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# A Longitudinal Analysis of Quality of Life and Associated Factors in Spanish Outpatients With Schizophrenia-Spectrum Disorders

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## Abstract

Background: Quality of Life (QoL) studies in outpatients with psychosis can improve patient support. This study evaluates changes in QoL among Spanish schizophrenia-spectrum outpatients receiving rehabilitation treatment and identifies factors associated with those changes.

Methods: A total of 127 outpatients with schizophrenia or schizoaffective disorder completed the EuroQOL five dimensions five levels (EQ-5D-5L) and the Schizophrenia Quality of Life Scale-Revision 4 (SQLS-R4) QoL questionnaires twice. The Signs and Symptoms of Psychotic Illness (SSPI) scale, the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB), the Personal and Social Performance (PSP) scale, and the Assessment of Activities of Daily Living and Instrumental Activities (VAVDI) scale were also administered. The frequencies of clinical, demographic and QoL variables were examined, followed by comparisons of questionnaire scores between the two assessments using Wilcoxon and chi-square tests. Linear mixed-effects models were used to evaluate longitudinal changes in QoL and interactions with clinical and demographic factors.

Results: At baseline, the EQ-5D-5L Visual Analogue Scale (VAS) score was 63.7, while the EQ-5D-5L utility index was 0.80. SQLS-R4 scores ranged from 36.8 to 39.3. Patients with lower cognitive functioning, higher SSPI total score, and higher negative and anxiety/depression symptoms showed lower QoL baseline scores. Significant improvements were observed in EQ-5D-5L VAS [$p = 0.001$] and all three SQLS-R4 domains [$p < 0.001$]. Greater QoL improvements were associated with female sex, lower baseline cognitive functioning, and more severe baseline total, negative and anxiety/depression symptoms.

Conclusions: General and specific QoL levels of schizophrenia-spectrum outpatients with stable disease treated at a community day centre were moderate. Improvements in QoL were observed after the rehabilitation intervention. These improvements were associated with general and psychosis-specific symptoms, as well as cognitive functioning and gender. Given the lack of a control group, these findings should be interpreted as associational rather than causal. These results could inform future rehabilitation interventions.

## Keywords

Quality of Life; schizophrenia; schizoaffective; rehabilitation; longitudinal

## Introduction

Quality of Life (QoL) is an important goal in the care of people with psychosis [1]. Interventions for patients with severe mental illness have become more community-based and include treatment provided in rehabilitation centres. A key objective of these centres is to preserve and enhance patients' QoL [2,3]. QoL has also become a central focus of research and an important measure of treatment outcomes

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in psychosis [4]. It is widely accepted that patients with psychosis should assess their QoL (subjective assessment) [2]. Some QoL studies in schizophrenia-spectrum disorders have been performed in Spain [5–8], but the number is limited [9].

Numerous cross-sectional studies have examined QoL and its demographic and clinical determinants in psychosis [9–11]. Lower QoL has tended to be found among patients with higher levels of symptoms (both general and psychosis-specific) and lower cognitive functioning [12–14]. Other factors associated with lower QoL include older age, earlier age at onset, unemployment, and lower educational achievement [15,16].

To improve interventions for patients with psychosis living in the community, there is increasing recognition of the need for longitudinal studies to determine the temporal dynamics of QoL: i.e., to assess whether improvements in patients' QoL occur over time [9,12,17]. A dominant idea has been that schizophrenia-spectrum disorders result in a progressive decline in QoL [18]. It is also crucial to examine the clinical and demographic factors that are associated with improvements in QoL to improve interventions for these patients [19]. In this context, depression, anxiety and (negative) psychotic symptoms are the factors that have most frequently been associated with changes in QoL [13]. Socio-demographic factors such as female gender [20], lower age [18], higher educational achievement [7] have also been associated but further studies are needed to clarify these associations [7,15,16].

Contradictory results have been reported in studies examining changes in QoL, for instance, in relation to the magnitude of QoL improvement [21] and its associated factors. Depression has been reported to show both positive (higher depression scores are associated with greater QoL improvements) [9] and negative associations with QoL improvements [22,23]. These limitations in obtaining more robust results may be due to differences in QoL assessment methods (e.g., patient- or professional-rated measures and the questionnaires administered), patients' clinical characteristics (e.g., age, diagnosis and illness duration), healthcare systems [14], or the heterogeneity of patient profiles, even within the same study [17,24]. Additionally, some QoL studies conducted with patients experiencing an exacerbation may be considered less suitable for analysing the impact of negative symptoms [7,25,26].

To improve comparability, these inconsistent findings warrant further investigation using the same measures across different samples [15]. Questionnaires that are common to other diseases, such as the EuroQOL five dimensions five levels (EQ-5D-5L) [27], the World Health Organization Quality of Life Assessment Instrument–Bref (WHOQOL-BREF) [28] and the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) [29] , as well as instruments that are specific to psychosis, such as the Lehman Quality of Life Inventory (L-QOLI) [30], the Manchester Short Assessment of Quality of Life (MANSA) [31], the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) [32], and the Lancashire Quality of Life Profile (LQoLP) [33], have been used to assess general QoL in psychosis. To capture the various QoL dimensions, it is recommended that a generic QoL questionnaire should be combined with a disease-specific instrument [34]. One example is the combination of EQ-5D-5L and Schizophrenia Quality of Life Scale (SQLS) (an earlier version of Schizophrenia Quality of Life Scale-Revision 4 (SQLS-R4)), as this covers psychotic symptoms, psychosocial performance and medication side effects and has been shown to be responsive to changes in QoL [7].

Rehabilitation programmes are recommended in the literature to combine different components addressing the entire spectrum of schizophrenia symptoms [24]. Some multidisciplinary interventions for psychosis have been associated with QoL improvements. Such programmes tend to include evidence-based treatment components (e.g., cognitive-behavioural therapies such as anxiety and depression management and insight treatment, pharmacotherapy, as well as social interventions and occupational therapy). Some programmes, e.g., Assertive Community Treatment (ACT) [13], address psychoses in general [35], while others address more specific groups such as first-episode psychoses [12,35,36].

The present study has several distinctive features: it is a longitudinal study conducted in Spain; it evaluates a rehabilitation programme that combines different components addressing the entire spectrum of schizophrenia symptoms; all patients participated in the same rehabilitation programme, which had not been previously evaluated; both a general and a disease-specific instrument were administered; and the study included a homogeneous group of patients, with the diagnosis restricted to schizophrenia-spectrum disorders with stable disease.

This study assesses general and disease-specific QoL and analyses how QoL changes following a rehabilitation intervention in a sample of clinically stable Spanish outpatients with schizophrenia-spectrum disorders. The study also examines whether longitudinal changes in QoL differ across groups based on demographic and clinical variables. It was hypothesised that QoL would be moderate and that it would improve after the rehabilitation intervention,


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with these improvements being associated with baseline demographic (gender) and clinical (cognitive impairment and symptomatology) variables.

## Materials and Methods

*Participants*

A consecutive sample of patients receiving treatment at a rehabilitation service (community day centre) was recruited between May 2023 and July 2025. The patients received a multidisciplinary intervention aimed at improving QoL and other aspects. All participants were adults aged 18–65 years diagnosed with clinically stable schizophrenia-spectrum disorders (schizophrenia or schizoaffective) with mild or no positive symptoms, who had been attending the rehabilitation service for at least three weeks. Stable psychosis was defined according to the APA criteria as "the absence of an acute psychotic episode; no psychiatric hospitalisation or major change in antipsychotic treatment during the previous three months, and clinically stable positive symptoms, with no more than mild symptom severity (Signs and Symptoms of Psychotic Illness (SSPI) reality distortion score <5) and no significant deterioration in functioning" [37]. Patients with cognitive impairment that prevented them from completing the questionnaires were excluded.

*Measures*

QoL Questionnaires

All patients completed two subjective QoL questionnaires. The first of these was the EQ-5D-5L, a generic QoL self-report measure comprising five health dimensions that can be combined to produce a societal preference-based health status value (EQ-5D-5L utility index value) [38]. Scores range from 0 to 1. Reference values are available for Spain [39]. The questionnaire includes a self-rated health status score (EQ-5D-5L), which is a Visual Analogue Scale (VAS) with scores ranging from 0 to 100. In both cases, higher scores represent a higher QoL. The person indicates the number that best represents their state of health that day. The second instrument was the SQLS-R4 [40], a self-administered questionnaire that measures subjective QoL specific to patients with schizophrenia. The scale comprises two subscales, vitality and psychosocial feelings, and a global QoL score. Scores in the two areas and the global score range from 0 to 100, with lower scores indicating a higher QoL. This questionnaire has been validated for use in Spain [41]. Questionnaires with <70% of the items completed were excluded from the study. If at least 70% of items were completed, missing items were prorated.

Other Instruments

The main signs and symptoms of psychosis were assessed by the treating clinician using the SSPI interview [42]. This instrument comprises six dimensions – negative symptoms (scores 0–16), disorganisation (0–16), reality distortion (0–12), anxiety-depression (0–8), psychomotor excitation (0–24), and insight level (0–4) – as well as a total score (0–80). Higher scores indicate greater symptomatologic severity. The Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB) [43] evaluates key neurocognitive domains in schizophrenia and related disorders. These domains include information processing speed, attentional vigilance, working memory, verbal learning, visual learning, reasoning, problem solving and social cognition. The MCCB also provides an overall composite score. More precisely, it provides T-scores for each area and an overall composite, with higher scores indicating better cognitive functioning. This instrument has been validated for use in Spain [44]. Raw scores from the Spanish version of the MATRICS are converted into age- and sex-adjusted T-scores (mean = 50, standard deviation [SD] = 10) using the official Spanish normative data and scoring program. The Overall Composite Score is calculated according to the standardised MATRICS scoring algorithm provided for the Spanish version and is also reported as a T-score (mean = 50, SD = 10) [44].

Treating clinicians assessed personal and social functioning using the Personal and Social Performance (PSP) scale [45]. This instrument assesses functioning across four domains: socially useful activities, personal and social relationships, self-care, and disturbing and aggressive behaviours. The PSP provides an overall functioning score ranging from 0 to 100, with higher scores indicating better functioning. The PSP has been validated for use in Spain [46]. Basic and instrumental Activities of Daily Living (ADL) were also assessed by treating clinicians using the Assessment of Activities of Daily Living and Instrumental Activities (VAVDI) [47]. This instrument, validated for use in Spain, evaluates basic and instrumental ADL and the level of support needed to perform them. VAVDI provides a summary score ranging from 14 to 70, with higher scores indicating lower ADL levels [48].

*Intervention*


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All patients took part in an intensive treatment programme provided by the rehabilitation service. This programme provides patients with multidisciplinary care addressing cognitive, social and physical functioning, insight, coping skills, leisure activities, and occupational activities (both in the centre and in the community). Patients also receive pharmacological treatment, as well as individual and group psychotherapy, mainly cognitive-behavioural therapy (see **Supplementary Table 1**). The multidisciplinary team comprises psychiatrists, clinical psychologists, nurses, occupational therapists, leisure therapists, and social workers. The scheduled treatment duration is six months, with patients attending the centre for six hours a day, Monday to Friday.

*Data Collection Procedures*

Patients who provided informed consent completed the QoL questionnaires twice: once in their third week of rehabilitation (baseline) and once two weeks before completing the intervention.

During the first three weeks in the rehabilitation unit, patients underwent an assessment period in which professionals from the unit conducted evaluation interviews. An individual rehabilitation programme was then designed for each patient. This programme was presented to the patient by the treating psychiatrist or psychologist, and participation was voluntary. The first assessment was then conducted during the third week of the programme. The second was conducted two weeks before completion of the intervention. In the final two weeks, patients tended to reduce the number of days they attended the unit in order to prepare their discharge from the rehabilitation programme.

Clinicians completed the SSPI, VAVDI and PSP, and administered the MCCB battery at these same assessment points. Sociodemographic variables (gender, age, educational level, cohabitance, employment status, and leisure and occupational activities) were obtained from the patients. Clinical data (diagnosis, time since diagnosis, number of acute episodes, and degree of disability) were obtained from clinical records.

*Statistical Analysis*

Descriptive statistics, including means and standard deviations, as well as frequencies and percentages, were used to summarise the characteristics of the sample, the scores on the QoL and clinical questionnaires, and the frequency of leisure and occupational activities. Mann-Whitney U tests and chi-square tests were used to compare the two main diagnostic groups (schizophrenia and schizoaffective disorders) in the EQ-5D-5L, SQLS-R4, PSP and VAVDI questionnaires as well as in the clinical and demographic variables (gender, education level, number of acute episodes and time since diagnosis). Wilcoxon and McNemar tests were used to compare the frequencies between the two assessments in the QoL (EQ-5D-5L, SQLS-R4) and clinical (MATRICS, SSPI, PSP and VAVDI) questionnaires, as well as in leisure and occupational activities.

Linear mixed-effects models were fitted to evaluate longitudinal changes in QoL, with time included as a fixed effect and individual as a random effect to account for the intra-correlation structure of the data. To assess whether longitudinal changes in QoL differed according to demographic and clinical features (sex, age, cognitive functioning using MATRICS composite score and symptoms using SSPI total score and individual areas), these models included as fixed effects time and each of these variables, together with an interaction term between them. Due to sample size constraints and the exploratory nature of the study, no other variables were included as covariates in the mixed models. No adjustment for multiple testing was applied as all analyses were pre-specified as exploratory. When the interaction term was significant, the estimated interaction values and the relationship between the specific feature and time were presented. When the interaction term was not significant, *p*-values for the additive model without interaction were presented. A significance level $p = 0.05$ was considered. SPSS program (version 28, IBM Corp., Armonk, NY, USA) was used for data analyses.

## Results

A total of 127 patients out of 133 candidates were interviewed (see flow diagram in **Supplementary Fig. 1**). Six patients did not complete the questionnaires due to administrative failure (three patients were not present in the Rehabilitation Unit when the QoL assessments were conducted) and patient refusal (three patients lacked the motivation to participate in the study). Of the 127 patients who completed the first assessment, 119 (93.7%) completed the second assessment. The reasons for not completing the second assessment were withdrawal from the rehabilitation programme (four patients withdrew because of a worsening of their clinical status and two because of a lack of motivation to continue treatment, corresponding to an attrition rate of 4.7%); and patient refusal (two patients lacked the motivation to participate in the study). No differences were found in baseline characteristics between patients who competed the follow-up assessment and those who did not (see


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**Table 1. Sociodemographic and clinical characteristics of the sample.**

| Variables | Categories | n | % |
|---|---|---|---|
| Gender | Female | 47 | 37.0 |
| | Male | 80 | 63.0 |
| Age | Range 19–64; mean (SD) | 41.6 | (11.4) |
| Cohabitance | Family of origin | 67 | 52.7 |
| | Partner, children, other relatives | 26 | 20.5 |
| | Alone | 18 | 14.2 |
| | Other (flat, institution) | 16 | 12.6 |
| Education level | University | 16 | 12.6 |
| | >Compulsory & <University level | 45 | 35.4 |
| | Compulsory | 50 | 39.4 |
| | Less than compulsory | 16 | 12.6 |
| Employment status | Working | 13 | 10.2 |
| | Student | 1 | 0.8 |
| | Sick leave | 8 | 6.3 |
| | Retired/incapacitated for work | 43 | 33.9 |
| | Unemployed | 60 | 47.2 |
| | Household | 2 | 1.6 |
| Diagnosis | Schizophrenia | 80 | 62.9 |
| | Schizoaffective disorder | 47 | 37.1 |
| Time since diagnoses (years) | Range 1–47; mean (SD) | 14.7 | (10.1) |
| Number acute episodes | Range 0–16; mean (SD) | 3.8 | (3.1) |
| Disability degree | Range 0–75; mean (SD) | 56.8 | (12.5) |
| Substance abuse last year | Alcohol | 13 | 10.2 |
| | Cannabis | 12 | 9.4 |
| | Amphetamines | 4 | 3.1 |
| | Cocaine | 1 | 0.8 |

SD, standard deviation.

**Supplementary Table 2**). All questionnaires included in the study had over 80% of their items answered.

The sociodemographic and clinical characteristics of the patients are shown in Table 1. The majority of patients were male (63.0%) and had a mean age of 41.6 years. 73.2% of patients were living with close family or other relatives, and the mean time since diagnosis was 14.7 years. A total of 26 patients (20.4%) had had substance abuse disorder in the year before entering the rehabilitation programme. These disorders were treated before they were admitted onto the programme. The mean baseline scores were moderate for the EQ-5D-5L VAS (63.7) and the SQLS-R4 total score (37.9), and high for the EQ-5D-5L utility index (0.80). No significant differences were found between patients with schizophrenia and those with schizoaffective disorder in terms of QoL, clinical variables or demographic characteristics (data not shown). The analyses were therefore performed with the two diagnostic groups combined.

Significant improvements in QoL were found between the two assessments for the EQ-5D-5L-VAS and the three SQLS-R4 scores, with effect size/sizes (ES) ranging from 0.35 to 0.39, indicating small effects [49]. Better cognitive functioning was found in the MATRICS composite score and in three dimensions, namely speed of processing, verbal learning and reasoning, and problem solving. ES ranged from 0.18 to 0.24, indicating small or very small effects. Symptom severity decreased in the SSPI total score and in five areas, with ES ranging from 0.53 to 1.13, suggesting medium-to-large effects. More precisely, the ES were large for the total score (1.13), negative symptoms (0.84), and anxiety/depression (0.94). Improvements were also observed in ADLs, with a VAVDI ES of 0.34, indicating a small effect, as well as in global functioning, with a PSP ES of medium magnitude (ES = 0.68). The frequency of leisure and occupational activities performed outside the rehabilitation service also increased significantly (see Table 2).

Table 3 shows the results of the mixed-effects model assessing whether the evolution of QoL differed according to sociodemographic and clinical global scores (MATRICS and SSPI). Additional results for specific SSPI scores are provided in **Supplementary Table 3**. Regarding socio-


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**Table 2. Changes in scores for the QoL, MATRICS, SSPI, PSP and VAVDI questionnaires, leisure and occupational frequencies.**

| Variable | Assessment | | Cohen's d | *p*-value |
|---|---|---|---|---|
| | 1st n = 127, mean (SD) | 2nd n = 119, mean (SD) | d ES | |
| QoL | | | | |
| EQ-5D-5L VAS[c] | 63.7 (22.5) | 71.9 (18.8) | 0.39 | 0.001[a] |
| EQ-5D-5L utility index[c] | 0.80 (0.2) | 0.83 (0.2) | | 0.089[a] |
| SQLS-R4 psychosocial[d] | 36.8 (21.9) | 29.5 (20.6) | 0.35 | <0.001[a] |
| SQLS-R4 vitality[d] | 39.3 (20.6) | 32.3 (17.8) | 0.38 | <0.001[a] |
| SQLS-R4 total[d] | 37.9 (20.9) | 35.1 (10.1) | 0.37 | <0.001[a] |
| MATRICS | | | | |
| Composite score[c] | 33.1 (12.8) | 38.1 (11.9) | 0.23 | <0.001[a] |
| Speed of processing[c] | 35.8 (11.1) | 40.1 (10.5) | 0.24 | <0.001[a] |
| Working memory[c] | 38.5 (11.1) | 40.1 (12.3) | | 0.094[a] |
| Social cognition[c] | 40.5 (13.6) | 41.1 (14.1) | | 0.254[a] |
| Attention/vigilance[c] | 38.5 (9.2) | 40.3 (9.1) | | 0.642[a] |
| Verbal learning[c] | 34.4 (14.9) | 38.1 (13.4) | 0.21 | 0.031[a] |
| Visual learning[c] | 35.9 (14.4) | 39.2 (14.4) | | 0.081[a] |
| Reasoning and problem solving[c] | 43.3 (10.5) | 46.6 (12.2) | 0.18 | 0.013[a] |
| SSPI | | | | |
| Total[d] | 10.9 (5.7) | 6.0 (3.9) | 1.13 | <0.001[a] |
| Insight level[d] | 1.8 (1.3) | 1.3 (1.2) | 0.39 | 0.025[a] |
| Negative symptoms[d] | 4.1 (2.6) | 2.5 (2.3) | 0.84 | <0.001[a] |
| Disorganisation[d] | 0.9 (1.1) | 0.7 (0.8) | | 0.075[a] |
| Reality distortion[d] | 1.1 (1.5) | 0.4 (1.1) | 0.53 | <0.001[a] |
| Anxiety-depression[d] | 1.7 (1.5) | 0.6 (0.7) | 0.94 | <0.001[a] |
| Psychomotor excitement[d] | 0.5 (0.9) | 0.1 (0.4) | 0.53 | 0.001[a] |
| ADL, PSP and activity | | | | |
| VAVDI[d] | 37.8 (8.9) | 35.1 (6.8) | 0.34 | 0.002[a] |
| PSP[c] | 39.2 (8.8) | 46.1 (11.3) | 0.68 | 0.001[a] |
| Leisure activity, n (%) | 19 (14.9) | 59 (49.6) | | <0.001[b] |
| Occupational activity, n (%) | 8 (6.3) | 35 (29.4) | | 0.003[b] |

ES, effect size/sizes (Cohen's d); QoL, Quality of Life; EQ-5D-5L, EuroQOL five dimensions five levels; SQLS-R4, Schizophrenia Quality of Life Scale-Revision 4; MATRICS, Measurement and Treatment Research to Improve Cognition in Schizophrenia; SSPI, Signs and Symptoms of Psychotic Illness; VAVDI, Assessment of Activities of Daily Living and Instrumental Activities; PSP, Personal and Social Performance; VAS, Visual Analogue Scale; ADL, Activities of Daily Living; SD, standard deviation. [a] Wilcoxon test; [b] McNemar; [c] higher scores indicate better results; [d] higher scores indicate worse results.

economic variables, neither age nor its interaction with time were significant. However, gender-differences were identified: baseline EQ-5D-5L VAS scores were nine points higher in men than in women, but men showed significantly less improvement (5 vs 16 points). A higher proportion of women were unemployed than men (61.7% vs 38.8%), but women were less likely to be retired or incapacitated (23.4% vs 40.0%), despite having a higher mean age. Women also had slightly higher total SSPI scores (11.4 vs 10.4) (**Supplementary Table 4**).

With regard to cognitive features, the baseline EQ-5D-5L VAS score was significantly higher in patients with high cognitive functioning than in those with low MATRICS composite scores. However, QoL improvement after the intervention was significantly greater among patients with lower MATRICS scores, and the relationship between EQ-5D-5L and MATRICS was no longer observed. Similarly, baseline SQLS-R4 scores correlated negatively with MATRICS scores, indicating that patients with higher cognitive values tended to have better Schizophrenia-related QoL. Improvements in this QoL were observed in most patients regardless of their level of cognitive functioning (see Table 3).

Finally, psychotic illness and anxiety-depression


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symptoms were also associated with changes in QoL. More specifically, baseline EQ-5D-5L scores were lower in patients with high symptomatology (higher SSPI total scores). However, QoL improved significantly more in these patients, and the correlation between EQ-5D-5L and SSPI total scores was no longer observed in the post-intervention assessment. Accordingly, baseline SQLS-R4 total scores were higher (indicating lower QoL) in patients with higher SSPI total scores, though QoL improved over time in most patients regardless of SSPI score (see Table 3).

The SSPI domain that clearly interacted with QoL evolution was negative symptomology. Specifically, EQ-5D-5L utility index and SQLS-R4 scores improved greatly in patients with more severe negative symptoms. Anxiety-depression also interacted with QoL evolution, with greater improvements in EQ-5D-5L VAS scores observed in patients with higher anxiety-depression scores. In addition, patients with higher levels of negative symptoms had higher baseline vitality scores (indicating lower QoL), whereas those with higher levels of anxiety-depression symptoms and reality distortion (which did not interact with QoL evolution) had lower baseline EQ-5D-5L VAS scores as well as higher scores (indicating lower QoL) on all three SQLS-R4 scales (see **Supplementary Table 3**).

## Discussion

This study shows that general and specific QoL levels of schizophrenia-spectrum outpatients with stable disease treated at a community day centre were moderate. Following a rehabilitation intervention, improvements were observed in both general and specific QoL, as well as in clinical variables (symptoms and cognitive functioning) and other activity areas (ADL, personal and social functioning by PSP, and leisure and occupational activities). Changes in QoL differed according to the following clinical variables: cognitive functioning, psychosis symptomatology (total, negative symptoms, and anxiety/depression) and gender. More precisely, baseline QoL was lower in women than in men and in patients with higher symptom levels and lower cognitive functioning than in those with lower symptom levels and higher cognitive functioning. However, patients with these same demographic (females) and clinical characteristics (higher symptom levels and lower cognitive functioning) showed significantly greater improvement.

No significant differences between patients with schizophrenia and those with schizoaffective disorder were observed. Similarly, no QoL differences were found between patients with schizophrenia and those with schizoaffective disorder in a sample of patients with a disease duration similar to that of our patients [21] and no differences were reported in a sample of patients with first-episode psychosis [50]. In the latter study, the authors attributed this lack of difference to similar levels of depressive symptoms in the two diagnostic groups. In our study, no differences were observed in SSPI scores.

Related to the QoL results, scores from the two QoL questionnaires show moderate QoL limitations. Scores from the first assessment were in line with those reported in an international study (including Spain) conducted with schizophrenia outpatients (with a similar time since diagnosis) in which the EQ-5D-5L and SQLS were administered [7]. In that study, the SQLS-R4 vitality score was slightly worse (by 10 points). Psychosocial feelings were similar to those found in a study of Macedonian outpatients with stable disease [51]. SQLS-R4 scores in our study were higher than those reported in a study of schizophrenia inpatients with non-symptom remission (>8 points in psychosocial, vitality and Global QoL) [52]. They were also higher than those reported in a study of schizophrenia patients experiencing acute exacerbations (differences of 16–20 points) [53]. Differences in patients' clinical status may have influenced these differences in QoL.

Improvements in QoL and other variables studied (e.g., symptoms, cognitive functioning, ADL, PSP and activity) may suggest that the rehabilitation intervention had a positive effect in several key areas. These results could support the positive effect of multiprofessional rehabilitation programmes for psychoses [13,16,21,54]. Improvements in SQLS scores were also reported in the international sample (including Spain) of schizophrenia outpatients mentioned earlier [7]. Improvements in EQ-5D-5L VAS were higher than the Minimal Clinical Important Difference (MCID) score and may be considered clinically relevant, whereas changes in the EQ-5D-5L utility index did not reach this MCID threshold [55].

Previous studies have reported differences in responsiveness between the EQ-5D-5L VAS and the EQ-5D-5L utility index in patients with schizophrenia [34,56–58], with some authors observing greater sensitivity to change for the EQ-5D-5L VAS [57,58], consistent with our findings.

Changes in general QoL (WHOQOL-BREF) have been reported in schizophrenia outpatients [15] and in patients in the early course of illness treated at a day centre [59]. Similarly, changes in SF-36 scores have been observed in outpatients with schizophrenia-spectrum disorders [60]. An increase in general QoL (L-QOLI) was found in first-episode psychosis [12,61] and in patients with schizophrenia-spectrum disorders (schizophrenia and


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**Table 3. Mixed-effect model results assessing differential evolution for EQ-5D-5L and SQLS-R4 by sociodemographic and clinical symptoms.**

| Variable | EQ-5D-5L | | SQLS-R4 | | |
|---|---|---|---|---|---|
| | VAS | Utility index | Total | Psychosocial | Vitality |
| Total | | | | | |
| Time (post vs pre) | 8.61 (3.91; 13.3) | 0.38 (–0.22; 0.99) | –7.99 (–12.05; –3.93) | –9.04 (–12.40; –3.68) | –7.44 (–11.31; –3.52) |
| Sex | | | | | |
| Men (vs Women) | 9.21 (1.26; 17.16) | 2.04 (–1.87; 5.84) | –0.73 (–7.96; 8.48) | –1.94 (–9.61; 5.23) | 0.42 (–6.56; 7.41) |
| Time (post vs pre) | 16.16 (8.13; 24.19) | 0.38 (–0.22; 0.98) | –7.97 (–12.04; –3.91) | –7.99 (–12.36; –3.61) | –7.45 (–11.33; –3.55) |
| Sex (men)*Time | –11.26 (–21.01; –1.51) | - | - | - | - |
| Interaction *p*-value | 0.024 | 0.442$^{\Omega}$ | 0.912$^{\Omega}$ | 0.774$^{\Omega}$ | 0.872$^{\Omega}$ |
| Age | | | | | |
| Age | –0.09 (–0.39; 0.21) | 0.02 (–0.15; 0.18) | –0.02 (–0.32; 0.29) | –0.02 (–0.33; 0.31) | 0.01 (–0.28; 0.30) |
| Time (post vs pre) | 9.65 (3.96; 13.35) | 0.38 (–0.22; 0.98) | –7.99 (–12.05; –3.93) | –8.04 (–12.40; –3.67) | –7.44 (–11.32; –3.56) |
| Age*Time | - | - | - | - | - |
| Interaction *p*-value | 0.089$^{\Omega}$ | 0.502$^{\Omega}$ | 0.892$^{\Omega}$ | 0.885$^{\Omega}$ | 0.714$^{\Omega}$ |
| MATRICS composite score | | | | | |
| MATRICS | 0.38 (0.02; 0.71) | 0.01 (–0.13; 0.14) | –0.40 (–0.70; –0.11) | –0.39 (–0.70; –0.07) | –0.42 (–0.71; –0.13) |
| Time (post vs pre) | 26.20 (10.02; 42.37) | 0.37 (–0.26; 1.01) | –7.65 (–11.88; –3.43) | –7.71 (–12.23; –3.19) | –7.01 (–11.07; –2.94) |
| MATRICS*Time | –0.49 (–0.92; –0.06) | - | - | - | - |
| Interaction *p*-value | 0.025 | 0.811$^{\Omega}$ | 0.512$^{\Omega}$ | 0.423$^{\Omega}$ | 0.245$^{\Omega}$ |
| SSPI total | | | | | |
| SSPI total | –1.18 (–1.97; –0.39) | 0.21 (–0.16; 0.57) | 0.72 (0.04; 1.40) | 0.65 (–0.93; 1.39) | 0.89 (0.25; 1.55) |
| Time (post vs pre) | –2.73 (–14.41; 8.92) | 0.42 (–0.33; 1.21) | –7.95 (–12.62; –3.29) | –7.82 (–12.84; –2.80) | –7.48 (–11.93; –3.03) |
| Total*Time | 1.18 (0.23; 2.14) | - | - | - | - |
| Interaction *p*-value | 0.015 | 0.262$^{\Omega}$ | 0.137$^{\Omega}$ | 0.054$^{\Omega}$ | 0.111$^{\Omega}$ |

Parameter estimates (*p*-values with 95% interval) are presented for the variables included in the models and for the interaction terms between these variables and time. $^{\Omega}$For models with interaction *p*-value $\geq$0.05, parameter estimates correspond to the coefficients of the additive models that result from adding the variables without including the interaction term. Scales: EQ-5D-5L, EuroQOL five dimensions five levels; SQLS-R4, Schizophrenia Quality of Life Scale-Revision 4; MATRICS, Measurement and Treatment Research to Improve Cognition in Schizophrenia; SSPI, Signs and Symptoms of Psychotic Illness; VAS, Visual Analogue Scale. The asterisk (*) represents the interaction effect.

schizoaffective disorder) treated for one year (Q-LES-Q) [53]. Contrary to our findings, no changes in QoL were reported in patients with stabilised illness from that study after a 10-year period [21]. In our study, patients were assessed during a period of intensive rehabilitation treatment.

The small ES observed for QoL improvements were consistent with those reported in a meta-analysis examining the impact of psychological treatments on QoL in people with schizophrenia-spectrum disorders. In that meta-analysis, a larger ES (Hedges g = 0.314) was observed, as in our study, when a combination of interventions was administered [24]. However, the ES for QoL changes in our study were larger than those reported in a sample of patients receiving community-based follow-up management [10]. This difference may be due to the greater intensity of our treatment programme. The low ES for cognitive outcomes may be related to the fact that our rehabilitation programme was not primarily focused on cognitive rehabilitation. These results are in line with those from other cognitive rehabilitation programmes for schizophrenia [62]. Factors such as illness duration may also influence these results [63]. The ES for SSPI scores was much larger than those observed for QoL. The afore-mentioned meta-analysis of randomised clinical trials examining the effect of interventions on QoL in schizophrenia also revealed larger ES for symptom improvement than for QoL improvement [24]. This difference may be related to the characteristics of the questionnaire used, including possible ceiling effects in QoL scores or greater sensitivity to change in symptom-measuring scales. In this regard, Liddle *et al.* [42] concluded that the SSPI was at least as sensitive to changes in illness severity as the Brief Psychiatric Rating Scale (BPRS) and the Positive and Negative Syndrome Scale (PANSS) scales. They also estimated that a one-unit increase in the Clinical Global Impression (CGI) score corresponded to a 31% reduction in SSPI global score. Another possible explanation for the large ES observed is the nature


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of the intervention: ours was delivered in a mental health centre rather than a psychosocial centre. The professionals in our team have extensive experience in interventions aimed at improving both positive and negative symptoms. Another meta-analysis also found large ES on symptoms, with figures of approximately 0.50–0.60 for global negative symptoms [64]. None of the studies included in the latter analysis used the SSPI scale. Another possible explanation for the large ES observed in our study is the high level of baseline global symptoms (mean (SD) = 10.9(5.7)), which may have left greater room for improvement. Furthermore, because this was an uncontrolled pre-post study, regression to the mean cannot be ruled out as a contributing factor to the observed improvement. Nevertheless, the sensitivity of the SSPI to clinical change and the symptom-focused nature of the intervention may also have contributed to the large ES.

Results from the mixed models are consistent with those of other studies. Lower QoL improvements in men than in women have been reported in patients with psychoses treated with extended-release quetiapine [65], consistent with our findings for EQ-5D-5L VAS, as well as in patients with other conditions, such as depression and alcohol use disorder [66]. In first-episode psychosis, changes in general QoL (L-QOLI) interacted with initial depression [12]. In contrast to our findings, no interaction was observed with negative symptoms or cognitive functioning, which may be explained by the lower levels of negative symptoms and better-preserved cognitive functioning in first-episode patients. Also in contrast to our findings, lower initial depressive symptomatology was associated with improvements in general QoL (MANSA) in elderly patients (mean age 66) with psychosis [67]. The patients in our study were younger and were receiving a more intensive intervention. Another study with first-episode patients also found no interaction between changes in WHOQOL-BREF scores and age; however, unlike in our study, no gender effects were observed [58]. De Winter *et al*. [18] (2024) found greater QoL improvements in younger patients with schizophrenia-spectrum disorders. One explanation for their findings is their higher proportion of younger participants, who also demonstrated greater improvements in symptoms and functioning. Taken together, the results of the mixed models suggest that demographic and clinical factors may be associated with QoL improvement [68]. More specifically, gender-related differences in QoL improvements have been associated with differences in cognitive and emotional status, which may in turn reflect hormonal influences, brain structure differences, and gender-related sociocultural factors [69]. In addition, women in our sample had lower initial EQ-5D-5L VAS scores and higher symptomatology (SSPI scores). They were also more likely to be unemployed but less likely to be retired or incapacitated than men. These differences may explain the greater improvements in EQ-5D-5L VAS scores among women than among men.

Negative symptoms and depression may be key mechanisms through which integrated care may be related to improvements in QoL among patients with schizophrenia-spectrum disorders treated at a rehabilitation centre. Persistent negative symptoms are considered to affect patients' QoL directly [70] but also indirectly: negative symptoms are a major driver of non-adherence to multiprofessional therapy, which may lead to persistent psychopathology, including increased depression and positive symptoms, as well as reduced social and overall functioning [1]. High levels of depressive symptoms may therefore mask the potential positive effects of other factors on QoL [9] and lead to a negative view of life as it is, resulting in lower subjective QoL [71]. Moreover, lower cognitive functioning may result in poorer psychosocial functioning and, consequently, lower subjective QoL [72]. Related to the group comparisons, group differences based on clinical variables, including cognitive functioning and symptoms, were consistent with those reported in previous studies of patients with first-episode psychosis [12,14,60,70] and schizophrenia-spectrum disorders [10,14] including those from a previous study conducted by our group [34].

Several clinical recommendations can be made. For example, for patients with schizophrenia-spectrum disorder and stable disease with prominent negative symptoms, intensive rehabilitation programmes combining various components targeting several symptoms of schizophrenia may be beneficial. These programmes could include interventions aimed at increasing activity levels (daily physical functioning interventions, occupational and leisure activities both in the centre and the community), cognitive remediation (two weekly group sessions), social skills training (weekly group sessions), insight training (individual and weekly group sessions), and cognitive behavioural therapy to address psychosis and general symptoms (also individual and weekly group sessions).

This study has several limitations. First, the study's single-centre design limits its external validity. However, it should be noted that the centre covers a very large part of the autonomous community of Navarre, including both rural and urban areas with a variety of neighbourhoods and socioeconomic levels, as patients came from 13 centres of the Mental Health Network of the community. This makes the sample representative of the region. Nevertheless, to increase generalisability, similar studies should be con-


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ducted across multiple centres in Spain. Second, the pre-post single-arm study design lacks a control group, meaning improvements in QoL cannot be specifically attributed to the rehabilitation programme as natural recovery has not been accounted for. For ethical reasons we did not design a two-arm study, as the programme is offered to all patients who meet the inclusion criteria due to the expected benefits. Third, there may be a potential selection bias because patients who agreed to participate may differ systematically from those who declined, as they may have been more motivated to improve their situation. We do not know how many patients met the clinical inclusion criteria but did not participate in the programme, so it is difficult to estimate the effects, though overestimation is inevitable as participation cannot be compulsory. In contrast, follow-up bias is expected to be low, as only six people left the programme and two others remained in it but declined to take part in the measurements. Moreover, their baseline characteristics did not differ from the completers. Fourth, the assessment of factors affecting QoL evolution did not include possible confounding factors, such as employment status or educational level, so caution is needed to avoid over-interpreting the results. Fifth, although there are reference MCIDs for some QoL scales, none exist for the SQLS-R4 questionnaire, which limits the interpretation of the statistical differences observed. Finally, only six months of follow-up were considered, which may be insufficient to assess long-term maintenance of QoL improvements. Future research with longer follow-up periods is needed to address this aspect.

## Conclusions

This study has observed that an intensive rehabilitation intervention is associated with improvements in general and disease-specific QoL in a sample of Spanish outpatients with clinically stable schizophrenia-spectrum disorders. General and psychosis-specific symptoms, as well as cognitive functioning and gender, were associated with these QoL improvements. These results support the expansion and improvement of available treatments–particularly for patients with depressive and negative symptoms, as well as cognitive rehabilitation–given their positive effects in improving patients' QoL and preventing its deterioration. Future research should examine whether gender-specific differences exist in treatment outcomes. Future research should also study QoL, the effects of treatments, and related factors in other groups, such as patients with psychotic and substance abuse disorders—a highly prevalent dual pathology that poses major challenges for professionals.

## Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Author Contributions

Conception and study design: JIA; Data acquisition: JIA, ACI, LL, AL, GG; Data analysis and interpretation: JIA, BI, JL; Drafting of the article: JIA, BI. All authors contributed to the critical revision of the article's intellectual content and approved the final version for submission. All authors participated fully in the work, took public responsibility for appropriate portions of the content, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or completeness of any part of the work were appropriately investigated and resolved.

## Ethics Approval and Consent to Participate

This study was approved by the Regional Ethics Committee for Biomedical Research of Navarra (protocol number 35/2013) to perform the study in the Rehabilitation Unit from Mental Health Network of Navarra (Spain). Participants provided written informed consent to take part in the study. This study adhered to the recommendations of the Declaration of Helsinki.

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## Conflict of Interest

The authors declare they have no conflict of interest.


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## Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.62641/aep.2441.

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