIDS-r	8.53 (10.85)	14.8 (15.76)	6.71 (7.90)	5.520	.005*	.08	<i>c</i>
T0_SelfBlame	4.1 (1.84)	3.83 (2.15)	4.63 (1.75)	2.050	.133	.03	
T0_Acceptance	6.67 (2.07)	7.23 (2.31)	6.5 (1.99)	1.249	.290	.02	
T0_Rumination	5.97 (2.27)	5.9 (2.19)	5.59 (1.80)	.430	.651	.01	
T0_PositiveRefocusing	5.23 (1.98)	5.2 (1.99)	4.68 (1.77)	1.259	.288	.02	
T0_RefocusPlanning	5.8 (1.80)	6.53 (2.34)	6.87 (1.65)	3.079	.050*	.05	<i>b</i>
T0_PositiveReappraisal	6.7 (2.38)	7.13 (2.59)	7.85 (1.83)	3.120	.048*	.05	<i>b</i>
T0_PuttingPerspective	7.17 (2.11)	7.27 (2.10)	6.31 (2.13)	2.825	.063	.05	
T0_Catastrophizing	4.47 (2.21)	4.87 (2.60)	3.61 (1.09)	5.267	.006*	.08	<i>c</i>
T0_Otherblame	3.03 (1.67)	3 (1.55)	3.66 (1.43)	2.727	.070	.04	
T0_MCQ30_POS	9.1 (3.58)	10.23 (4.77)	10.53 (3.69)	1.346	.264	.02	
T0_MCQ30_NEG	13.7 (3.94)	14.9 (3.74)	14.05 (3.24)	.936	.395	.02	
T0_MCQ30_CC	10.2 (3.73)	9.73 (3.79)	9.40 (3.71)	.465	.629	.01	
T0_MCQ30_NC	12.3 (3.37)	11.77 (3.63)	10.92 (3.52)	1.706	.186	.03	

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T0_MCQ30_CSC	17.27(3.30)	15.93(4.13)	16.05 (3.06)	1.549	.217	.03
T0_MCQ30_TOT	62.57(12.28)	62.63(11.98)	61 (10.41)	.307	.736	.01

Table 2. Means and standard deviations. F value and p values of univariate tests between patients with Low pain (LP), High Pain (HP), and control group (CG) for all psychological characteristics.

^a p < 0.05 LP vs HP
^b p < 0.05 LP vs CG
^c p < 0.05 HP vs CG

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Variables	β	t	p	Partial R
Block 1 ($R^2 = .546$)				
T0_FSDS-r	.759	4.634	.000*	.711
T0_MPQ-SF	- 0.47	- .286	.778	- .062
(Constant)		1.311	.204	
Block 2 ($R^2 = .635$)				
T0_FSDS-r	.720	4.754	.000*	.728
T0_MPQ-SF	-.042	-.282	.781	-.063
T0_MCQ30	.299	2.198	.040*	.441
(Constant)		-1.728	.099	

Table 3. Multiple linear regression analyses for Sexual distress at T1 (at three-months follow-up).
 FSDS-r: Female Sexual Distress Scale; MPQ-SF: McGill Pain Questionnaire – short version; MCQ30: Metacognitive Questionnaire