



Health-related quality of life associated with different symptoms in women and in men who suffer from schizophrenia

Cristina Domenech^{1,2} · Corrado Bernasconi³ · Maria Victoria Moneta^{2,4} · Anna-Lena Nordstroem³ · Paula Cristobal-Narvaez^{2,4} · Ellen Vorstenbosch² · Jesus Cobo⁵ · Susana Ochoa^{2,4} · Josep Maria Haro^{1,2,4} 

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Abstract

Health-related quality of life (HRQoL) in patients with schizophrenia is related to the severity of psychiatric symptoms. The objective of this study is to analyze whether the symptoms that influence HRQoL are similar in women and men. Data were part of the Pattern study, an international observational investigation which collected data from 1379 outpatients with schizophrenia. Patients were evaluated with the Mini International Neuropsychiatric Inventory, the Clinical Global Impression-Schizophrenia, and the Positive and Negative Syndrome Scale (PANSS), and reported their quality of life using the Schizophrenia Quality of Life Scale (SQLS), the Short Form-36 (SF-36), and the EuroQoL-5 Dimension (EQ-5D). Men reported higher HRQoL on all scales. PANSS total score was 80.6 (SD 23.6) for women and 77.9 (SD 22.1) for men. In women, a higher PANSS negative score and a higher PANSS affective score were associated with a lower SQLS score. In men, a higher PANSS positive score and a higher PANSS affective score were associated with a lower SQLS score. The same pattern appeared with EQ-VAS and EQ-5D tariff. In women, greater age and higher PANSS affective score were associated with a lower SF-36 mental component score. In men, higher PANSS affective, positive, and cognitive scores were associated with a lower SF-36 mental component score. This study shows that HRQoL is influenced by different psychiatric symptoms in women and men. This may have significant implications when deciding the main treatment target in patients with schizophrenia.

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Keywords Gender · Schizophrenia · Health-related quality of life · Positive symptoms · Negative symptoms

✉ Josep Maria Haro
jmharo@pssjd.org

Cristina Domenech
cdomenech@pssjd.org

Corrado Bernasconi
corrado.bernasconi@roche.com

Maria Victoria Moneta
mvictoria.moneta@pssjd.org

Anna-Lena Nordstroem
anna-lena.nordstroem@roche.com

Paula Cristobal-Narvaez
pcristobal@pssjd.org

Ellen Vorstenbosch
e.vorstenbosch@pssjd.org

Jesus Cobo
jcobo@tauli.cat

Susana Ochoa
sochoa@pssjd.org

- 1 Universitat de Barcelona, Barcelona, Spain
- 2 Parc Sanitari Sant Joan de Déu, Institut de Recerca Sant Joan de Déu, Sant Boi de Llobregat, Barcelona, Catalonia, Spain
- 3 F. Hoffmann-La Roche Ltd, Basel, Switzerland
- 4 Centro de Investigación Biomédica en Red, CIBERSAM, Madrid, Spain
- 5 Corporació Sanitària Parc Taulí, Hospital Universitari - UAB Sabadell, Barcelona, Catalonia, Spain

Background

The move to a more patient-centered approach in mental health requires assessment of the patient's perspective of his or her health status. Accordingly, self-reported health-related quality of life (HRQoL) measurements are increasingly seen as an important way of evaluating the treatment and care offered to patients with schizophrenia. The use of HRQoL measures as treatment outcomes, as they represent the patient's perspective, may contribute to increased satisfaction with care, enhanced adherence to therapeutic interventions, and improved health outcomes (Awad and Voruganti 2012).

HRQoL is a complex concept which depends on many aspects of a patient's life, from sociodemographic characteristics to living conditions, but is especially influenced by symptoms the patient experiences (Katschnig 2000). Several reviews have analyzed how psychiatric symptoms influence quality of life in patients with schizophrenia (Eack and Newhill 2007; Papaioannou et al. 2011). Many studies found that overall level of symptoms is related to HRQoL (Eack and Newhill 2007; Galuppi et al. 2010). Most found that the presence of depressive symptoms is associated with lower HRQoL. However, the studies that analyzed the relationship between positive and negative symptoms and HRQoL showed discordant results (Papaioannou et al. 2011), with some finding a relationship and others not. Eack and Newhill (2007) in their review on the relationship between symptoms and HRQoL in schizophrenia concluded that positive and negative symptoms seem to be more strongly related to poor HRQoL in studies with outpatients, whereas general psychopathology shows a consistent negative relationship with HRQoL across all study samples and treatment settings.

A number of studies have examined gender differences in HRQoL in patients with schizophrenia. Some of them found differences in HRQoL between men and women, but some did not. For instance, Jarema and Koniecznyńska (2001) evaluated 100 patients with schizophrenia treated with classic or atypical neuroleptics in a day hospital. They found that the HRQoL of women and men did not differ at baseline, but the improvement after treatment was greater in women. Conversely, another study, which included patients from five European countries, did not find differences in self-reported quality of life (Thornicroft et al. 2002). Interestingly, Galuppi et al. (2010) found that the differences in HRQoL between men and women depended on the age of the individual. In people younger than 45 years of age, women tended to have better HRQoL than men, but after that age, the relationship appeared to be the opposite. Only a scarce number of studies have investigated gender differences in the association of symptoms with HRQoL. Röder-Wanner and Priebe (1998) analyzed the HRQoL of men and women at first admission for schizophrenia. They conducted stratified analyses by gender and reported that psychopathology, measured with the BPRS scale, was not

related to subjective HRQoL in either gender. Jarema and Koniecznyńska (2001) reported that the severity of depressive symptoms correlated inversely with HRQoL in all patients and that, in women, the improvement in HRQoL correlated positively with the improvement in Positive and Negative Syndrome Scale (PANSS) general symptoms.

The aim of this study is to examine whether there are gender differences in HRQoL in schizophrenia and investigate the relationship between the symptoms of schizophrenia and HRQoL by gender. If these differences exist, they should be taken into account when tailoring schizophrenia treatments for women and men.

Methods

Study design

Data used in this paper are derived from the Pattern study, an international, multicentric, observational study designed to collect data from outpatients with schizophrenia who were attending psychiatric centers (Haro et al. 2015).

Adult patients with schizophrenia who were treated at psychiatric outpatient clinics were eligible for study entry. To maximize the generalizability of study findings, minimal entry criteria were applied. Participants had to be at least 18 years old and meet criteria for schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision, or the International Classification of Diseases, 10th revision (American Psychiatric Association 2000). Diagnosis was confirmed with an abridged version of the Mini International Neuropsychiatric Inventory (Leclercq et al. 1997). Exclusion criteria were an acute psychotic exacerbation in the 3 months prior to baseline (e.g., hospitalization or increased psychiatric care in order to avoid hospitalization), enrollment in an interventional study at baseline, and an inability or unwillingness to comply with the study protocol.

The study was conducted by psychiatrists working in outpatient facilities who recruited the patients using sequential selection. From a list of current clinic patients generated for each site, those patients who fulfilled the inclusion criteria and did not meet any exclusion criteria were invited to participate in the study.

Patient care and treatment followed the routine local clinical practice and proceeded at the discretion of the treating clinician. The study was conducted in eight countries, namely Argentina (4 sites), Brazil (4 sites), Canada (9 sites), France (25 sites), Germany (33 sites), Italy (25 sites), Spain (25 sites), and the UK (15 sites). Patient recruitment took place from September 2012 until December 2013. The target sample size was 1500 patients. The protocol and consent procedures were approved by all local institutional review boards/ethics

committees before study initiation. All patients voluntarily participated in the study and provided informed consent.

Patient assessment

Psychiatrists and patients utilized an electronic hand-held tablet to capture all clinical assessments and HRQoL. Patients recorded their HRQoL prior to completion of other study assessments. The assessment by the participating psychiatrists included sociodemographic and clinical variables, the Positive and Negative Syndrome Scale (PANSS) (Kay and Fiszbein 1987), and the Clinical Global Impression-Schizophrenia (CGI-SCH) Scale (Haro et al. 2003). Participating psychiatrists were provided with training in the use of the questionnaires, and ratings were not blinded since no defined intervention was evaluated. PANSS dimensions were calculated based on Lindenmayer et al.'s five factors (Lindenmayer et al. 1995): positive, negative, cognitive/disorganized, affective, and excitement.

HRQoL data were assessed by patients using two generic scales and one disorder-specific scale. Generic scales were developed to measure HRQoL across different health conditions, while condition-specific scales focus on the symptoms and difficulties experienced by individuals presenting a particular health problem (Papaioannou et al. 2011; Brazier et al. 2014). The two generic scales were the Short Form-36 (SF-36) (Ware and Sherbourne 1992), the EuroQol-5 Dimension (EQ-5D) (Rabin and de Charro 2001) questionnaire, and the disorder-specific Schizophrenia Quality of Life Scale (SQLS) (Wilkinson et al. 2000).

The SF-36 is a generic health status profile measure consisting of eight dimensions of general health, bodily pain, physical functioning, role-physical, mental health, vitality, social functioning, and role-emotional. The eight dimensions can be used to generate physical and mental health summary scores (SF-36-physical component score, SF-36 PCS and SF-36 mental component score, SF-36 MCS). The population mean of these summary scores has been established at 50, with higher ratings indicating a better health-related quality of life.

The EQ-5D questionnaire includes five questions assessing different dimensions of HRQoL (mobility, self-care, usual activities, pain, and anxiety/depression) and a visual analogue scale (EQ-5D VAS) which indicates the responder's self-rated evaluation of his/her current quality of life from 0 (worst imaginable health state) to 100 (best imaginable health state). The five questions allow the calculation of a health preference measure or tariff. This tariff ranges from 0 (death) to 1 (perfect health).

The EuroQol 5-D population tariffs, SF-36 mental component score (SF-36 MCS), and physical component score (SF-36 PCS) were calculated using UK validation studies (Jenkinson et al. 1993; Dolan et al. 1995). Both scales have

shown good validity and reliability in different populations (Jenkinson et al. 1994; Fransen and Edmonds 1999; Linde et al. 2008).

The Schizophrenia Quality of Life Scale (SQLS) includes 30 items divided over three subscales. The three subscales correspond to (a) psychological aspects, including various emotional problems such as feeling lonely, depressed or hopeless, as well as feelings of difficulty in social situations and feeling worried about the future; (b) motivation and energy, which addresses various problems of motivation and activity, such as lacking the will to do things and engage in positive aspects of life; and (c) symptoms and side-effects such as sleep disturbance, blurred vision, dizziness, muscle twitches, and dry mouth, which can be caused by medication (Wilkinson et al. 2000). In this scale, higher ratings represent lower HRQoL. Given that in the other HRQoL scales used in this study higher ratings mean better HRQoL, the rating of this scale was reversed to facilitate comparability. The internal reliability of the SQLS ranges from 0.78 to 0.93 for the three subscales (psychosocial, motivation and energy, and symptoms and side-effects) (Wilkinson et al. 2000).

Statistical analysis

The analyses included all patients who fulfilled all the eligibility criteria. Descriptive statistics are provided for all variables of interest by gender. Statistical significance was calculated using the *t* test or chi-square test. Pearson correlation coefficients between symptom dimensions and HRQoL were calculated. Differences between coefficients between women and men were calculated using the Fisher *r*-to-*z* transformation.

Linear regression models stratified by gender were fitted to study the baseline factors associated with HRQoL ratings (in case of the EQ-5D tariff, Tobit regression was used to take into account ceiling effects). Age and country were included in all regression models regardless of statistical significance. The rest of the covariates were chosen based on a stepwise selection model. The initially tested variables were PANSS (positive, negative, cognitive/disorganized, affective, and excitement), age at onset, time since onset, number of comorbidities, type of comorbidity (respiratory, cardiovascular, gastrointestinal, genitourinary, musculoskeletal, neurological in extremities, endocrine/metabolic, hematopoietic, dermatological, cancer, and others), extrapyramidal symptoms, tardive dyskinesia and akathisia, obesity, and substance use (including prior or current use of alcohol, recreational drugs, and other substances). All the entered variables had their association with the outcome variable tested in bivariate analyses. Additionally, a linear regression model including all patients was fitted to test for gender differences in overall HRQoL when adjusting for covariates. Finally, the analyses we

repeated stratify the sample in two age groups, people younger and older of 45 years of age, for each gender.

All statistical analyses were conducted with SAS version 9.

Results

The sample included 391 women and 954 men. Mean age was 45.7 (SD 12.3) years for women and 40.5 (SD 10.7) years for men ($P < 0.0001$) (Table 1). Duration of illness was 16.2 (SD 11.1) and 14.6 (SD 10.0) for women and men, respectively ($P < 0.05$). PANSS total score was 80.6 (SD 23.6) for women and 77.9 (SD 22.1) for men. PANSS positive and negative symptom scores for women were 16.0 (SD 6.7) and 23.4 (SD 7.4), respectively. The figures for men were 16.0 (SD 6.3) and 22.2 (SD 7.2).

Men reported higher HRQoL as assessed by all scales. For example, the EQ-5D VAS score was 66 for men and 62 for women ($P < 0.001$). However, the magnitude of the difference was not large. The linear regression model that tested whether these differences were maintained when adjusting for the influence of covariates also found significant gender differences, with men reporting higher HRQoL than women.

Table 2 presents the Pearson correlation coefficients for the relationship between each of the HRQoL scales and the PANSS symptoms for women and men. In all but five of the 25 estimates, the correlation between symptom dimensions and HRQoL was numerically higher for women than for men. However, only in the case of the relationship between EQ-VAS and EQ-5D and PANSS negative score, the difference reached statistical significance. The magnitude of the correlation was moderate, except for the SF-36 PC score, which had a lower correlation with symptoms. The correlations between symptom dimensions and HRQoL were higher for the affective dimension, followed by the positive and negative dimensions.

Table 3 presents the results of the ten linear regression models on the factors associated with the scores of each of the HRQoL scales for each gender. Each row shows a regression model. In women, a higher PANSS negative symptom score and a higher PANSS affective symptom score were associated with a lower SQLS score. In men, a higher PANSS positive symptom score and a higher PANSS affective symptom score were associated with a lower SQLS score.

The same pattern by gender also appeared in the EQ-VAS and EQ-5D tariff. In women, a higher PANSS negative symptom score and a higher PANSS affective symptom score were associated with a lower EQ-VAS and EQ-5D tariff. Moreover, obesity was included in the EQ-5D tariff model. However, in men, a higher PANSS positive symptom score and a higher PANSS affective symptom score were associated with lower EQ-VAS and EQ-5D tariff scores. In women, the SF-36 mental component score was lower with increasing age and

increasing severity of the PANSS affective score. In men, the SF-36 mental component score was lower with increasing severity of the PANSS affective, positive, and cognitive scores. In both men and women, the SF-36 physical component score was lower with increasing age, increasing PANSS affective score, and in those individuals who were obese. Additionally, a higher PANSS positive score was associated with a lower SF-36 PC score.

The stratified analysis by age group (younger and older than 45 years of age) showed very similar results than the total sample (data not shown).

Discussion

The three main conclusions of the present study are that men with schizophrenia tend to report a higher health-related quality of life (HRQoL) than women in spite of overall similar severity of schizophrenia symptoms; that the presence of psychiatric symptoms seems to have a larger impact on HRQoL for women than for men; and that HRQoL is associated with the severity of affective and negative symptoms in women and with the severity of affective and positive symptoms in men.

Our study is in accordance with a vast amount of evidence showing that depressive (affective) symptoms are related to HRQoL (Hansson 2006; Schram et al. 2009; Mauriño et al. 2011; Guajardo et al. 2015; Alessandrini Lançon et al. 2016). Our data show that this relationship is present in both women and men. Of all the types of symptoms associated with HRQoL in patients with schizophrenia, depressive symptoms seem to be the most relevant (Galuppi et al. 2010).

The most remarkable finding of this study is that negative symptoms seem to influence HRQoL only in women, while positive symptoms seem to influence HRQoL in men. In their meta-analysis of psychiatric symptoms and quality of life in schizophrenia, Eack and Newhill (2007) found that both positive and negative symptoms influence HRQoL. However, they do not mention in their report any gender difference in that relationship. They do report that positive symptoms seem to have a larger influence than negative symptoms, but other studies have found that negative symptoms are more relevant (Katschnig 2000, 2006; Zeng et al. 2015). However, neither these studies take gender differences into account.

Compared to men, women with schizophrenia have usually been reported to have a better social functioning (Usall et al. 2002; Ochoa et al. 2012) and lower severity of negative symptoms (Bardenstein and McGlashan 1990; Shtasel et al. 1992). Additionally, a number of studies have associated negative symptoms with psychosocial functioning (Ochoa et al. 2005; Kurtz 2006; Lysaker et al. 2009; Ventura et al. 2013) and psychosocial functioning with HRQoL (Browne et al. 1996). Accordingly, a possible explanation for our findings is that women may be more vulnerable to the presence of negative

Table 1 Sociodemographic and clinical characteristics of the patients, by gender

	Women <i>N</i> = 391 Mean (sd)	Men <i>N</i> = 954 Mean (sd)	<i>P</i> value
Age	45.74 (12.34)	40.46 (10.69)	< 0.0001
Years since onset	16.16 (11.09)	14.61 (9.97)	0.0426
Age at onset	29.09 (11.31)	25.35 (8.15)	< 0.0001
PANSS total score	80.62 (23.60)	77.94 (22.07)	0.1046
PANSS positive score	16.03 (6.71)	15.95 (6.27)	0.9927
PANSS negative score	23.36 (7.42)	22.52 (7.19)	0.0511
PANSS cognitive/disorganized score	18.37 (6.16)	17.93 (5.86)	0.2902
PANSS affective score	12.90 (4.67)	12.06 (4.53)	0.0046
PANSS excitement score	9.96 (4.38)	9.48 (4.15)	0.0567
SQLS total score	39.73 (16.1)	36.99 (15.13)	0.0053
Inverse SQLS total score	60.27 (16.1)	63.01 (15.13)	0.0053
EQ-5D tariff score	0.69 (0.28)	0.74 (0.25)	0.0023
EQ-5D VAS score	62.34 (20.52)	66.14 (19.12)	0.0010
SF-36 mental component	39.15 (11.58)	41.04 (10.84)	0.0055
SF-36 physical component	48.5 (8.94)	50.37 (8.09)	0.0004
	Number (%)	Number (%)	
Comorbidities			0.0817
None	210 (53.71)	584 (61.22)	
One	90 (23.02)	176 (18.45)	
Two	44 (11.25)	93 (9.75)	
3 or more	47 (12.02)	101 (10.59)	
Any substance abuse			< 0.0001
Never	332 (84.91)	548 (57.44)	
Past	51 (13.04)	349 (36.58)	
Current	8 (2.05)	57 (5.97)	
Extrapyramidal symptoms, dyskinesia, or akathisia	56 (14.32)	100 (10.48)	0.0458
Obesity	131 (33.50)	245 (25.68)	0.0037

PANSS, Positive and Negative Syndrome Scale; SQLS, Schizophrenia Quality of Life Scale; SF-36 PC, Short-Form 36 Physical Component; SF-36 MC, Short-Form 36 Mental Component; EQ-5D, EuroQol-5 Dimensions; EQ-VAS, Euro-Qol Visual Analogue Scale

symptoms since negative symptoms affect psychosocial functioning. In contrast, men usually have more hostility and behavioral problems. Hostility and behavioral problems are associated with lower quality of life (Galuppi

et al. 2010). Furthermore, behavioral problems have been related to the presence of positive symptoms (Volavka and Citrome 2011). Vila-Rodriguez et al. (2011) found that social functioning in men was better

Table 2 Pearson correlation between PANSS scales and Outcomes

	Gender	SQLS	SF-36 MC	SF-36 PC	EQ-5D VAS	EQ-5D tariff
PANSS positive score	Women	-0.30	-0.23	-0.15	-0.22	-0.24
	Men	-0.30	-0.26	-0.18	-0.23	-0.24
PANSS negative score	Women	-0.29	-0.25	-0.14	-0.29*	-0.26*
	Men	-0.18	-0.17	-0.13	-0.15	-0.13
PANSS cognitive/disorganized score	Women	-0.24	-0.19	-0.16	-0.22	-0.26
	Men	-0.19	-0.13	-0.17	-0.13	-0.20
PANSS affective score	Women	-0.36	-0.38	-0.21	-0.31	-0.38
	Men	-0.35	-0.32	-0.19	-0.25	-0.30
PANSS excitement score	Women	-0.24	-0.25	-0.09	-0.19	-0.22
	Men	-0.20	-0.16	-0.09	-0.13	-0.18

All correlation coefficients are statistically significant at the *P* < 0.001 level

**P* < 0.05, women and men correlation coefficients are statistically different from one another

PANSS, Positive and Negative Syndrome Scale; SQLS, Schizophrenia Quality of Life Scale; SF-36 PC, Short-Form 36 Physical Component; SF-36 MC, Short-Form 36 Mental Component; EQ-5D, EuroQo-5 Dimensions; EQ-VAS, Euro-Qol Visual Analogue Scale

Table 3 Multiple linear regression models on the factors associated with difference in the ratings of the quality of life scales. Figures are coefficients (95% CI)

	Intercept	Age	PANSS positive	PANSS negative	PANSS cognitive/ disorganized	PANSS affective	Obesity
SQLS	Women 70.1 (60.3, 79.9)	0.02 (-0.10, 0.14)		-0.31 (-0.54, -0.07)*		-0.99 (-1.34, -0.63)***	
	Men 79.8 (74.6, 85.1)	-0.03 (-0.11, 0.06)	-0.31 (-0.48, -0.13)**			-0.97 (-1.20, -0.73)***	
EQ-VAS	Women 86.4 (73.5, 99.3)	-0.15 (-0.31, 0.01)		-0.63 (-0.94, -0.32)***		-0.90 (-1.37, -0.43)**	
	Men 83.9 (77.1, 90.7)	-0.12 (-0.23, -0.02)*	-0.36 (-0.58, -0.13)*			-0.82 (-1.13, -0.52)***	
EQ-5D	Women 0.93 (0.75, 1.10)	-0.01 (-0.03, 0.001)		-0.01 (-0.01, -0.00)*		-0.02 (-0.03, -0.01)**	-0.08 (-0.14, -0.03)*
TARIFF	Men 1.05 (0.96, 1.14)	-0.002 (-0.004, -0.001)*	-0.004 (-0.007, -0.002)*			-0.01 (-0.02, -0.01)***	
SF-36 MCS	Women 45.8 (39.0, 52.7)	0.10 (0.01, 0.18)*			0.28 (0.14, 0.42)**	-0.94 (-1.17, -0.70)***	
	Men 50.7 (47.0, 54.5)	0.04 (-0.02, 0.10)	-0.32 (-0.45, -0.18)***			-0.80 (-0.97, -0.62)***	
SF-36 PCS	Women 55.5 (50.1, 60.9)	-0.19 (-0.26, -0.12)***				-0.42 (-0.60, -0.23)***	-4.47 (-6.26, -2.69)***
	Men 59.1 (56.1, 62.1)	-0.13 (-0.18, -0.08)***	-0.14 (-0.24, -0.05)*			-0.20 (-0.33, -0.07)*	-2.79 (-3.95, -1.64)***

* $P < 0.05$ ** $P < 0.001$ *** $P < 0.0001$

PANSS, Positive and Negative Syndrome Scale; SQLS, Schizophrenia Quality of Life Scale; SF-36 PC, Short-Form 36 Physical Component; SF-36 MC, Short-Form 36 Mental Component; EQ-5D, EuroQol-5 Dimensions; EQ-VAS, Euro-Qol Visual Analogue Scale

explained by positive and disorganized (cognitive) symptoms. The effect of positive symptoms on behavioral problems and psychosocial functioning could be the link between positive symptoms and HRQoL. Our results are also consistent with Siegrist et al.'s findings (Siegrist et al. 2015). In a follow-up study that included more than one thousand patients with schizophrenia, Siegrist et al. reported a link between social contact frequency and negative symptom scores, social functioning, and quality of life at baseline. However, they did not conduct an analysis stratified by gender, and we do not know if these relationships are present for both genders.

In our study, we have also found that women have a lower HRQoL than men. Women tend to report lower levels of HRQoL than men in general population samples (Bisegger et al. 2005) and in many clinical studies in individuals with physical health conditions (Gijsberts et al. 2015; French et al. 2004), coinciding with our results. These differences persist even when adjusting for sociodemographic differences (Cherepanov et al. 2010) or for the prevalence of chronic health conditions (Orfila et al. 2006). However, in individuals with schizophrenia, findings on gender differences in quality of life have been less consistent to date. Some studies, (Xiang et al. 2007; Kumar et al. 2010) including ours, have found that women tend to have lower HRQoL than men. Conversely, other studies have found no differences (Becker et al. 2005) or have reported that women have higher HRQoL than men (Galuppi et al. 2010; Carpiniello et al. 2012; Zhao et al. 2017).

The intensity of the relationship between symptoms and HRQoL was numerically greater in women than in men in most of the correlations between HRQoL and symptom dimensions, but only in two of the cases the crude comparison reached statistical difference. One possible explanation for this finding is that women may be more aware of the impairment of schizophrenia than men given that they seem to have better cognitive functioning (Caqueo-Urizar et al. 2018). Krysta et al. (2013) conducted a review of studies reporting gender differences in neuropsychological functioning. They concluded that most of the studies postulate worse performance on neuropsychological tests by men. However, not all studies provide the same results (Fond et al. 2018).

In our data, there was a partial effect of age in HRQoL. Increasing age was associated with lower quality of life in the SF-36 PCS in both genders and in the EQ-VAS and the EQ-5D in males. These are HRQoL scales that include a physical dimension. However, there was no effect in the other scales. The results did not vary when stratifying the analysis by age groups (younger and older of 45 years of age).

The choice of the specific HRQoL scales we used merits some discussion since there is great diversity in the available instruments. We used the most widely employed generic HRQoL scales in Europe and the USA. Regarding the

disorder-specific HRQoL scales, the diversity is even greater (Bobes and A-Portilla 2005; Cramer et al. 2000). When choosing a condition-specific HRQoL scale, we searched for a scale which covered the areas described by Awad and Voruganti (2012) of being relevant in the assessment of patients with schizophrenia. According to Awad et al., HRQoL is defined as the outcome of the dynamic interaction among three primary determinants: psychotic symptoms and their severity, medication side-effects, and psychosocial performance. The SQLS has three dimensions, namely psychosocial, motivation and energy, and symptoms and side-effects (Wilkinson et al. 2000).

In evaluating these findings, we need to take a number of limitations into account. First, we present a cross-sectional analysis, and the direction of causality cannot be inferred from the data. Second, we included a community sample of patients with stable symptoms in the study, and the results may be different in patients presenting psychotic exacerbation. Third, we employed the most-used five-factor model of the PANSS as described by Lindenmayer et al. (1995), although other models have also been proposed (Perez et al. 2013). Fourth, cognition was not measured. Not only cognition may influence HRQoL but also it may vary by gender. Finally, the factors that we analyzed in relation to HRQoL were mostly sociodemographic and clinical, and we did not include information about other factors associated with quality of life such as marital status, education, psychological aspects, and living conditions (Ruggeri et al. 2005; Zeng et al. 2015).

Conclusion

In conclusion, these findings show that HRQoL may be influenced by different types of symptoms in women than in men. While positive symptoms seem more important in men, in women negative symptoms play a more relevant role. This may have implications when targeting the treatment of schizophrenia. While all patients should be treated for the affective symptoms, negative symptoms may be the second most important target for women, while in men, positive symptoms should be addressed. These results are novel since previous analysis has not been able to distinguish the different effects of symptom dimensions on HRQoL in each gender. Additional strengths of the study are its large sample size, the inclusion of patients coming from a diversity of centers and countries, and the consistency of findings using different HRQoL scales. However, these results are cross-sectional and need to be confirmed with longitudinal studies.

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Authors' contribution The statistical analysis and manuscript content were directed, conducted, and approved by the authors.

Compliance with ethical standards

Ethical approval The protocol and consent procedures were approved by all local Institutional Review Boards/Ethics Committees before study initiation. All patients and caregivers provided informed consent.

Conflict of interest CD, JE, RC, and MVM have no conflict of interest. CB is a contractor of F. Hoffmann- La Roche, Ltd. ALN is an employee of F. Hoffmann- La Roche, Ltd. JMH has acted as a consultant, participated in advisory boards or given educational presentations for Eli Lilly and Co., Lundbeck, Otsuka, F. Hoffmann- La Roche Ltd., and Takeda.

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