



Perceived stress, social functioning, and quality of life in first-episode psychosis: a 1-year follow-up study

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4 **Original research.**
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8 **Perceived stress, social functioning, and quality of life in first-episode**
9 **psychosis: a 1-year follow-up study**
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11 *Functioning in first-episode psychosis*
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LO and JL designed the study, managed the literature, carried out the interviews, data collection and data entry, and writing of the manuscript. JL participated in the design of the study, carried out the statistical analysis of data and the data collection. RM, IM and LM carried out to the interviews, data collection and data entry. MDB, VSG and EV contributed to the planning of the study, supervised the first draft written and revised the manuscript critically. All authors contributed to and approved the final manuscript version.

ABSTRACT

Aim: Quality of life (QoL) has been widely studied in people with schizophrenia. In the early phases of psychosis, it remains often impaired even after the remission of psychotic symptoms. The aim of this study was to explore QoL and social functioning during the first year after a first-episode psychosis (FEP), and to study potential moderating effects of stress measures.

Methods: 61 FEP subjects and 55 healthy controls (HC) were included. Sociodemographic data and clinical variables were collected through a semi-structured interview. Stress measures, social functioning and QoL were assessed with the Holmes-Rahe Social Readjustment Rating Scale, the Perceived Stress Scale, the Social Adaptation Self-Scale and the Euro-QoL-5D, respectively. ANOVA was employed with repeated measures and a mediation analysis at baseline and at 1-year follow-up was carried out.

Results: Patients reported lower QoL, poorer social functioning and more stress than HC. FEP patients significantly improved in QoL and stress measures over time, but not in social functioning. Perceived stress mediated the association between poorer social functioning and lower QoL.

Conclusions: Social functioning at baseline may determine QoL over a 1-year follow-up period. Despite the improvement in most measures, patients do not achieve the level of wellbeing as the healthy group.

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4 **KEYWORDS:** first-episode psychosis; social functioning; quality of life; social
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6 adaptation; stress.
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For Peer Review

INTRODUCTION

Quality of life (QoL) is a variable that has been widely studied in people with schizophrenia (Bobes, Garcia-Portilla, Bascaran, Saiz, & Bousoño, 2007; Degnan et al., 2018) and that is already affected prior to the onset of first psychotic symptoms (Bechdolf et al., 2005). Together with depression, social functioning seems to be important for subjective QoL in FEP patients (Gardsjord et al., 2016) as mediates the association between positive symptoms and QoL.

QoL shows a natural overlap with social functioning (Watson et al., 2018) and with depressive and negative symptoms (Cotton, Gleeson, Alvarez-Jimenez, & McGorry, 2010; Malla & Payne, 2005). It has been suggested that psychopathology (positive and negative symptoms) and duration of untreated psychosis (DUP) are associated to a worse QoL in FEP patients (Watson et al., 2018), while other studies suggest that depressive symptoms have the greatest effect on QoL (Ohmuro et al., 2017; Ruhrmann et al., 2008). In general, longitudinal studies that have researched QoL after a first psychotic episode have shown significant improvement during recovery (Addington, Young, & Addington, 2003; Gardsjord et al., 2016; Góna, Jaracz, Rybakowski, & Rybakowski, 2008; Priebe et al., 2010; Tan et al., 2019). Despite the finding of an improvement in social functioning in FEP individuals after the 1-year follow-up, they often do not reach the healthy population level of wellbeing when compared to a non-psychiatric control group (Addington et al., 2003).

Furthermore, stress is another a variable that can influence the QoL of patients with a psychotic disorder. People with psychotic disorders who use negative coping strategies in response to stress report poorer QoL (Cohen, Hassamal, &

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4 Begum, 2011; Holubova et al., 2015). Previous studies that explore the
5 relationship between vocational status and perceived stress in FEP patients have
6 surprisingly reported increased levels of perceived stress and more intense daily
7 problems in unemployed patients (Allott et al., 2013). Other studies on FEP
8 cohorts have reported that more daily activities and being employed are likely to
9 be associated with a better QoL (Addington et al., 2003; Gardsjord et al., 2016;
10 Tan et al., 2019). In line with these findings, a previous study by our group
11 (Ortega, Montalvo, Monseny, Vilella, & Labad, 2019) focused on ultra-high-risk
12 (UHR) individuals found that UHR people with low social functioning reported
13 more unemployment, increased perceived stress and less QoL than UHR people
14 with normal social functioning and with healthy controls. Moreover, perceived
15 stress mediated the relationship between social functioning and QoL.

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32 To address these outstanding issues, we aimed to explore QoL and social
33 functioning during the first year after a first-episode psychosis (FEP) and to study
34 potential moderating effects of stress measures. With all the above, we
35 hypothesized that over the first year after a FEP, patients would improve QoL,
36 social functioning, and stress measures. We also hypothesized that perceived
37 stress would mediate the relationship between social functioning and QoL. To our
38 knowledge, there are no longitudinal studies exploring the potential influence of
39 stress variables on QoL in FEP patients.

40 41 42 43 44 45 46 47 48 49 50 51 52 **METHODS**

53 54 55 **Study setting and participants**

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4 The study included 61 FEP subjects with a mean age (standard deviation) of 24.1
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6 (4.3) years, who were attending the Early Psychosis Programme in Reus (HPU
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8 Institut Pere Mata, Tarragona, Spain). This Programme covers a population area
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10 of approximately 194,000 inhabitants, and has an incidence of 30-40 FEP cases
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12 every year. Outpatients referred to the Early Psychosis Programme are offered
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14 mental health care by a multidisciplinary team (that includes psychiatrists, clinical
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16 psychologists, mental health nurses and social workers) during at least 3 years
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18 (most of them for 5 years). All patients are prospectively assessed while being
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20 attended at the Early Psychosis Programme and are invited to participate in
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22 active research projects by consecutive sampling if they meet the **exclusion**
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24 **criteria**.

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29 The exclusion criteria for participating in the current study were pregnancy,
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31 **intellectual disability**, severe head injury or neurological disease, active
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33 glucocorticoid treatment, active substance dependence (other than tobacco or
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35 cannabis) and type 1 diabetes, as well as refusing to participate. We included a
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37 control group of 55 healthy people (HCs) without a past or current history of
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39 psychiatric disorders. Additionally, they were screened with the 28-item General
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41 Health Questionnaire (GHQ-28) and scored less than 7 (Goldberg & Hillier,
42
43 1979). This cut-off point has been reported to be effective for detecting cases with
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45 psychiatric disorders in Spanish populations (Lobo, Pérez-Echeverría, & Artal,
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47 1986). HCs were recruited from the community through advertisements, patient
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49 friends and college students. They were living in the same population area that
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51 is covered by the Early Psychosis Programme.
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4 Ethical approval was obtained from the local Ethics Committee. Written informed
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6 consent was obtained after the participants had been given a complete
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8 description of the study.
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11 12 13 **Assessments**

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15 All patients were assessed with the Schedules for Clinical Assessment in
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17 Neuropsychiatry (SCAN) (Wing et al., 1990) by a trained psychiatrist, and
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19 diagnoses were obtained with OPCRIT 4 for Windows. Sociodemographic data
20
21 and clinical variables (age, occupation, living situation, use of substances and
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23 antipsychotic drugs) were collected through a semi-structured interview that was
24
25 conducted by a mental health nurse.
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29 The Positive and Negative Syndrome Scale (Kay, Fiszbein, & Opler, 1987;
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31 Peralta & Cuesta, 1994) was used to assess the severity of positive and negative,
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33 and general psychopathology symptoms.
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37 We evaluated stress with the Holmes-Rahe Social Readjustment Rating scale
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39 (HRSRRS) (Holmes & Rahe, 1967), which includes two types of measures: the
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41 number of stressful life events in the past six months and the total score, obtained
42
43 by adding the scores of all present life events. The Perceived Stress Scale (PSS)
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45 (Cohen, Kamarck, & Mermelstein, 1983; Remor, 2006) was used to assess the
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47 psychological perception of stress. This 14-item self-report questionnaire
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49 measures how stressful have been experienced life situations in the last month,
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51 in a range from 0 to 40, where higher scores indicate higher perceived stress.
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55 The Social Adaptation Self Scale (SASS) (Bosc, Dubini, & Polin, 1997) was used
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57 to assess social functioning. This self-report scale assesses several aspects
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4 related to social functioning, including individuals and the environment, as well
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6 as behaviour and social motivation. It includes 21 items with four response levels
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8 (from 0 to 3) and explores a variety of areas, such as work, family, leisure, social
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10 relationships and motivation/interests. The total score ranges between 0 and 60.
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12 The proposed cut-off points are <25 (social imbalance), 25-52 (normal
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14 parameters), and >52 (over-adaptation) (Bosc et al., 1997).
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18 Euro-QoL-5D (Badia, Schiaffino, Alonso, & Herdman, 1998) was used to assess
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20 QoL. The 3-level version (EQ-5D-3L), validated for the Spanish population by
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22 Badia et al. (1998), was used to evaluate self-perception of health-related QoL.
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24 This self-report instrument is composed of three parts: (i) a descriptive part with
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26 five domains and three response levels (EQ-5D-3L); (ii) a Visual Analog Scale
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28 (EQ-5D-VAS) or 'health thermometer' that records the health self-assessment
29
30 from 0 ('worse state of health imaginable') to 100 ('the best state of health
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32 imaginable'); and (iii) the EQ-5D 'health profile' (EQ5D- HP). The descriptive EQ-
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34 5D-3L system has five dimensions (mobility, self-care, daily activities,
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36 pain/discomfort and anxiety/depression) and three levels of response ('no
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38 problem', 'some problems' or 'serious problems'). Scores in these five
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40 dimensions can be presented as a health profile represented by five digits (e.g.
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42 11111, meaning no problems in any dimension, or 33333, meaning serious
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44 problems in all dimensions) with 243 possible health states. For example, an EQ-
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46 5D-3L health state 21123 represents a patient who indicates some problems on
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48 the mobility dimension, no problems on the self-care and usual activities
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50 dimensions, some pain or discomfort and serious problems on the
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52 anxiety/depression dimension. The health states defined by the EQ-5D scale can
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4 be converted into a single summary index by applying a formula, using a value
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6 set for the Spanish population, that gives a specific weight to each of the levels
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8 in each dimension. This index is referred to as EQ-5D-HP in our study.
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11 The psychometric properties of the scales described above are provided in Table
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13 S1.
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16 17 18 **Statistical analysis**

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20 SPSS version 21.0 (IBM Corp., Armonk, New York) was used for the statistical
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22 analyses. Continuous or categorical measures for diagnostic groups (UHR vs
23
24 HC) were compared using the T test and χ^2 tests, respectively. Longitudinal
25
26 changes over time in FEP patients were assessed with a paired T test with a p
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28 value <0.05 (two-tailed).
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31 We also conducted an ANOVA for repeated measures to explore longitudinal
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33 changes in QoL and test for the potential moderating effects of stress measures
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35 or social functioning. These analyses were only performed with FEP patient data
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37 and the following independent variables were considered: gender, baseline social
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39 functioning, perceived stress, stressful life events, and positive and negative
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41 symptoms. We conducted two ANOVA for repeated measures using two different
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43 QoL variables (EQ-5D-VAS and EQ-5D-HP), which were considered the
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45 dependent variables.
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50 Concerning psychopathology symptoms, 45 out of 61 (73.7%) patients had a
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52 repeated PANSS assessment at the end of the follow-up period (1 year). We
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54 conducted exploratory analyses to study psychopathology changes over time and
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4 to explore whether psychopathology symptoms at each visit (baseline, 1 year)
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6 were associated with social functioning and stress measures.
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9 A mediation analysis (for a detailed explanation of this analysis see Box S1) was
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11 conducted to explore whether the relationship between social functioning and
12
13 QoL was mediated by stress measures. The PROCESS macro for SPSS
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15 (available at <https://processmacro.org/index.html>) (Preacher & Hayes, 2008) was
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17 used to conduct these analyses. This macro allows multiple mediators and
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19 covariates to be included. Social functioning (SASS scores) was considered the
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21 main independent variable in the mediation analysis. QoL was used as the
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23 dependent variable. We conducted two independent mediation analyses
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25 considering two QoL measures (EQ-5D-VAS and EQ-5D-HP). Stress measures
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27 (PSS scores) were tested as potential mediators. Bootstrapping was used to test
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29 the indirect effect of mediation (Preacher & Hayes, 2008).
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36 **RESULTS**

37 **Sociodemographic characteristics**

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39 There were no significant differences in the age or gender distribution between
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41 the two groups. We found significant differences in employment status (fewer
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43 FEP individuals were working or studying), marital status (more FEP individuals
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45 were single) and living situation (more individuals were living with their family of
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47 origin). FEP individuals reported higher consumption of tobacco, cannabis and
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49 alcohol than healthy control individuals. The characteristics of the sample are
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51 described in Table 1. Baseline perceived stress and stressful life events were not
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4 significantly correlated in either HCs ($r= 0.196$, $p= 0.160$) or FEP individuals ($r= -$
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7 0.098 , $p= 0.452$).
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11 Insert Table 1 above here.
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14 15 **QoL, stress measures and social functioning: group differences and** 16 17 **longitudinal changes in FEP patients** 18 19

20 In the baseline characteristics, FEP patients reported lower QoL, poorer social
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22 functioning and more stress (perceived stress and stressful life events) than HCs
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24 (Table 2). The analysis of longitudinal changes over time (1-year follow-up)
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26 showed that FEP patients significantly improved in QoL measures (they reported
27
28 greater EQ5DHP and EQ5D-VAS at follow-up) and stress measures (they
29
30 reported reduced perceived stress and less stressful life events at follow-up).
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33 There were no significant changes in social functioning over time. Although an
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35 improvement was observed in QoL in FEP patients over time, they did not
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37 achieve the same level as HCs in QoL. The same cannot be said about perceived
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39 stress, as FEP patients had very similar scores to HC individuals.
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50 The ANOVA for repeated measures, adjusting for gender, baseline social
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52 functioning, perceived stress, stressful life events, and positive and negative
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54 symptoms, showed a significant interaction by time and social functioning in
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56 EQ5D-VAS (within-subject effects; $F= 4.77$, $p= 0.034$). No significant
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4 associations were found for time and no other interactions were found between
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6 time and other covariates. No significant interactions were found for EQ5D-HP.
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11 Insert Figure 1 above here.
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16 The time by social functioning interaction in EQ5D-VAS is represented in Figure
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18 1. Those FEP patients with lower scores in the SASS (in the first two terciles)
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20 showed an improvement in QoL, whereas those patients with greater social
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22 functioning (last tercile) did not improve over time.
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26 27 **Longitudinal changes in psychopathology: exploratory analyses**

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29 Longitudinal changes in **positive and negative, and general psychopathology**
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31 symptoms are described in Table S2. FEP patients improved in positive and
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33 general psychopathology symptoms at the follow-up visit, with no significant
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35 changes in negative symptoms. The PANSS positive score at the 1-year visit
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37 suggests that most patients were on remission taking into account positive
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39 symptoms.
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44 Correlation analyses between PANSS scores, stress measures and social
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46 functioning are reported in Table S3. Baseline negative and general
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48 psychopathology symptoms showed a high correlation with these symptoms at
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50 follow-up, whereas the correlation was non-significant for positive symptoms.
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52 Negative symptoms at both visits (baseline and follow-up) were significantly
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54 associated with poorer social functioning at both visits. At the baseline visit,
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56 general psychopathology was associated with stress measures (perceived stress
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4 and stressful life events) and poorer quality of life. At the follow-up visit, positive
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6 symptoms were associated with more perceived stress and poorer QoL (EQ5D-
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8 HP).
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10 11 12 13 **Mediation analyses**

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16 The mediation analyses, which explored whether perceived stress could mediate
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18 the relationship between social functioning and QoL at baseline or at one-year
19
20 follow-up, only found a mediating effect for the baseline assessment (Figure 2).
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22 In the unadjusted model (Figure 2A), social functioning was associated with QoL.
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24 This effect was fully mediated by perceived stress (Figure 2B) as the relationship
25
26 between social functioning and QoL lost its significance when this mediator was
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28 included in the equation. Bootstrap results for indirect effects were significant for
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30 perceived stress (95% confidence interval: 0.021 to 1.017).
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Insert Figure 2 above here.

41 **DISCUSSION**

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43 Our study shows a significant improvement at a 1-year follow-up of FEP subjects
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45 in QoL and stress measures (perceived stress and stressful life events) but not
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47 in social functioning. These results corroborate the findings of previous studies in
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49 this field (Addington et al., 2003; Gardsjord et al., 2016; Melle et al., 2010);
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51 however, they contrast with other studies that found only minimal variation in QoL
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53 over time (Górna et al., 2008; Priebe, Roeder-Wanner, & Kaiser, 2000). The
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55 changes in QoL in early stages of psychosis spectrum disease have been shown
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4 to have an important impact on long-term QoL (Karow, Wittmann, Schöttle,
5 Schäfer, & Lambert, 2014). In a previous study by our group (Ortega et al., 2019)
6 we concluded that social functioning was affected before the onset of psychosis
7 in the prodromal phase. Thus, as expected in our sample, employment rates were
8 lower in FEP individuals than in HCs, which is in line with previous studies on
9 early psychosis disorder (Cotton et al., 2017; Rinaldi et al., 2010). Employment
10 has been shown to have a positive effect on QoL and on wider social functioning
11 in psychotic disorders (Charzyńska, Kucharska, & Mortimer, 2015; Tan et al.,
12 2019), and it plays an important role because it influences relationships, leisure
13 activities and daily time organization, for example, which not only affect QoL but
14 also social functioning. In general terms, a longer duration of compromised
15 function (Melle et al., 2005) or DUP (Renwick et al., 2017) have been associated
16 with worse QoL. We also need to take into account that FEP patients are
17 responsive to integrated early intervention programme, which have been shown
18 to have a positive impact on the recovery of psychosis in young people (Macbeth,
19 Gumley, Schwannauer, & Fisher, 2015; Maddigan, LeDrew, Hogan, & Le
20 Navenec, 2018)). In addition, as Renwick et al. (2017) demonstrated, it is
21 necessary to carry out interventions to preserve social connectedness, especially
22 for those patients with longer DUP, as psychosis studies associate QoL with
23 larger social networks (Degnan et al., 2018). Early intervention services for FEP
24 have proven to be effective in improving QoL over time with greater
25 improvements in those with shorter DUP (Kane et al., 2016). However, other
26 studies have not reported significant associations between DUP and longitudinal
27 changes in QoL in FEP patients over time (Melle et al., 2010).

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4 In our study, EQ5D-VAS but not the EQ5D-HP was associated with social
5 functioning. The EQ5D-HP is an index that uses an algorithm that includes the
6 values of the general population responses to the questions asked, whereas the
7 EQ5D-VAS does not and relies in the subjective response of the participant. In
8 previous studies that included patients with psychotic disorders and that
9 assessed the relationship between mental health outcomes (including social
10 functioning and welfare) and dimensions of QoL (EQ5D-VAS and EQ5D-HP),
11 EQ5D-VAS also showed a slightly greater association with functioning when
12 compared to EQ5D-HP (Vergunst et al., 2017)

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25 Although social functioning did not improve after the follow-up period in our study,
26 it became an influential variable on the evolution of QoL. The QoL improved more
27 in FEP patients with lower social functioning at baseline than it did in to those
28 patients with a high social functioning, who reported a decrease in QoL. In
29 contrast with patients with poorer social functioning, those with higher social
30 functioning may have a greater sense of loss although they have a similar level
31 of insight after their FEP (Cotton et al., 2010). This could explain the different
32 pattern in longitudinal changes between patients with higher and lower social
33 functioning.

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46 Despite the improvement in QoL, FEP subjects do not achieve the same QoL
47 level as HCs one year later. Our findings are in line with the Addington et al.
48 (2003) study, which followed up subjects after a FEP admission. These authors
49 found that symptomatic remission differs from functional remission, and the latter
50 often takes longer to recover. In another study from this same group (Addington
51 & Addington, 2005), it has been suggested that negative symptoms in FEP
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4 patients contribute to the poorer social functioning at both 1 and 2-years. Our
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6 results regarding the significant association between negative symptoms and
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8 poorer social functioning at both baseline and follow-up visits are in accordance
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10 with the previous study.
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13 Similar to the results in a previous study by Ortega *et al.* (2019), we also found
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15 that perceived stress is a mediating variable of the relationship between social
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17 functioning and QoL. We found a mediating effect on the baseline visit but no
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19 effect one year later. As FEP patients improved in perceived stress one year later,
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21 a potential explanation for the lack of mediating effects at this point is that the
22
23 level of perceived stress was too low for significant mediating effects to be found.
24
25 Moreover, all FEP patients attended an Early Intervention Service and were
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27 offered group psychotherapy (which includes psychoeducation and social skills
28
29 training) and individual psychotherapy. Therefore, it is possible that they could
30
31 have received treatment during the first year that might have helped them to
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33 improve their style of coping with stress. Our study highlights the need to screen
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35 for perceived stress in people who have suffered a FEP and to address these
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37 symptoms in order to improve QoL over time.
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45 **Strengths and limitations**

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47 The major strength of this study is the one-year follow-up of FEP individuals and
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49 the reassessment of functioning variables in the prospective design, as well as
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51 having a control group to compare patients' results. The main weakness is the
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53 use of self-report QoL measures, since these measures can be influenced by the
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55 patients' depression and lack of insight (Malla & Payne, 2005). Indeed, these
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4 measures may overlap with depression and QoL questionnaires, particularly
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6 concerning negative perceptions of life events and negative outlook on life
7
8 (Cotton et al., 2010). Nonetheless, self-reported measures are the best way for
9
10 the patients to express their feelings and experiences of their illness, and most
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12 studies conclude that self-reported satisfaction or subjective QoL is a valid
13
14 outcome measure in schizophrenia and other psychotic disorders (Melle et al.,
15
16 2005). We did not control the patients' attendance to the health care professional
17
18 visits, and therefore we must assume that all of them received similar care.
19
20 Finally, the lack of longitudinal assessment of the studied measures in HCs is
21
22 another limitation that does not allow to test potential fluctuations over time in this
23
24 non-clinical group.
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29 Considering the limitations described above, this is one of the first studies to
30
31 assess the potential effect of stress variables on QoL in FEP patients during the
32
33 first year after a psychotic episode. Quality of life is a complex concept, which is
34
35 sometimes difficult to address, and understanding and explaining its components
36
37 can help us jointly develop actions to improve it. Social functioning at baseline
38
39 may determine QoL perception over a 1-year follow-up period. Despite the
40
41 improvement over time in QoL and stress measures, young patients do not
42
43 achieve the same level of wellbeing as the healthy group. Therefore, it is
44
45 important to monitor and continue to give care to these patients even though
46
47 psychotic symptoms have remitted. We might focus on those patients with
48
49 apparently proper social functioning and follow closely, as well as those with
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51 lower social functioning. Mental health professionals' interventions for improving
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53 stress management skills and being aware of social functioning in young FEP
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4 individuals could mitigate the effect of stress and overall social functioning on
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6 QoL.
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40 **Authors declare no conflict of interest.**
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44 **DATA AVAILABILITY STATEMENT**

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46 The data that support the findings of this study are available from the corresponding
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48 author upon reasonable request.
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For Peer Review

FIGURE LEGENDS

Figure 1. Longitudinal changes in quality of life over the 1-year follow-up period in relation to social functioning groups.

Figure 2. Results of the mediation analysis exploring the relationship between social functioning and quality of life. β , beta regression coefficient; SE, standard error; CI, confidence interval.

For Peer Review

Table 1. Sample characteristics

	FEP	Healthy controls	P value
	N= 61	N= 55	
Age	24.1 (4.3)	24.7 (4.9)	0.430
Gender			
Male	46 (75.4)	38 (69.1)	0.534
Female	15 (24.6)	17 (30.9)	
Employment status			
No work/no studies	42 (68.9)	8 (14.5)	<0.001*
Working/studying	19 (31.1)	47 (85.5)	
Marital status			
Single	50 (82)	37 (67.3)	0.036*
Stable couple	9 (14.8)	18 (32.7)	
Divorced	2 (2)	0	
Living situation			
Family of origin	50 (82)	31 (56.4)	0.014*
Own family (couple)	7 (11.5)	11 (20)	
Friends	1 (1.6)	7 (12.7)	
Alone	3 (4.9)	6 (10.9)	
Substance abuse			
Smoking			
No	20 (32.8)	40 (72.7)	<0.001*
Yes	41 (67.2)	15 (27.3)	
Cannabis			
None	29 (47.5)	43 (78.2)	<0.001*
Occasional	5 (8.2)	8 (14.5)	
Daily	27 (44.3)	4 (7.3)	
Alcohol			
None	26 (42.6)	9 (16.4)	<0.001*
Occasional	26 (42.69)	44 (80)	
Daily	9 (14.89)	2 (3.6)	
Antipsychotic drug			
No	0	55 (100)	<0.001*
Yes	55 (100)	0	
Monotherapy	36 (65.5)	0	
Polytherapy	17 (27.99)	0	
PANSS scores			
PANSS positive	12.7 (5.5)	-	
PANSS negative	15.6 (7.6)	-	
PANSS general	33.0 (10.0)	-	

Data are mean (SD) or N (%)

Abbreviations: FEP= First episode of psychosis; PANSS= Positive and Negative Syndrome Scale

Table 2. Quality of life, social adaptation and stress measures by diagnostic group, at baseline and after the 12-month follow-up.

	HC N= 55		FEP N= 61				P value † HC vs FEP (Baseline)	P value‡ HC vs FEP (Follow-up)	P value‡ (Change over time in FEP patients)
	Baseline		Baseline		Follow-up				
	Mean	SD	Mean	SD	Mean	SD			
EQ-5D HP	0.93	0.14	0.70	0.24	0.80	0.18	<0.001	<0.001	0.004*
EQ-5D VAS	81.7	15.3	59.1	17.9	68.1	17.9	<0.001	<0.001	0.003*
Social Adaptation self-Scale	43.7	5.9	35.0	6.6	35.6	7.6	<0.001	<0.001	0.511
Perceived Stress Scale	18.5	7.6	27.7	9.4	22.9	8.5	<0.001	0.004	0.002*
Holmes-Rahe Social Readjustment Scale									
Number of Stressful Life Events	3.98	3.3	7	5.7	4.2	2.3	0.001	0.755	<0.001*
Stress score	113.0	96.0	200.5	199.5	114.4	74.0	0.004	0.933	0.001*

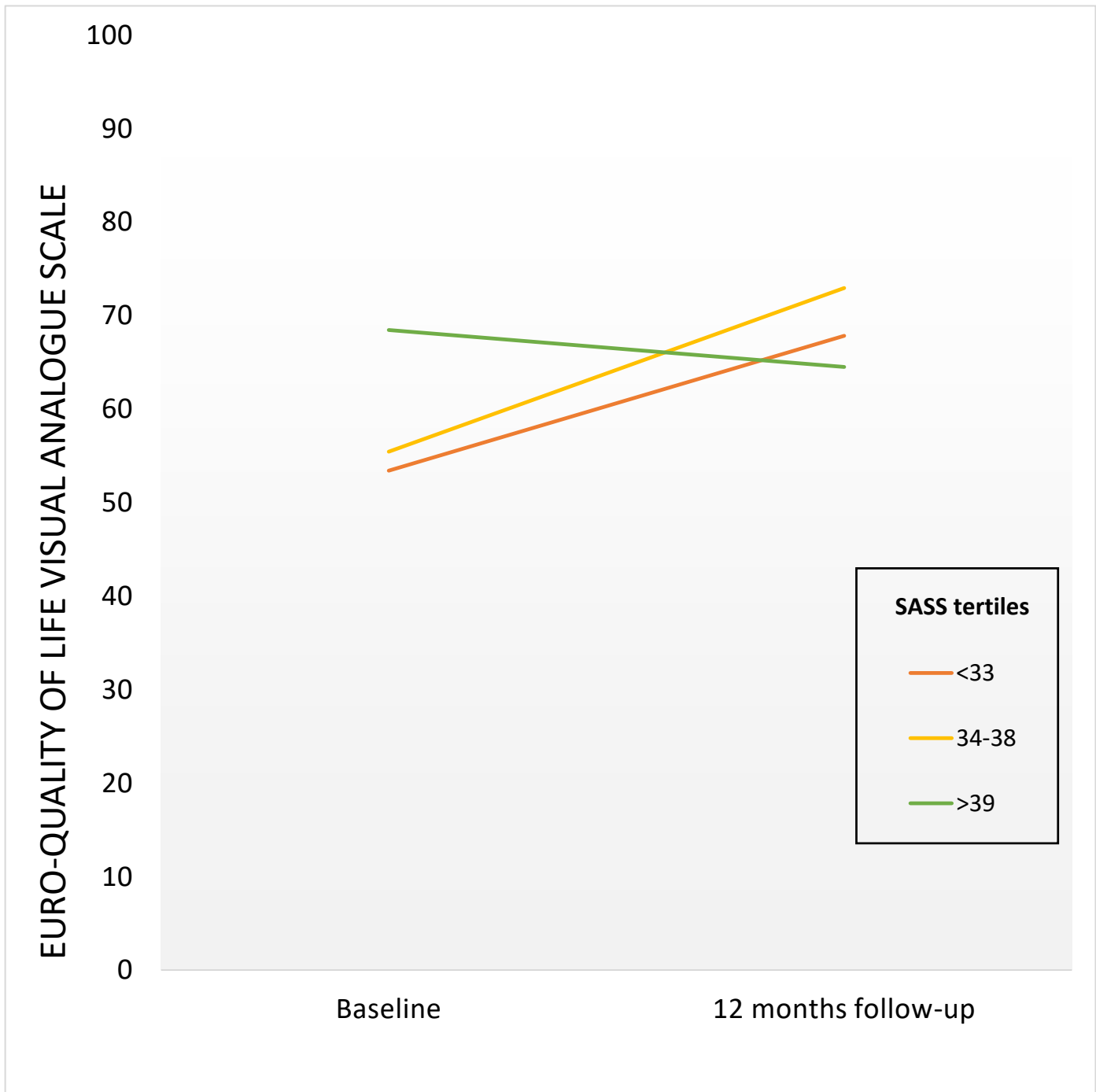
†Independent T-test.

‡Paired T-test.

Abbreviations: HC= Healthy controls; FEP: First episode of psychosis subjects; EQ-5D-HP= Euro Quality of Life-5 dimensions health profile;

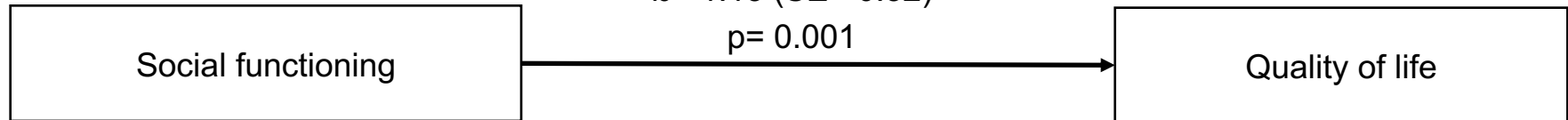
EQ-5D-VAS= Euro Quality of Life-5 dimensions visual analogical scale.

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a. Direct effect

$\beta = 1.13$ (SE= 0.32)
p= 0.001

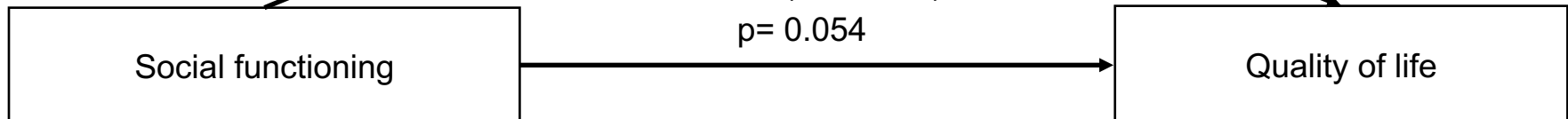
**b. Mediated effect**

$\beta = -0.70$ (SE= 0.16)
P=0.001

Perceived stress

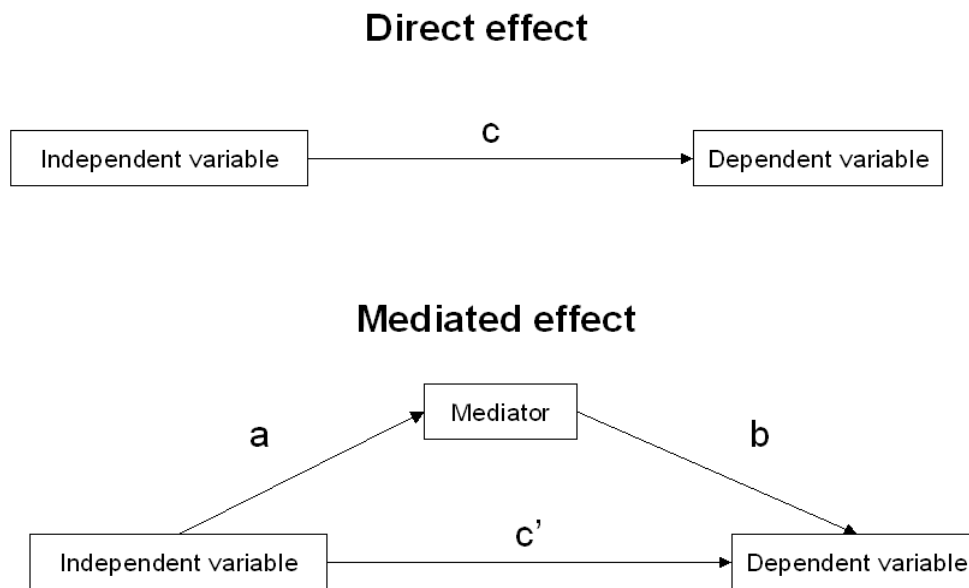
$\beta = -0.62$ (SE= 0.25)
P=0.015

$\beta = 0.70$ (SE= 0.36)
p= 0.054



Indirect effect (bootstrapping) effect=0.43 Boot SE=0.24
CI 95%: 0.021 to 1.017

Box S1. Explanation of the mediation analysis.



According to Baron and Kenny (Baron & Kenny, 1986), the following regression equations should be estimated in a mediation analysis:

- 1) the association between the independent variable and the dependent variable (c)
- 2) the association between the independent variable and the mediator (a)
- 3) the association between the mediator and the dependent variable (b), controlling for the effect of the independent variable (c').

In order that mediation exists, the strength of the relation between the independent variable and the dependent variable (c) is significantly reduced when the mediator is added to the model (c'). If perfect mediation exists, the effect of the independent variable on the dependent variable controlling for the mediator should be zero.

The amount of mediation is called indirect effect. An increasingly popular method of testing the indirect effect is bootstrapping (Shrout & Bolger, 2002). Bootstrapping is a non-parametric method based on resampling with replacement which is done many times. From each of these samples the indirect effect is computed and a sampling distribution can be empirically generated. Because the mean of the bootstrapped distribution will not exactly equal the indirect effect a correction for bias is usually made. With the distribution, a confidence interval (CI), a p value, or a standard error can be determined. Very typically a CI is computed and it is checked to determine if zero is in the interval. If zero is not in the interval, then the researcher can be confident that the indirect effect is different from zero (For a full explanation of the mediation analysis, see <http://davidakenny.net/cm/mediate.htm>).

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Instrument	References	Measurement	Items (N)	Type of instrument (administration)	Domains	Reliability	Validity
PANSS	Peralta & Cuesta, 1994	Schizophrenia symptoms	30	Semi-structured/ Clinician rated	3 subscales: - Positive - Negative - General	Internal reliability: $\alpha = 0.73$ for the positive scale $\alpha = 0.83$ for the negative scale $\alpha = 0.87$ for the general scale	Concurrent validity with BPRS, SAPS, SANS and CGI from 0.52 to 0.77
PSS	Remor, 2006	Perceived stress	14	Structured/ Self-reported		Internal consistency: $\alpha = 0.81$ Test-retest reliability of 0.73	Concurrent validity with HADS-T and HADS-A of 0.71 and 0.64
HRSRS	Holmes & Rahe, 1967 Rahe et al., 1970 Gerst et al., 1978	Stressful life events	43	Structured/ Self-reported		Inter-rater reliability: Kendall's coefficient of concordance of 0.47 Test-retest reliability of psychiatric group of 0.08 at 6-12 months, and 0.41 at 12-24 months Test-retest reliability of non-psychiatric group of 0.83 from initial to 3 months, 0.69 at 6-12 months, and 0.59 at 12-24 months	Concurrent validity with dispensary visits (an indicator of illness behaviour) of 0.42, and a multiple correlation of the combined HRSRS and CMI with dispensary visits of 0.66
SASS	Bobes et al., 1999	Personal and social functioning	21	Structured/ Self-reported		Internal reliability: from $\alpha = 0.88$	Concurrent validity with HDRS, CGI, GAF of -0.40, 0.37 and -0.39
Euro-QOL-5D	Buchholz et al., 2018 Badia et al., 1998	Health-related quality of life	5+1 (VAS)	Structured/ Self-reported	5 dimensions (mobility, self-care, daily activities, pain/discomfort and anxiety/depression) A Visual Analogical Scale (from 0 to 100)	Test-retest reliability across different studies: Intra-class correlations: 0.52 to 0.83 Kappa: 0.39 to 0.93 Percentage of agreement: 0.78 to 0.97	Construct validity: correlations with GHQ from 0.1 (self-care dimension) to 0.3 (mood dimension) Concurrent validity: self-perceived overall health (excellent, very good, good, fair, poor) with VAS of 0.55 and tariff values for health of 0.53

Table S1. Psychometric properties of the instruments used in the current study.

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3 Abbreviations: PANSS: Positive and Negative Syndrome Scale; BPRS: Brief Psychiatric Rating Scale; SAPS: Scale for the Assessment of Positive Symptoms; SANS: Scale for the
4 Assessment of Negative Symptoms; CGI: Clinical Global Impression; PSS: Perceived Stress Scale; HADS-T: Hospital Anxiety and Depression Scale Global Distress measure; HADS-A:
5 Hospital Anxiety and Depression Scale Anxiety subscale ; HRSRS: Holmes-Rahe Social Readjustment Scale; CMI: Cornell Medical Index ; SASS: Social Adaptation Self-evaluation Scale;
6 HDRS: Hamilton Depression Rating Scale; GAF: Global Assessment of Functioning; Euro-QOL-5D: Euro-QOL-5 dimensions; VAS: visual analogical scale; GHQ: General Health
7 Questionnaire;

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Table S1. Longitudinal changes in psychopathology in 45 patients with a first episode psychosis who had two PANSS assessments over time.

	Baseline		Follow-up		P value (Paired T-test)
	Mean	SD	Mean	SD	
PANSS positive	13.2	5.4	8.7	2.4	<0.001
PANSS negative	16.1	7.8	15.0	8.0	0.228
PANSS general psychopathology	33.2	10.0	24.8	8.6	<0.001

Abbreviations: PANSS= Positive and Negative Syndrome Scale; SD= Standard deviation.

Table S2. Correlation analyses between baseline and follow-up PANSS scores and stress, QoL and social adaptation measures.

	PANSS-P V1	PANSS-N V1	PANSS-GP V1	PANSS-P V2	PANSS-N V2	PANSS-GP V2
PANSS-P V1	1	0.250	0.540***	0.207	0.404**	0.254
PANSS-N V1	0.250	1	0.650***	0.331*	0.735***	0.556***
PANSS-GP V1	0.540***	0.650***	1	0.305*	0.559***	0.492**
PSS V1	0.147	0.258*	0.409**	0.195	0.242	0.308*
Number SLE V1	-0.140	-0.227	-0.275	-0.126	-0.246	-0.254
HRSRS Score V1	-0.125	-0.219	-0.276*	-0.115	-0.250	-0.238
EQ-5D VAS V1	-0.188	-0.232	-0.304*	-0.065	-0.238	-0.211
EQ-5D HP V1	-0.011	-0.170	-0.109	-0.129	-0.316*	-0.363*
SASS V1	-0.135	-0.476***	-0.397**	-0.443**	-0.530***	-0.559***
PANSS-P V2	0.207	0.331*	0.305*	1	0.404**	0.701***
PANSS-N V2	0.404**	0.735***	0.559***	0.404**	1	0.746***
PANSS-GP V2	0.254	0.556***	0.492**	0.701***	0.746***	1
PSS V2	0.017	0.070	0.147	0.397**	0.142	0.357*
Number SLE V2	-0.223	-0.205	-0.122	-0.110	-0.285	-0.277
HRSRS Score V2	-0.166	-0.146	-0.089	-0.171	-0.234	-0.274
EQ-5D VAS V2	0.107	-0.042	-0.056	-0.044	-0.122	-0.259
EQ-5D HP V2	-0.038	0.002	-0.071	-0.327*	-0.127	-0.256
SASS V2	0.113	-0.350**	-0.180	-0.232	-0.323*	-0.369*

*p<0.05; **p<0.01; ***p<0.001

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4 Abbreviations: PANSS= Positive and Negative Scale; PANSS-P= PANSS positive subscore; PANSS-N= PANSS negative subscore; PANSS-
5 GP= PANSS general psychopathology subscore; QoL= Quality of Life; V1= Baseline visit; V2= Follow-up visit (1 year); EQ-5D-HP= Euro
6 Quality of Life-5 dimensions health profile; EQ-5D-VAS= Euro Quality of Life-5 dimensions visual analog scale; SLE= Stressful life events;
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8 HRSRS= Holmes-Rahe Social Readjustment Scale; SASS= Social Adaptation Self-Scale.
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