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Symptomatic remission and patient quality of life in an observational study of schizophrenia: is there a relationship?

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Abstract

This analysis aimed to examine the association between remission and quality of life (QOL) in schizophrenia. In *post-hoc* analyses of the 3-year, prospective, observational Schizophrenia Outpatients Health Outcomes (SOHO) study, we compared the QOL of patients who achieved symptomatic and clinical remission with those who did not, and the factors associated. Symptomatic remission was defined as achieving a score of ≤ 3 on the Clinical Global Impressions-Schizophrenia (CGI-SCH) scale, maintained for at least 6 months and without hospitalization. QOL was patient self-rated using the European-QOL. Of the 6516 patients analysed, 38% were in symptomatic remission 12 months post-baseline and 52% at 36 months. Functional remission remained fairly constant from 12 months to 36 months (22.4% at both time points). At all visits from 12 to 36 months, patient QOL and social functioning were significantly higher for patients in symptomatic remission. QOL was higher in patients in functional remission compared to those not in functional remission at all time points. Patients with maintained symptomatic remission over the 3-year follow-up had a much greater improvement in QOL than patients with no symptomatic remission or symptomatic remission for part of the period. Factors associated with a better QOL included symptomatic remission, paid employment, socially active, having a higher CGI-SCH cognitive score, good compliance, and a better baseline QOL. Achieving symptomatic remission in schizophrenia is associated with an increase in patient self-perceived QOL, even when adjusting for confounding factors.

Keywords

Observational study; Quality of life; Remission; Schizophrenia

1 Introduction

A few years ago, the Remission in Schizophrenia Working Group (Andreasen et al., 2005) proposed that treatment effects should be assessed using measures that have a significant meaning for the patient. Most clinical trials have used a clinical severity scale, such as the Positive and Negative Syndrome Scale (PANSS) or the Brief Psychiatric Rating Scale (BPRS), as the main outcome measure. However, a decrease in such scale scores cannot easily be translated into patient clinical status. The Working Group proposed 'remission' as a construct that has a clear meaning for patients and, thus, has direct implications for their well-being. Remission has been defined as having none or a minimal level of symptoms in key areas of schizophrenia for a period of 6 months or more (Andreasen et al., 2005).

Since then, this definition of symptomatic remission has been applied in a number of studies with different samples of patients with schizophrenia in an attempt to validate it (Lasser et al., 2007; Boden et al., 2009; Ciudad et al., 2009). These validation studies applied an external validity criterion by comparing the key functioning and quality of life aspects of patients who were in symptomatic remission with those who were not in symptomatic remission. The findings of better social functioning for patients in symptomatic remission were highly consistent (Lasser et al., 2007), whereas the quality of life results were discordant (van Os et al., 2006; Emsley et al., 2007; Wunderink et al., 2007; Boden et al., 2009). Some studies found that patients in symptomatic remission did not have a better quality of life than patients not in symptomatic remission (van Os et al., 2006; Wunderink et al., 2007), while others found a difference in quality of life between remitters and non-remitters (Emsley et al., 2007; Boden et al., 2009). The differences may be

explained by the use of different measures of quality of life, and because some studies had small sample sizes.

Quality of life is complex and influenced by many social, psychological and clinical factors, including the patient's age and sex, insight into illness, severity of current symptoms, and side effects of medications (Hofer et al., 2004). Katschnig (2000) proposed that quality of life encompassed three areas; subjective wellbeing/satisfaction, and two objective aspects related to functioning and external resources. Among psychiatric patients, the relationship between these areas is complex, and the different areas have more or less influence on overall quality of life depending on the impact of disease at that point in time; when disease has a large impact on functioning, quality of life is reduced (Becker et al., 2005). A variety of measures are used to assess quality of life, including patient self-report measures (e.g. a summary measure on a visual analogue scale, VAS) and clinician-rated scales (e.g. the Heinrich's QOL). There is, however, a discrepancy between self-reported and clinician-rated quality of life, as many of the clinician-rated scales measure functioning rather than subjective well-being (Lazalvia et al., 2002; Jung et al., 2010). In this analysis, we were interested in self-reported quality of life as the impact of multiple relevant factors in a single, global, subjective judgement as a summary rating on a VAS. The setting of studies of quality of life is also important; quality of life measures have been applied in naturalistic settings and in clinical trials, but only the former setting characterizes the broader range of patients seen in everyday clinical practice. As quality of life profiles are reported by patients, not their clinicians, they are of interest to purchasers and providers of psychiatric services.

Some of the studies that found an association between quality of life and symptomatic remission did not take into account the presence of confounders (Boden et al., 2009): factors such as gender, age, or medication are known to be associated with both quality of life and symptomatic remission frequency, and may confound the relationship. van Os et al. (2006) did take confounding factors into account, but did not find an association between quality of life and symptomatic remission. In addition to these clinical factors, there are many other social factors that influence quality of life and may also confound the results.

The Schizophrenia Outpatients Health Outcomes (SOHO) study, a 3-year prospective, observational study on the course of schizophrenia in the outpatient setting (conducted from September 2000 to January 2005), provides an excellent opportunity to address the issue of whether remission and quality of life are related. The objectives of these *post-hoc* analyses are to compare the quality of life of patients who achieve symptomatic remission of schizophrenia with those who do not achieve symptomatic remission. We also analyse whether the association between symptomatic remission and quality of life, if present, can be explained by the presence of confounding factors. For this, the regression model can be adjusted for other factors known to impact on quality of life and to be associated with remission (e.g. age, gender and medication) (Haro et al., 2006; Yen et al., 2008; Potkin et al., 2009). Finally, we have described the relationship between functional remission and quality of life.

2 Methods

The SOHO study was a prospective, observational study conducted in 10 European countries. The rationale, design and methods of the study have been described in detail elsewhere (Haro et al. 2003b). Full ethical approval (including patient consent) was obtained in all countries, either at the site, region or national level, depending on country regulations. The study was carried out in accordance with the Declaration of Helsinki. A total of 1096 psychiatrists offered enrolment to patients who were: initiating or changing antipsychotic medication for the treatment of schizophrenia (diagnosed using ICD-10 or DSM-IV criteria); presenting within the normal course of care in the outpatient setting or in the hospital when admission was planned for the initiation or change of antipsychotic medication and discharge planned within 2 weeks; at least 18 years of age; and not participating in an intervention study. Patients were included irrespective of the reason for treatment change (e.g. lack of response, side effects, etc.), and regardless of whether an antipsychotic drug was being initiated as a replacement for a previous medication, was an addition to existing treatment, or was being initiated for the first time or after a period of no treatment.

Since the initial objective of the SOHO study was to compare treatment with olanzapine versus treatment with other antipsychotics, the study was designed to provide two patient cohorts of approximately equal size: patients who initiated therapy with or changed to olanzapine; and patients who initiated therapy with or changed to a non-olanzapine antipsychotic. To achieve approximately equal numbers in the olanzapine and non-olanzapine groups, different sample fractions entered each cohort. This resulted in a stratified sample, with the olanzapine group as the ‘over-sampled’ stratum. In the present analyses, however, the non-olanzapine

group was divided into groups according to the specific antipsychotic medication prescribed.

Effort was made to avoid interference with clinical practice. Investigators were instructed to make treatment decisions independently of the study and then evaluate whether patients were eligible for inclusion based on the entry criteria and the alternating structure of enrolment. The recruitment period was intentionally long and no minimum number of cases was required by each investigator.

Patients were evaluated during visits occurring within the normal course of health care, which were planned at approximately 3, 6, 12, 18, 24, 30 and 36 months after baseline. The routine outpatient visit at which patients were enrolled served as the time for baseline data collection.

Clinical severity was assessed using the Clinical Global Impression-Schizophrenia scale (CGI-SCH) (Haro et al., 2003c), which evaluated positive, negative, cognitive, depressive and overall symptoms in the week before the day of assessment. This physician-rated scale ranges from 1 (not ill) to 7 (among the most severely ill).

Health-related quality of life (HRQL) was assessed using the European Quality of Life Questionnaire (EQ-5D, formerly EuroQol) (Brooks et al. 2003). This is a patient self-rated, generic, HRQL instrument that includes a visual analogue scale (EQ-VAS) which patients use to assess their perceived current level of health on the day of scoring from 0 (worst imaginable health state) to 100 (best imaginable health state).

Other data collected included socio-demographics, psychiatric history, patient functioning, medication use and adverse events. Data on baseline variables such as employment and social activities were collected using single-item questions completed by the participating investigators to the best of their knowledge including onformtion from the patient and other sources and assessing the status during the previous four weeks.

Further details about the design of the SOHO study and the results at 6 months and 3 years have been provided elsewhere (Haro et al., 2003a; 2003b; 2003c; Haro et al., 2005; Haro et al., 2006).

2.1 Definition of remission

In this analysis, remission was described in two ways; symptomatic remission (based on the CGI-SCH) and functional remission (based on social functioning).

Symptomatic remission was defined as achieving a score of 3 (mild severity) or less on the 1–7 scale for each of the CGI-SCH items of overall severity, positive, negative and cognitive symptoms, and maintained for a period of 6 months or more. In addition, the patient must not have been hospitalized for their schizophrenia during this period. This definition has been shown to have an excellent agreement (Cohen's kappa value of 0.80) with the Remission in Schizophrenia Working Group definition (Haro et al., 2007). In order to avoid a bias in favour of patients who entered the study with a good clinical status, symptomatic remission was defined starting at the 6-month visit.

Functional remission was based on good social functioning and was defined at each visit. To achieve functional remission required the patient to fulfill three criteria: i) positive occupational/vocational status (i.e. paid or unpaid full- or part-time employment, being an active student in university, or housewife); ii) living independently; iii) socially active (i.e. having more than one social contact during the last 4 weeks or having a spouse or partner).

2.2 Statistical analysis

Only patients assessed at all visits or having at most one missing visit were included in the analysis. For patients with one missing visit, values from the previous visit were imputed for that visit (n = 6752). Of these, 236 (3.5%) had missing information on CGI-SCH ratings and were not included in the analysis. Thus, a total of 6516 patients were included in the analysis.

Baseline characteristics of the study sample were summarized using descriptive statistics. Quality of life (EQ-VAS) and functional remission (percentage of patients in a relationship, living independently, in paid employment, and socially active) at each visit from 12 months onwards were compared with patients in functional remission and not in remission at that visit using Student's *t*-tests and χ^2 tests.

Based on the above definition of symptomatic remission, patients were also classified into one of three symptomatic remission groups based on their symptomatic remission status over the whole 3-year follow-up period:

i) Those not achieving symptomatic remission at any time during follow-up (no symptomatic remission);

ii) Those starting symptomatic remission at 6 months and maintaining symptomatic remission during the 3 years (always symptomatic remission);

iii) Patients achieving symptomatic remission only for part but not all of the 6-month periods during the 3-year follow-up period (some symptomatic remission).

Patients were classified into the following treatment groups: olanzapine, risperidone, quetiapine, amisulpride, clozapine, oral typical antipsychotics, depot typical antipsychotics and combination therapy. Patients taking any other atypical antipsychotics at baseline were excluded from the analysis because of the small number of patients in those groups.

To analyse factors associated with quality of life, a generalized estimating equation (GEE) linear regression model was fitted with EQ-VAS as the dependent variable, including all observations from 6 months onwards. An observation was included in the model for each visit of each patient. An auto-regressive correlation structure (AR(1)) matrix was defined. The covariates in the model were chosen based on a backward reduction method. The initial list of covariates were country, gender, never treated before SOHO, age at first treatment contact, time since first treatment for schizophrenia, current alcohol abuse or dependence, current substance abuse or dependence, suicide attempts in past 6 months, CGI-SCH overall score, CGI-SCH positive score, CGI-SCH negative score, CGI-SCH cognitive score, CGI-SCH depressive score, hostility/aggression in past 6 months, compliance, body mass index, relationship with spouse or partner, living independently, work status

(employed and paid versus not), social activities in past 4 weeks, anticholinergic, antidepressant, anxiolytics/hypnotics and mood stabilizer concomitant medication, EQ-VAS score at baseline. As patients could change medication at any point during the study, the medication that was included in each observational period as a dependent variable was the medication the patient was taking upon presentation to that visit. The final model was repeated including only those patients who maintained the same antipsychotic medication throughout the 3-year follow-up period.

All statistical analyses were performed with SAS version 9.1 (SAS Institute, Inc., Cary, NC, USA).

3 Results

A total of 6516 (63.8%) patients were included in the analysis, and 3702 (36.2%) were excluded; there were no relevant differences between the patients included and excluded from the analysis. For example, mean overall symptom scores for included patients were 4.4 (SD 1.0) and for excluded patients were 4.5 (SD 1.0) and mean EQ-VAS scores for included patients were 46.3 (SD 21.0) and for excluded patients were 46.1 (SD 21.7). A total of 24 patients (0.2%) of patients were excluded from the analysis because they took other atypical antipsychotics at baseline.

The characteristics of the included population at baseline are summarized in Table 1. Of these patients, 3984 (61.1%) maintained their baseline medication at 36 months. The mean age of the sample was 40.2 years and 57.6% were men. Patients had a long duration of illness (mean 11.8 years) and moderate-to-severe symptoms

(CGI-SCH overall mean 4.4). Patient social functioning at baseline was as follows: 29.4% were in a relationship (spouse or partner), 47% lived independently, 19.6% were in paid employment, and 68.2% were socially active. The patients' quality of life at baseline was a mean EQ-VAS rating of 46.3 (SD 21.0).

Of the 6516 patients analysed, 38% of patients were in symptomatic remission at the 12-month post-baseline visit. The percentage of patients in symptomatic remission had increased to 45% at the 18-month visit and to 52% at the 36-month visit. Patient quality of life and social functioning by symptomatic remission status at each follow-up visit from 12 months to 36 months are presented in Table 2 and Fig. 1, respectively. Patients in symptomatic remission had a significantly higher EQ-VAS score at all visits compared with patients not in symptomatic remission ($P < 0.001$). Likewise, at all visits, a significantly higher percentage of patients in symptomatic remission were in a relationship, living independently, in paid employment and socially active compared with patients not in symptomatic remission ($P < 0.001$).

When the patients were classified according their symptomatic remission status over the 3-year follow-up period, 35% had no symptomatic remission, 38% had always symptomatic remission, and 26% had some symptomatic remission. All three patient groups experienced improvements in their quality of life during follow-up, but the improvement was much greater in the always symptomatic remission group compared with the other two groups. Mean EQ-VAS in the always symptomatic remission group was 48.5 (SD 20.2) at baseline and 79.3 (SD 14.2) at 36 months. In the never symptomatic remission group, the corresponding mean EQ-VAS scores were 44.9 (SD 21.4) and 60.5 (SD 19.1), respectively. Finally, in the group of

patients experiencing some remission, mean EQ-VAS ratings were 46.0 (SD 21.0) at baseline and 72.1 (SD 16.5) at 36 months. At each of the time points, differences between the three patient groups were statistically significant.

The percentage of patients in functional remission remained constant over time; the number of patients in functional remission was 1439 (22.4%) at 12 months, 1426 (22.2%) at 18 months, 1407 (22.0%) at 24 months, 1421 (22.2%) at 30 months, and 1368 (22.4%) at 36 months. EQ-VAS scores at each visit were compared for patients achieving functional remission with patients not achieving functional remission. At 12 months, mean EQ-VAS scores were 69.0 (SD 18.4) for those achieving functional remission versus 63.4 (SD 19.1) for those not achieving remission (table 2). At 18 months these scores were 71.7 (SD 17.9) versus 65.0 (SD 19.2); at 24 months these scores were 72.6 (SD 17.9) versus 66.4 (SD 18.3); at 30 months these scores were 74.3 (SD 17.7) versus 67.0 (SD 18.5); and at 36 months these scores were 76.0 (SD 17.2) versus 68.5 (SD 18.4), for those achieving functional remission versus those not achieving remission, respectively. There were significant differences between these scores at all time points ($P<0.0001$).

Factors independently associated with quality of life (EQ-VAS) during the 3-year follow-up period are summarized in Table 3. The value of the estimate in Table 3 represents the estimated difference in EQ-VAS ratings for patients in that category. As higher EQ-VAS values represent better quality of life, when the estimate is positive, that factor is associated with better quality of life. Being in symptomatic remission was strongly associated with a better quality of life as perceived by patients using the EQ-VAS. Other factors associated with a better quality of life

were being in paid employment, being socially active, having a higher CGI-SCH cognitive score, a better quality of life at baseline, and compliance. Compared to patients who were not compliant at baseline, patients who were always compliant or partially compliant had a better quality of life at followup. Also patients who were not taking medication at baseline (some patients had never received antipsychotic treatment before baseline) had better quality of life outcomes. In contrast, factors associated with a worse quality of life were: male gender, older age at first treatment, longer duration of illness, higher CGI-SCH negative and depressive symptom scores at baseline, being prescribed anxiolytics or mood stabilizers, and treatment with amisulpride, typical antipsychotics (depot, oral), quetiapine, risperidone or combination therapy versus olanzapine (Table 3).

Similar results were obtained when the analysis included only those patients who maintained the antipsychotic treatment prescribed at baseline during the 3 year follow-up (data not shown but available on request).

4 Discussion

The objective of treatment in schizophrenia must be to improve patient quality of life. Our results show that achieving symptomatic remission in schizophrenia is associated with an improvement in patient self-perceived health-related quality of life, even when confounding factors are taken into account. Furthermore, because SOHO was an observational study in outpatients with schizophrenia, our results not only provide support for the external validity of the symptomatic remission construct, but also the usefulness of measuring symptomatic remission in everyday clinical practice, especially in patients requiring a change of antipsychotic treatment.

The findings of this analysis should be considered in the context of patient self-reported quality of life (as specifically assessed using the EQ-5D, Brooks et al., 2003), rather than clinician-reported quality of life, which as discussed previously, tend to measure functioning rather than subjective quality of life (Lazalvia et al., 2002; Jung et al., 2010).

Previous studies examining the relationship between symptomatic remission and quality of life showed inconsistent results (van Os et al. 2006; Emsley et al. 2007; Wunderink et al., 2007; Boden et al., 2009). Our study goes beyond previous studies, which were limited by small sample sizes or did not adjust for confounding. In addition, most previous studies were cross-sectional in design or based on the highly controlled clinical circumstances of randomized clinical trials. In contrast, SOHO was a large, naturalistic, prospective study in the outpatient setting, which increases the generalizability of the findings. Moreover, our analyses controlled for the presence of other important factors that frequently affect quality of life and symptomatic remission, such as age, duration of illness, antipsychotic treatment, social activity and employment status.

In the present study, 52% of patients were in symptomatic remission at the 36-month visit. Similar percentages of patients achieved symptomatic remission in the 3-year extension study of a controlled clinical trial, where symptomatic remission rates ranged from 41% in haloperidol-treated patients to 50% in ziprasidone-treated patients (Potkin et al., 2009).

Symptomatic remission status, however, can change over time, and so can patient quality of life. We have shown that patients who achieve symptomatic remission continue to experience improvements in their quality of life over time if symptomatic remission is maintained. This indicates that quality of life continues to improve when symptomatic symptomatic remission is maintained and this is consistent with previous research (Dunayevich et al., 2006). This finding, together with the need for good compliance with medication, signals the relevance of maintenance treatment in schizophrenia.

Patients in symptomatic remission reported having a better quality of life compared with patients not in remission. The mean EQ-VAS score at 3 years for remitters was similar to that reported for the general population (König et al., 2009). Previous reports have found that quality of life in patients with schizophrenia in symptomatic remission is lower than in healthy individuals (Yen et al., 2008). However, the study by Yen et al. (2008) did not use a representative sample of general population subjects and did not specify for how long the patients included had been in remission.

In agreement with other studies (van Os et al., 2006; Lasser et al., 2007; Ciudad et al., 2009), we found that patients who achieved symptomatic remission had better social functioning (as measured with the frequency of having paid employment, living independently, being in a relationship, and being socially active) than patients not achieving symptomatic remission.

There is an emphasis on psychosocial functioning after clinical remission as the most important outcome in schizophrenia. Quality of life has usually been given less attention, but it should be of great relevance for the well-being of the patient (Cardoso et al., 2006; Juckel et al., 2008). Although related, clinical remission, social functioning and quality of life are different entities that depend on different factors (Lambert et al., 2006).

The proportion of patients in functional remission was much lower than those in symptomatic remission. Besides, the proportion of patients in symptomatic remission increased during follow-up, while the proportion of patients in functional remission presented a much more stable course. This highlights the difficulty of improving patient functioning when disability has been established.

Gender is a potential confounding factor in the association between symptomatic remission and quality of life. In a previous report of the 3-year results of the SOHO study, men with schizophrenia were less likely to achieve symptomatic remission than women (Haro et al., 2006). Moreover, in the present analysis, we found that men had a slightly worse quality of life (EQ-VAS) than women. In contrast, in the general population, women report a lower HRQL than men (Gallicchio et al., 2007). Moreover, previous studies in schizophrenia have shown inconsistent results. Women with serious mental health problems (including schizophrenia) reported poorer HRQL than men across several domains of the Short Form (36) Health Survey (SF-36), but reported better self-perceived health (Teh et al., 2008). In a cross-sectional study using the Quality of Life scale, women with schizophrenia had better quality of life scores than men (Cardoso et al., 2006). Further studies

exploring the effect of gender on symptomatic remission and HRQL in schizophrenia are needed.

Longer duration of illness was associated with a lower quality of life during follow-up. There may be two explanations for this. Firstly, quality of life decreases with age. Secondly, quality of life decreases with a chronic course of illness; that is, patients who continue experiencing symptoms at older ages have a more disabling illness.

In the present study, patients with more severe depressive or negative symptoms had a lower quality of life. This is consistent with previous studies (Yamauchi et al., 2008). These symptoms are more important than positive symptoms in explaining patients' quality of life during the maintenance treatment of schizophrenia. They are also associated with higher costs (Knapp et al., 2008).

Patients with a higher level of cognitive symptoms reported a somewhat better quality of life. This finding must take into account that self-evaluation of quality of life by patients with cognitive impairment may be more problematic. Higher cognitive impairment has been associated with a lower quality of life in patients with bipolar disorder (Brissos et al., 2008), but the results are not consistent for schizophrenia (Patel et al., 2006). Moreover, Brissos et al. (Brissos et al., 2008) did not adjust for the presence of symptoms.

Compliance has a favourable effect on patient quality of life. We found that patients who were compliant with their antipsychotic medication had a better quality of life

(EQ-VAS). Furthermore, patients treated with olanzapine showed a better quality of life than patients treated with oral or depot typical antipsychotics, quetiapine, amisulpride and risperidone. This is in accordance with previous studies (Silva de Lima et al., 2005), and is consistent with the 6- and 36-month results from the SOHO study (Haro et al., 2007; Alonso et al., 2009).

Several limitations must be considered when analysing these results. Firstly, our definition of symptomatic remission was based on the CGI-SCH scale, and not on the scales initially recommended by the Remission in Schizophrenia Working Group (Andreasen et al., 2005). Nevertheless, the definition used in this analysis has shown high agreement with the Consensus Group Definition (Haro et al., 2007). Secondly, patients enrolled in the SOHO study were not representative of all patients with schizophrenia, but of patients changing treatment in the outpatient setting. However, the socio-demographic characteristics of the patients included in the SOHO study are similar to those in studies including prevalence samples of patients with schizophrenia. Finally, SOHO is an international study and we have not analysed country differences in the relationship.

In conclusion, this study in the real-life clinical practice setting provides further evidence of an association between remission and quality of life. Patients who achieved remission had better self-rated social functioning and quality of life than patients not meeting the remission criteria. Moreover, the association between quality of life and remission persisted even when confounding factors were taken into account.

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Conflict of interest

Josep Maria Haro has consulted for Astra-Zeneca, Eli Lilly, Glaxo-Smith-Kline, and Lundbeck. Diego Novick is an employee of Eli Lilly and Company, UK. Elena Perrin is an employee of Eli Lilly and Company, Paris, France. Jordan Bertsch conducted the statistical analysis under a contract between Eli Lilly and Company and Fundació Sant Joan de Déu. To obtain the protocol used in statistical analysis please contact the first author.

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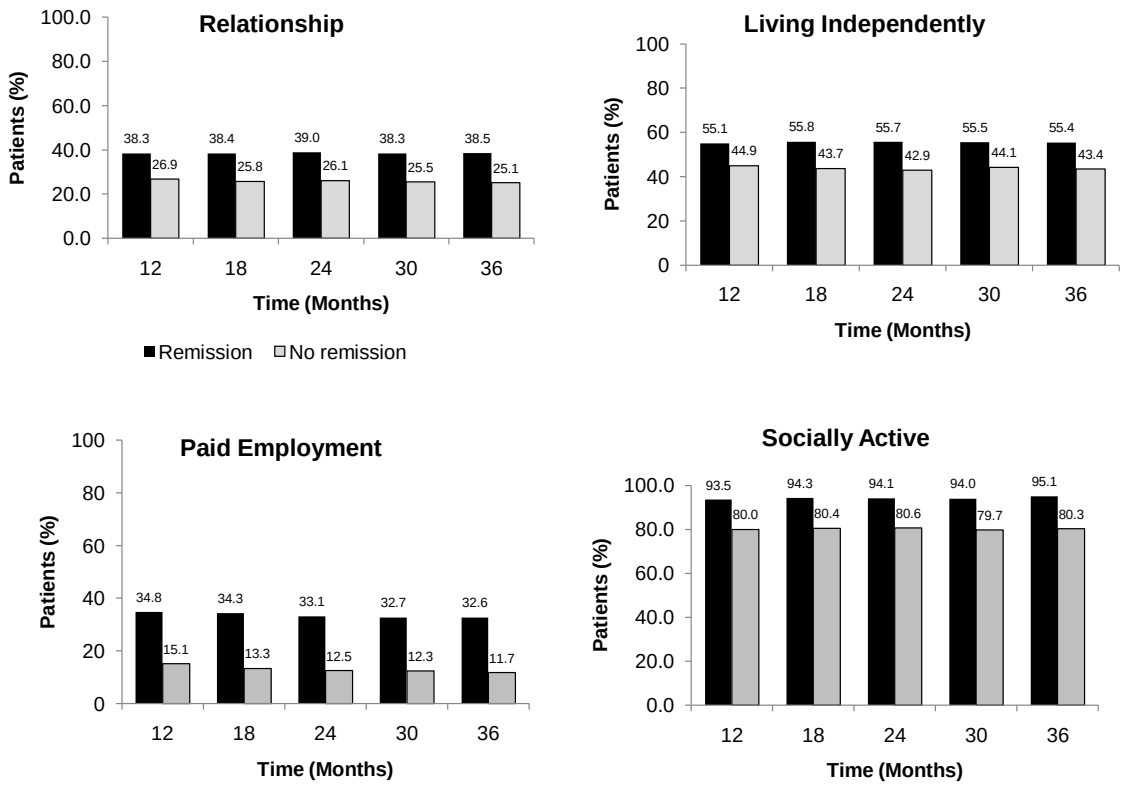

Fig. 1.

Social functioning by remission status at each follow-up visit.

Table 1

Demographic and clinical characteristics of the study sample at baseline (*n* = 6516).

Parameter	Mean (SD) or number (%)
Gender (% male)	3729 (57.6)
Age (years)	40.20 (12.9)
Age at first contact (years)	28.46 (10.2)
Duration of illness (years)	11.78 (11.0)
Body mass index (kg/m^2)	26.25 (4.8)
CGI-SCH overall severity score	4.40 (1.0)
CGI-SCH positive symptom score	3.80 (1.4)
CGI-SCH negative symptom score	4.08 (1.3)
CGI-SCH cognitive symptom score	3.76 (1.3)
CGI-SCH depressive symptom score	3.44 (1.3)
EQ-VAS	46.3 (21.0)
Alcohol abuse at baseline (%)	165 (2.5)
Substance abuse at baseline (%)	141 (2.2)
Suicide attempts in six months before baseline (%)	264 (4.3)
Relationship (spouse or partner) (%)	1857 (29.4)
Living independently (%)	3058 (47.0)
Being in paid employment (%)	1267 (19.6)
Being socially active (%)	4390 (68.2)
Compliance at baseline (%)	
Not prescribed antipsychotic	1327 (20.4)
Always complies to antipsychotic	3986 (61.4)
Half complies to antipsychotic	879 (13.5)
Never complies to antipsychotic	304 (4.7)
Treatment initiated at baseline (%)	
Olanzapine	3408 (52.3)
Risperidone	1266 (19.4)

Quetiapine	486 (7.5)
Amisulpride	192 (2.9)
Clozapine	226 (3.5)
Oral typical	444 (6.8)
Depot typical	333 (5.1)
2+ antipsychotics	161 (2.5)
Anticholinergics prescribed at baseline (%)	1219 (18.7)
Antidepressants prescribed at baseline (%)	1165 (17.9)
Anxiolytics/hypnotics prescribed at baseline (%)	2384 (36.6)
Mood stabilizer prescribed at baseline (%)	611 (9.4)

CGI-SCH, Clinical Global Impression-Schizophrenia scale (range 1–7); EQ-VAS, European Quality of Life Questionnaire-Visual Analogue Scale

Table 2

Quality of life (EQ-VAS) by symptomatic and functional remission status at each follow-up visit.

Visit	Symptomatic remission		No symptomatic remission		Functional remission		No functional remission	
	Mean (SD)	Median	Mean (SD)	Median	Mean (SD)	Median	Mean (SD)	Median
12 months	73.9 (15.1)	75	58.7 (19.0)	60	69.0 (18.4)	70	63.4 (19.1)	65
18 months	75.2 (14.8)	76	59.3 (19.3)	60	71.7 (17.9)	75	65.0 (19.2)	67
24 months	75.7 (14.5)	78	60.2 (18.6)	60	72.6 (17.9)	75	66.4 (18.3)	70
30 months	76.6 (14.7)	79	60.3 (18.6)	60	74.3 (17.7)	77	67.0 (18.5)	70
36 months	77.3 (14.6)	80	61.4 (18.8)	63	76.0 (17.2)	80	68.5 (18.4)	70

All $P < 0.001$ for remission versus no remission

EQ-VAS, European Quality of Life Questionnaire-Visual Analogue Scale

Table 3

Factors associated with quality of life as measured with the EQ-VAS[*].

Variable (reference category)	Estimate	95% CI	*P* value
In remission (versus not in remission)	5.903	237.288, 564.508	< 0.0001
Male (versus female)	–0.876	0.205, 0.846	0.0155
Age at first treatment (per year)	–0.069	0.898, 0.969	0.0003
Duration of illness (per year)	–0.140	0.839, 0.900	< 0.0001
CGI-SCH negative score at baseline	–0.346	0.501, 1.000	0.0500
CGI-SCH cognitive score at baseline	0.622	1.358, 2.557	0.0001
CGI-SCH depressive score at baseline	–0.848	0.306, 0.599	< 0.0001
In paid employment at baseline (versus not in paid employment)	2.874	7.320, 42.805	< 0.0001
Socially active at baseline (versus not socially active)	1.869	2.945, 14.262	< 0.0001
Compliance with antipsychotic treatment at baseline (versus never complies)			
Always complies	2.724	2.525, 91.944	0.0030
Complies half the time	2.352	1.487, 74.273	0.0184
Not prescribed	3.252	3.826, 174.409	0.0008
Body mass index	–0.058	0.874, 1.019	0.1412
Treatment (versus olanzapine)			
Amisulpride	–1.919	0.028, 0.771	0.0234
Clozapine	–1.158	0.067, 1.477	0.1425
Depot typical	–3.978	0.005, 0.071	< 0.0001
None	–0.741	0.101, 2.239	0.3479
Other atypical	–0.035	0.069, 13.555	0.9792
Oral typical	–4.837	0.002, 0.029	< 0.0001
Quetiapine	–2.721	0.017, 0.251	< 0.0001
Risperidone	–1.921	0.060, 0.359	< 0.0001
2+ antipsychotics	–3.663	0.011, 0.058	< 0.0001

Prescribed anxiolytics at baseline (versus no anxiolytics)	–1.181	0.145, 0.648	0.0020
Prescribed mood stabilizers at baseline (versus no mood stabilizers)	–1.336	0.078, 0.881	0.0303
Baseline EQ-VAS	0.284	1.303, 1.356	< 0.0001

*GEE model including all visits after 6 months; the model is also adjusted for visit and country

EQ-VAS, European Quality of Life Questionnaire-Visual Analogue Scale; CGI-SCH, Clinical Global Impressions-Schizophrenia scale

Variables not included in the model for lack of significance were: never treated before SOHO, current alcohol abuse or dependence, current substance abuse or dependence, suicide attempts in past 6 months, CGI-SCH overall score, CGI-SCH positive score, hostility/aggression in past 6 months, relationship with spouse or partner, living independently, antidepressant, concomitant medication.