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RESEARCH ARTICLE

# Recovering quality of life in outpatients with psychosis spectrum disorders and its association with the symptom domains

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**Competing interests:**

The authors have declared that no competing interests exist

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## Summary

Quality of life (QoL) as a measure of subjective well-being is an important indicator in the everyday functioning of patients with psychosis spectrum disorders (PSD). The aim of this study was to explore the association between QoL and five symptom domains in outpatients with PSD. Our hypothesis was that negative and affective symptom domains would be associated with lower QoL.

Socio-demographic and clinical data were collected from 68 participants who met the prerequisite for the current study – adult outpatients diagnosed with F20.x-29 (according to ICD-10), qualified by the attending physicians as stable. Their symptoms were assessed using the expanded version of the Brief Psychiatric Rating Scale (BPRS-E) on the basis of which five symptom domains were quantified: positive symptoms, negative symptoms, affective symptoms (anxiety/depression), activation and disorganization. QoL was measured with the ten-point Recovering Quality of Life (ReQol) scale.

Mean age (SD) of the sample was 43.3 (11.0) years, and 60.3% of participants were male. ReQoL mean (SD) score was 25.4 (8.4) and BPRS-E mean total score was 1.9 (0.5). Regarding the BPRS-E and QoL score differences between males and females, educational level or marital status were not observed. Linear regression analyses showed that two out ot five symptom domains were significantly associated with ReQoL: Affective domain (β coeff.=-.717, p<.001) and Negative symptom domain (β coeff.=-.299, p=.001).

The present study of real-world clinically stable patients with PSD demonstrated that affective symptoms (depression/anxiety) had the strongest negative association with QoL in comparison with other symptom domains. This information could be useful for clinicians who should try to alleviate distress in order to improve the PSD treatment outcome.

**Keywords:** Quality of Life, Psychotic Disorders, Symptom domains, Outpatients

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## INTRODUCTION

Psychotic spectrum disorders (PSD) are multifactorial complex conditions with a huge impact on quality of life (QoL) (1). QoL can be defined as a person's sense of well-being and satisfaction with his/her life circumstances, as well as a person's health status and access to resources and opportunities (2). Personal recovery and QoL are especially important in clinically stable outpatients striving towards employment and stable work, socialization, as well as taking charge of their own health and preventing future episodes of mental health deterioration (2). Symptoms of patients diagnosed with schizophrenia and other psychosis spectrum disorders, in particular positive symptoms (perceptual and thought disorders), can be minimized by medication ("clinical recovery"), but their QoL seems to be lower than the QoL of the general population ("personal recovery") and this could be due to several different factors.

Several sociodemographic factors such as age, gender, marital status, and education level were associated with QoL in patients with schizophrenia in previous studies (3). Higher rates of QoL were consistently reported in females compared to male patients with schizophrenia (4). According to Meesters et al, 2010 (5), sociodemographic factors could explain up to 20% of the variance in QoL while the intensity of the clinical symptoms could explain around 50% of it. When patients with schizophrenia, schizoaffective and bipolar disorder were compared, the schizoaffective disorder was associated with the largest losses of QoL (6) and most of the losses in this and other studies (5) were explained by the current depressive symptom levels. Depressive symptoms correlated with QoL in several studies, but not in all (7). Moreover, reports were also showing significant associations between negative symptoms and QoL (4).

Typically, the assessment of symptoms in patients with PSD includes the Positive and Negative Symptoms Scale (PANSS), which measures negative, positive and general symptom domains (8) and additional scales (for example, Calgary Depression Scale for Schizophrenia or other specific scales (9)) would be necessary to address depressive symptoms. However, there are scales such as the BPRS-E (10,11) which could be easily used to get comprehensive information on the major symptom dimensions in PSD including affective symptoms. The BPRS-E was developed to assess the severity of symptoms in patients with psychosis and it is also a sensitive measure of symptom reduction following clinical remission (11). Moreover, this scale was also explored outside the psychosis spectrum. For example, Zanello et al (2013) showed that the 24-item BPRS could be a useful measure of symptom severity and change in symptom status in unipolar depression (12). A recent study performed on a sample of outpatients with psychosis from the Western Balkans which investigated the fitting of the three competing BPRS-E factor models derived in the literature suggested acceptable to good reliability of the five BPRS-E factors/groups of symptoms: Affect, Negative symptoms, Positive symptoms, Activation, and Disorganisation (13).

Understanding the relationship between the different symptom domains with QoL is important because interventions that focus on psychotic symptoms alone may fail to improve subjective QoL (4). Thus, the present study aimed to explore clinically stable outpatients with psychotic disorders to analyze the associations between QoL, socio-demographic characteristics and the five above mentioned symptom domains. Our hypothesis was that negative and affective domains, as assessed by BPRS-E, would be associated with lower QoL. If this hypothesis holds, it means that busy psychiatric services and clinicians could be provided by a simple-to-administer reliable instrument such as BPRS-E to identify patients whose symptoms need further improvement towards recovery.

## MATERIALS AND METHODS

The present study was a cross-sectional observational study performed at two psychiatric institutions (the Clinic for Psychiatry, University Clinical Center of Serbia in Belgrade, and the Special Hospital for Psychiatric Diseases "Dr Slavoljub Bakalović" in Vrsac, Serbia) during 2019/2020. The patients included in this study were involved in the large multicentric IMPULSE study which explored the implementation of the psychosocial intervention DIALOG+ for patients with PSD in low-middle income countries from Southeast Europe (for more information about the IMPULSE see Jovanovic et al, 2020; Grant agreement no.779334)) (14).

The inclusion criteria were the same as those for the IMPULSE study: outpatients with the primary diagnosis of PSD (ICD-10 codes F20-29), aged 18–65, with at least one psychiatric hospital admission during their lifetime (this means the diagnosis had been confirmed under comprehensive clinical evaluation), and the capacity and will to provide informed consent. Patients who had an organic brain disorder or severe cognitive deficits were excluded, as well as those who had been considered unstable by the treating clinician.

The information about gender, age, marital status (i.e. married, single, divorced/separated, and widow/widower) and education (i.e. below the level of elementary school, elementary school graduate, high school graduate, university, or college graduate) have been collected, as well as the information about the diagnosis and the number of psychiatric hospitalizations.

The study was conducted in accordance with the Declaration of Helsinki and its design was approved by the Medical Ethics Committee of the Faculty of Medi-

cine University of Belgrade, as well as by the relevant professional boards. All participants provided informed consent before the initiation of the study.

### Instruments of measurement

Symptoms were assessed using the Brief Psychiatry Rating Scale-Expanded (BPRS-E) with 24 items (10,11). It was applied to assess psychopathological symptoms in the participants of this study. Trained research assistants interviewed patients and used rated guidelines to provide the scoring. Each symptom was rated on a 7-point Likert scale indicating the symptom severity ranging from "0 - not present" to "7 - extremely severe"(Cronbach's alpha = .797). A higher score indicated more severe symptomatology. For additional information about particular symptom domains, five BPRS-E domains were calculated according to the factor analyses provided by Blazhevska Stoilkovska et al. (submitted): positive symptoms (hallucinations, unusual thought content, suspiciousness, grandiosity ), negative symptoms (blunted affect, emotional withdrawal, motor retardation), affective symptoms (anxiety, guilt, depression, suicidality), activation (excitement, motor hyperactivity, elevated mood, distractibility) and disorganization (conceptual disorganization, disorientation, self-neglect, mannerisms and posturing).

Patients were also assessed using the Recovering Quality of Life (ReQoL) scale (2), a generic psychometric self-evaluation. The non-somatic domains of QoL are the most relevant for psychiatric patients and therefore should be the main core (15). This scale measures rather non-physical domains of health-related QoL than pain or disability. It is composed of 10 questions ranging from "never" to "always" and it contains a mixture of positive and negative items. ReQoL had excellent acceptability and feasibility in clinical practice as well as good reliability and construct validity. The positively and negatively worded items score 0–4, where zero on the scale represents the poorest quality of life and four the highest (Cronbach's alpha = .874). ReQoL-10 score up to 24 is considered as falling within the clinical range (2).

## STATISTICAL ANALYSIS

All statistical analyses were performed by the SPSS version 20.0 statistical software.

Descriptive statistical values were used to summarize participants' demographic and clinical characteristics (minimum and maximum values, medians and means/standard deviations). Initially, all data were tested for normality and accordingly analyzed using the appropriate parametric or non-parametric tests. Univariable relations were investigated by ANOVAs for associations between categorical and continuous variables, and by correlations between continuous variables (Pearson's correlation). Multivariable associations between QoL (dependent variable) and all potential variables were investigated in linear regression analyses with potential predictors of QoL - the first block consisted of socio-demographic variables whereas the second block contained the symptom domains. All p-values less than 0.05 were considered significant.

## RESULTS

Our sample consisted of 68 adult patients, whose mean age was 43.3±11.0 and out of which 60.3% were male. Other socio-demographic and clinical characteristics of the participants are shown in **Table 1**. Diagnoses (according to ICD-10 criteria) are listed in **Table 1**. Most of the participants had schizophrenia or unspecified psychosis that was not caused by a substance or any known physiological condition. The mean number of hospitalizations was 4.7±3.4 (median: 4.0; range:1-15)

The mean total BPRS-E score was 1.9±0.5. Of the five symptom dimensions, BPRS Affective domain was scored by mean 2.4±1.0, Negative symptoms by mean 2.1±0.9, Disorganization was rated mean 1.7±0.7, Positive symptoms were scored 1.6±0.8 and Activation was scored 1.6±0.6. The mean of the total ReQol-10 score was 25.4±8.4. The lowest score was found in relation to the items: "I felt confident about myself" (1.7±1.2), "I felt hopeful about my future" (1.9±1.2) and "I felt happy" (2.1±1.1 ).

In terms of the BPRS-E and QoL scores, differences between males and females, educational level or marital status were not observed. Also, no differences in the symptom intensity or QoL were found between the diagnostic subgroups. Age and number of hospitalizations did not correlate with the aforementioned outcomes.

The first block of the variables (socio-demographic variables) explained 7.1% of the variance associated with QoL (R2= .071; adjusted R2=.012), while the second block which consisted of all symptom domains explained over 60% of the variance (R2 =.662; adjusted R2=.609).

In the final structure of the regression function, the only significant predictors of QoL were Affective and Negative symptom domains. The participants with more pronounced affective (depression/anxiety) and negative symptoms had lower scores on ReQoL - see **Table 2**.

## DISCUSSION

Our research involved real-world outpatients to explore how five different symptom domains measured by one single instrument correlated with QoL. We found that the affective domain of the BPRS-E scale, which includes depression, anxiety, and guilt, had the strongest impact on QoL, followed by the negative dimension (blunted

**Table 1.** Symptom domains and quality of life by socio-demographic and clinical characteristics

| **Sociodemographic data** | | **BPRS-E total score, Mean±SD 1.9±0.5** | | **ReQoL total score, Mean±SD 25.4±8.4** | |
|---|---|---|---|---|---|
| | Mean±SD | | | | |
| Age# | 43.3±11.0 | *r=.109; p=.377* | | *r=-.028; p=.824* | |
| Sex | n (%) | | Between group differences | | Between group differences |
| Male | 60.3 | 1.8±0.5 | p=.959 | 25.9±8.3 | P=.529 |
| Female | 39.7 | 1.9±0.4 | | 24.6±8.7 | |
| Education | n (%) | | | | |
| Elementary School or Less | 4 (5.9) | 1.9±0.4 | p=.805 | 30.0±7.2 | p=.527 |
| High School | 54 (79.4) | 1.9±0.5 | | 25.1±8.7 | |
| University/College | 10 (14.7) | 1.8±0.5 | | 25.4±8.4 | |
| Marital Status | n (%) | | | | |
| Married | 8 (11.8) | 1.7±0.3 | p=.367 | 30.1±5.0 | p=.178 |
| Single | 52 (76.5) | 1.9±0.4 | | 24.4±8.7 | |
| Separated/Divorced, Widow(er) | 8 (11.8) | 2.0±0.8 | | 26.8±8.1 | |
| Clinical characteristics | | | | | |
| Diagnosis (ICD-10) | n (%) | | Between group differences | | Between group differences |
| Schizophrenia- F20 | 25 (31.3) | 2.0±0.5 | p=.171 | 25.8±8.6 | p=.746 |
| Schizoaffective disorder – F25 | 11 (13.8) | 1.7±0.4 | | 26.0±6.0 | |
| Unspecified psychosis not due to a substance or known physiological condition- F29 | 22 (32.4) | 1.8±0.4 | | 25.9±9.0 | |
| Other: F21, F22 and F23 | 10 (14.7) | 1.9±0.5 | | 25.4±8.4 | |
| | | | | | |
| Number of hospitalizations# | 4.7±3.4 | *r=0.53; p=.667* | | *r=-0.85; p=.505* | |
| #Pearson's correlations | | | | | |

BPRS - Brief Psychiatric Rating Scale; ReQoL - Recovery Quality of Life

affect, emotional withdrawal, motor retardation). Thus, the hypothesis of this study was confirmed. Socio-demographic factors such as female gender or age, educational level or marital status did not significantly influence QoL in this study. In line with the previous research, the socio-demographic group of variables accounted for QoL variance only to a small extent. However, the symptoms have explained QoL variance to a very large extent in our study and it was in line with the earlier findings (5,16).

**Table 2.** Multivariable relationships between quality of life (ReQoL) and five symptom domains

| BPRS-E symptom domains | β coeff. | p value |
|---|---|---|
| Affective | -.717 | >.001* |
| Negative | -.299 | .001* |
| Positive | .035 | .705 |
| Activation | -.083 | .332 |
| Disorganized | .145 | .119 |

BPRS - Brief Psychiatric Rating Scale; ReQoL - Recovery Quality of Life

In our study, we found that especially anxiety-depression symptoms and negative symptoms measured by BPRS-E determine worse self-evaluation of QoL. These results are in line with what was reported by other authors even though they used different instruments to measure QoL. For example, in comparison with WHO-QoL-BREF used by Gallupi et al. (16) which included 26 items, a 10-item self-rated ReQoL used in the present study is much shorter. Besides being very easy to complete, it is also straightforward to score, quick to interpret and has advantages over similar scales such as EQ-5D-5L (which has an emphasis on pain and disability) or MANSA (which could be strongly associated with depressive symptoms) (15). As mentioned before, busy psychiatric services and clinicians need a simple-to-administer and reliable instrument to identify patients whose symptoms need further improvement.

To enable better daily life for clinically stable PSD outpatients, physicians should try to detect and treat depressive symptoms which seem to have a huge impact on QoL. Challenges to treating depression in PSD include

an additional diagnostic procedure and pharmacological and non-pharmacological management of the symptoms. In a patient with PSD, a clinician should investigate organic factors such as drug misuse, as well as endocrine and other medical problems, as this might be causal or at least contributory to the depressive/anxiety symptoms (17). CBT could be an effective adjunct to medications, however non-pharmacological approach to depressive/anxiety symptoms in psychosis is less explored in comparison to the medication. Drug therapy of affective symptoms in PSD is relying mainly on the results of small-scale trials and reviews. Certain second-generation antipsychotics (quetiapine, lurasidone, amisulpride, aripiprazole, olanzapine, clozapine) could be superior to other antipsychotics in the reduction of depressive symptoms and clozapine could be the therapy of choice in the management of patients at risk from suicide (18). The adjunctive therapy with antidepressants is still debated. Systematic review and meta-analysis (19) suggested small beneficial effects of adjunctive antidepressants, as patients taking add-on antidepressants had more adverse events such as abdominal pain, constipation, dizziness, and dry mouth. On the other hand, long term benzodiazepines adjunctive to antipsychotic drugs could be associated with cognitive impairments (20) and other severe adverse events (21), therefore its prolonged administration needs special caution. Finally, transcranial magnetic stimulation and electroconvulsive therapy could be considered, but they are only indicated when several previous therapeutic approaches proved to be ineffective.

Negative symptoms are an area of unmet therapeutic need in psychotic patients (22). Symptoms such as alogia, asociality, anhedonia, blunted affect or avolition have been associated with a limited response to pharmacotherapies and poor functional outcomes (23). Relatively new drugs such as cariprazine and amisulpride have shown some evidence of their efficacy towards negative symptoms (24, 25). In addition, psychoeducation and psychosocial interventions should be important components in helping patients and their families to cope with the disturbing aspects of avolition, anhedonia and social withdrawal.

There are several limitations of our study. Firstly, the clinical stability of our patients was confirmed by the treating clinician, instead of using scales to confirm the remission. However, the clinical judgment was in line with the level of QoL, i.e ReQoL mean score in our sample was above 24 (up to 24 is considered falling within the clinical range). Secondly, our findings are based on the cross-sectional design of a relatively small and convenient sample of psychosis spectrum patients, which could be considered a limitation to finding how socio-demographic factors could influence QoL or exploring further different types of PSD. Future research needs to include a larger sample and longitudinal design to further explore if several conditions included in PSD have specific associations between symptom domains and QoL in outpatients. Finally, we have not evaluated the possible effects of pharmacotherapy on symptoms or QoL, nor the patients' perception of their treatment. Our recommendation is that future studies also focus on these clinically highly relevant topics, as suggested by the recent study which used machine learning methods to explore QoL in schizophrenia (26).

## CONCLUSION

The emergence of the recovery movement in several European countries increased interest in the QoL assessment. The present study of real-world patients with PSD demonstrated that affective and negative psychotic symptoms had the strongest negative impact on QoL. This information could be useful for clinicians who should try to alleviate distress in order to improve the PSD treatment outcome. The better insight into the QoL of our patients, the more we can do to provide them with a seamless journey to recovery.

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## Conflict of interest

None to declare.

## Author Contributions

NJ, NM - funding acquisition, project administration, supervision
NM, NJ - conceptualization, methodology
SAP, IR, SJ, BS, MZ - investigation, resources
NM, SJ, KS, TT - writing the first and original draft
NM, IR directly accessed and verified the underlying data reported in the manuscript.
All authors - revisions of the manuscript
All of the authors provided important intellectual content and approved of the final version of the manuscript.

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## Ethical approval

The study was conducted in accordance with the Declaration of Helsinki and its design was approved by the Medical Ethics Committee of the Faculty of Medicine University of Belgrade (No:2650/VI-3; date 26.06.2018.), as well as by the professional boards of the Clinic of Psychiatry, University Clinical Centre of Serbia (No:350; date 09.05.2018.) and Special Hospital for Psychiatric Diseases "Dr Slavoljub Bakalović" in Vrsac, Serbia (No:01-36/1; date 15.01.2019.).

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# KLINIČKI SINDROMI POREMEĆAJA IZ SPEKTRA PSIHOZA I NJIHOVA POVEZANOST SA KVALITETOM ŽIVOTA TOKOM OPORAVKA

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**Sažetak**

Kvalitet života (QoL) se može definisati kao percepcija lične dobrobiti i blagostanja i važan je pokazatelj funkcionalnosti osoba sa poremećajima iz spektra psihoza (PSD). Cilj aktuelnog istraživanja koje se odnosi na vanbolničke pacijente sa PSD je da se ispita postoji li povezanost QoL sa jačinom pojedinih grupa simptoma posmatranih kroz pet sindroma. Hipoteza rada je da će QoL biti niži kod osoba sa izraženijim negativnim i afektivnim sindromom.

Uključeno je 68 ispitanika, od kojih su prikupljeni socio-demografski i klinički podaci i koji su bili dispanzerski pacijenti sa dijagnozama F20.x-29 (MKB-10) u stabilnoj fazi osnovnog poremećaja. Simptomi su procenjeni korišćenjem kratke psihijatrijske skale procene (BPRS-E), a zatim su računate vrednosti za pet sindoma: pozitivni, negativni, afektivni (anksiozno/depresivni spektar), sindrom aktivacije i sindrom dezorganizacije. Za ispitivanje QoL korišćena je skala sa 10 stavki (ReQoL) kojom se meri kvaliteta života tokom oporavka pacijenata.

Ispitanici su u proseku (SD) bili stari 43.3 (11.0) godine (60.3% muškog pola). ReQoL je u proseku (SD) iznosio 25.4 (8.4), dok je na BPRS-E zabeležena srednja vrednost (SD) od 1.9 (0.5). Socio-demografski parametri (pol, obrazovni nivo ili bračni status) nisu bili povezani sa BPRS-E ili QoL. S druge strane, od kliničkih parametara linearnom regresijom je pokazano da su dva od pet sindroma bila značajno povezana sa QoL: afektivni sindrom (β coeff.=-.717, p<.001) i negativni sindrom (β coeff.=-.299, p=.001).

Aktuelno ispitivanje klinički stabilnih vanbolničkih pacijenata sa poremećajima iz spektra psihoza ukazalo je da afektivni simptomi (anksiozno/depresivni spektar) imaju najjači uticaj na QoL. Ova informacija je korisna kliničarima jer ukazuje gde treba usmeriti napore da bi se poboljšao ishod lečenja osoba sa poremećajima iz spektra psihoza.

**Ključne reči:** Kvalitet života, Psihoza, Sindrom, Vanbolnički pacijenti

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