



Predictors of Real-World Functioning Improvement in a Sample of Psychiatric Outpatients

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Abstract

Objective: the aim was to identify in 511 outpatients, with diagnoses of schizophrenia, major depressive disorder (MDD), bipolar disorders (BD), and borderline personality disorder (BPD), what clinical variables predict the improvement of real-world functioning during 12 months of usual treatment.

Methods: sociodemographic variables were evaluated. Patients were assessed at baseline and endpoint with: Clinical Global Impression Scale - Severity (CGI-S); Satisfaction Profile (SAT-P), Drug Attitude Inventory-10 (DAI-10), and Personal and Social Performance (PSP). Statistical analysis was performed with Chi-square test and Pearson's correlation. Significant variables were included in a multiple regression analysis. Dependent variable was the difference of PSP after one year (Δ PSP). $P \leq 0.05$ was significant.

Results: in the total sample, Δ PSP was related to age of onset, SAT-P and psychotherapy and inversely related to suicide attempts and CGI-S. In schizophrenia, Δ PSP was related to SAT-P and DAI-10 and inversely related to CGI-S. In MDD, Δ PSP was related to SAT-P and psychotherapy and inversely related to suicide attempts and CGI-S. In BD, Δ PSP was related to SAT-P and inversely related to CGI-S. In BPD, only psychotherapy was related to Δ PSP.

Conclusion: Symptoms severity predicted a worse community functioning in the total sample and in each group, except for BPD. Suicide attempts were inversely associated to functional improvement in the total sample and depression. Quality of life was related to the change of functioning in each group, except for BPD. Patients with MDD and BPD receiving psychotherapy gained a better functional improvement. Attitude to pharmacotherapy was related to functional improvement only in schizophrenia.

Keywords

Real-world functioning, Schizophrenia, Bipolar disorder, Major depressive disorder, Borderline personality disorder, Outpatients, Naturalistic study.

Introduction

Real life disability produced by mental illness is responsible for the considerable costs of psychiatric disturbances in terms of expensive medical care and lost days at work. In the last years, after obtaining significant results in treating symptoms of mental disorders, authors

focused their investigations on the real-world functioning of severe psychiatric patients. The everyday performance includes general organization, communication skills, finance management, independent living, medication management, and social interactions. With regard to this concept, there is a core distinction

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between functional capacity (the ability to obtain a good level of functioning under optimal conditions) and real-world functioning (the patient's actual performance when he has to face the real circumstances of his life and environment) [1].

Initial studies in this field were performed in patients with a diagnosis of schizophrenia, a major psychiatric disturbance inducing a high degree of impairment in main areas of everyday life (independent living, employment, marital status, and social relationships) [2-4]. Several studies aimed to identify the predictive factors of functioning concluded that the achievement of the real-life functional milestones, such as educational level, independence in housing, current work situation, marital status, and quantity and quality of social contacts, depends on different variables, related to the characteristics of the disorders, the individual resources, and the context of patient's life [5-8].

In more recent years studies on this topic were extended to other mental disorders, in particular bipolar disorder (BP). Because of the chronic course of BP patients showed a rate of achievement of functional milestones significantly lower than general population [9,10]. Main findings suggested that mood symptoms and illness characteristics had a significant impact on a broad range of everyday expressions of functioning. Impaired community functioning has been reported in all phases of illness, including periods of euthymia [11,12]. In addition, authors found that episodes of depression are more detrimental to real-life functioning than mania [13]. In particular, attitudes such as giving up and self-blame are significant predictors of real-world functioning beyond sub-threshold depressive symptoms [14].

Only one systematic review is available on assessment of real-world functioning in patients with major depressive disorder (MDD) [15]. Authors evaluated the negative impact of major depression on quality of life, disability, work, family, and general psychosocial functioning. They concluded that depressive symptoms negatively affect real-life functioning and that the impairment of quality of life and functioning at baseline is significantly related to poor treatment outcome [15-17].

At the moment, a few authors [18,19] have investigated in samples of patients with severe personality disorders concepts such as social and occupational functioning. However, these

concepts are partly different from that of real-world functioning that measures the actual performance obtained in everyday context and combines the patient's functional capacity with the real opportunities available in the environment.

The present study is a naturalistic investigation aimed to identify in a sample of outpatients, including patients with schizophrenia; bipolar disorders; major depressive disorder, and borderline personality disorder, whether different variables, including psychiatric symptoms, onset and duration of illness, attitude to treatments, type of treatment and subjective quality of life may predict a change of the real-world functioning.

Methods

This study was conducted on 511 outpatients who attended the Psychiatric Clinic of the Department of Neuroscience of the University of Turin and completed a period of 12 months of usual treatment. They were recruited between June 2015 and May 2016. Inclusion criteria were a diagnosis of: 1) major depressive disorder; 2) bipolar disorders; 3) schizophrenia; 4) borderline personality disorder, according to DSM-5, and an age ranged between 18 and 60 years. Exclusion criteria were: a lifetime diagnosis of delirium, major and mild neurocognitive disorders. Diagnoses were made by an expert clinician and were confirmed using the Structured Clinical Interview for DSM-IV Axis I or II disorders [20,21].

All subjects were submitted to standard care, provided in community mental health centers in Italy, including pharmacological treatments as recommended by the guidelines, clinical monitoring at least on a monthly basis, and psychological interventions for selected patients. In particular, the two groups of patients with major depressive disorder (MDD) and borderline personality disorder (BPD) were treated with interpersonal psychotherapy. Subjects with MDD received traditional IPT lasting 16 weeks (International Society of Interpersonal Psychotherapy - isIPT, www.interpersonalpsychotherapy.org), while BPD patients received the adaptation of IPT to BPD (IPT-BPD), lasting 40 weeks [22]. Patients in the other two diagnostic categories (schizophrenia and bipolar disorder) were not treated with psychotherapy in our study.

The study was approved by the Ethical Committee of our University Hospital. Written informed consent was obtained from all patients prior to their participation. Declaration of Helsinki guidelines were followed.

At baseline, a series of sociodemographic variables were evaluated with a semi-structured interview.

Categorical variables were recorded as “yes/no” and included: gender (male/female), positive psychiatric anamnesis (previous request of psychiatric assistance/treatment), suicide attempts, treatment with antipsychotics, mood stabilizers, antidepressants, and/or psychotherapy. Treatment with medications was recorded asking directly to the patients and caregivers what they had been taking.

Continuous variables included age (years), age at onset (age of first psychiatric visit), education (years at school), and illness duration (years from the first psychiatric visit).

Patients were assessed at baseline with the following instruments: the severity item of the Clinical Global Impression Scale (CGI-S) [23]; the Personal and Social Performance (PSP) [24]; the Satisfaction Profile (SAT-P) [25]; and the Drug Attitude Inventory-10 (DAI-10) [26]. The same instruments were re-administered after 12 months of usual care.

The CGI is a clinician-rated instrument to make global assessment of illness and consists of three different measures: severity of illness, global improvement, and efficacy index (comparison between patient’s baseline condition and a ratio of current therapeutic benefit and severity of side effects). In this study, we considered the first scale: severity of illness. It is a 7-point scale that requires the clinician to rate the severity of illness at the time of assessment: (1) normal, (2), borderline mentally ill, (3) mildly ill, (4) moderately ill, (5) markedly ill, (6) severely ill, (7) extremely ill.

The PSP is a clinician-rated scale to assess the real-world functioning in patients with a variety of psychiatric conditions. This instrument was developed from Social and Occupational Functioning Assessment Scale - SOFAS [27]. PSP measures social functioning within four domains: (1) socially useful activities; (2) personal and social relationships; (3) self-care; and (4) disturbing and aggressive behaviours. The score is ranged between 1 and 100. Higher score is linked to better functioning.

The SAT-P is a self-administered questionnaire consisting of 32 scales which provides a satisfaction profile in daily life and can be considered as an indicator of subjective quality of life. The SAT-P considers five different factors: (1) psychological functioning; (2) physical functioning; (3) work; (4) sleep; (5) food, and (6) free time; (7) social functioning. The SAT-P asks the patient to evaluate his satisfaction in the last month for each of the 32 life aspects on a scale ranging from “extremely dissatisfied” (0) to “extremely satisfied” (100). The score used in this study is the “factors-related score”. For each factor was attributed a score range between 0 and 100.

The DAI-10 is the short-version of the DAI-30. It is a self-report scale measuring patients’ subjective response and attitude toward drugs therapy. The DAI-10 scoring ranges from -10 to +10 with a total score >0 indicating a positive attitude toward psychiatric medications and a total score of <0 indicating a negative attitude toward psychiatric medications.

Attainment in functional milestones were recorded as follows: (1) employment status (employed/not employed); (2) residential status (independent/dependent); (3) marital status/stable relationships (married/separated/divorced subjects or individuals with long-term relationship or equivalent versus not married patients or subjects without long-term relationship or equivalent).

Statistical analysis was performed using the software Statistical Package for the Social Sciences, SPSS, version 22 for Windows (SPSS, Chicago, IL, USA). Chi-square test for categorical variables and Pearson’s correlation for continuous variables were performed. Pearson’s correlation between the following continuous variables and change of PSP score were calculated: age, level of education, age of illness onset, duration of illness, number of hospitalizations, drug attitude (DAI-10 score), level of global symptoms (CGI-S score), subjective perception of quality of life (SAT-P score). The following categorical variables were evaluated with the chi-square test: gender, positive psychiatric anamnesis, psychiatric diagnosis, record of suicide attempts, use of antipsychotics; use of antidepressants, use of mood stabilizers, and ongoing psychotherapies.

All variables that were found significant were included in a multiple regression analysis (stepwise backward). Dependent variable was

the difference of PSP score between one year and baseline (Δ PSP).

At first time, bivariate analyses and multiple regression were performed in the whole sample of patients. Afterwards, analyses were repeated in each subsample of patients with diagnosis of schizophrenia; major depressive disorder; bipolar disorders; borderline personality disorder. Significance level was $P \leq 0.05$.

Results

Among the 511 outpatients of our sample the diagnoses were distributed as following: 16.4% patients had a diagnosis of schizophrenia; 49.5% patients a diagnosis of major depressive disorder; 17.6% patients of bipolar disorders, and 16.4% patients of borderline personality disorder. One hundred and eighty nine patients were male (36.98%), the mean age was 50.99 ± 16.41 (Mean \pm SD) years and the level of education was 11.28 ± 4.167 (Mean \pm SD). Baseline characteristics of the total sample and of the four diagnostic groups are described in **Table 1**.

In the whole sample of 511 outpatients continuous variables that were found significant were: age of illness onset ($r = 0.126$; $P = 0.007$); DAI-10 ($r = 0.212$; $P = 0.001$); CGI-S ($r = -0.109$; $P = 0.01$); and SAT-P ($r = 0.606$; $P = 0.001$). Significant categorical variables were: record of suicide attempts ($\chi^2 = -61.30$; $P = 0.007$); use of antipsychotics ($\chi^2 = 54.81$; $P = 0.03$) and use of antidepressants ($\chi^2 = 53.77$; $P = 0.04$); and psychotherapy ($\chi^2 = 118.742$; $P = 0.001$).

All significant variables were included in a multiple regression analysis (stepwise backward). Change of PSP score was the dependent variable. Results showed that age of illness onset ($P = 0.009$); SAT-P ($P = 0.001$); and psychotherapy ($P = 0.001$) were significantly and independently related to the change of PSP score. Record of suicide attempts ($P = 0.02$) and CGI-S ($P = 0.001$) were inversely related to the change of PSP score.

In the subgroup of patients with schizophrenia, we found the following significant variables with Pearson's correlation and Chi-square test: SAT-P ($r = 0.659$; $P = 0.001$), DAI-10 ($r = 0.774$; $P = 0.001$), and CGI-S ($r = -0.229$; $P = 0.036$). All these variables were significantly and independently related to PSP change in the multiple regression analysis (respectively $P = 0.001$, $P = 0.001$, and $P = 0.02$).

In the subsample of patients with major depressive disorder, we found the following significant variables with Pearson's correlation and Chi-square test: age ($r = -0.149$; $P = 0.02$); DAI-10 ($r = 0.267$; $P = 0.001$); CGI-S ($r = -0.242$; $P = 0.001$); SAT-P ($r = 0.788$; $P = 0.001$); record of suicide attempts ($\chi^2 = 48.89$; $P = 0.03$); use of mood stabilizers ($\chi^2 = 50.56$; $P = 0.02$); use of antidepressants ($\chi^2 = 64.58$; $P = 0.001$); and psychotherapy ($\chi^2 = 103.97$; $P = 0.001$). Variables significantly related to PSP change with the multiple regression analysis were: SAT-P ($P = 0.001$) and psychotherapy ($P = 0.001$). Record of suicide attempts ($P = 0.04$) and CGI-S ($P = 0.003$) were inversely related to PSP change.

In the subgroup of patients with a diagnosis of bipolar disorders the following variables were found significant with Pearson's correlation and Chi-square test: age of illness onset ($r = 0.254$; $P = 0.02$); duration of illness ($r = -0.224$; $P = 0.04$); CGI-S ($r = -0.489$; $P = 0.001$); DAI-10 ($r = 0.398$; $P = 0.001$); and SAT-P ($r = 0.731$; $P = 0.001$). Variable significantly related to PSP change with the multiple regression analysis was SAT-P ($P = 0.001$). CGI-S ($P = 0.006$) was inversely related to PSP improvement.

Finally, in the subgroup of patients with borderline personality disorder we found the following significant variables with Pearson's correlation and Chi-square test: DAI-10 ($r = 0.384$; $P = 0.001$); CGI-S ($r = -0.361$; $P = 0.001$); use of antidepressants ($\chi^2 = 33.59$; $P = 0.04$); and psychotherapy ($\chi^2 = 81.23$; $P = 0.001$). Variable significantly related to PSP change with the multiple regression analysis was psychotherapy ($P = 0.006$).

Significant results of multiple regression analyses calculated in the total sample and in the four diagnostic groups are summarized in **Table 2**.

Discussion

Impairment in real-world functioning is a common feature of major psychiatric disorders. It is characterized by difficulties in achieving life milestones, including independent living, employment, and stable interpersonal relationships. Recent literature data suggested that several factors may influence the functional outcome in real world, in particular quality of life, adherence to treatments and severity of psychiatric symptoms [7,8,28,29]. The aim of the present study was to identify whether several

Table 1: Demographic and clinical variables in the whole sample of 511 outpatients and in the four subgroups: schizophrenia, major depressive disorder, bipolar disorder, and borderline personality disorder.

Variables	Total sample	Schizophrenia N = 84	MDD N = 253	BP N = 90	BPD N = 84
Age (Mean ± SD)	50.99 ± 16.41	45.55 ± 16.65	54.43 ± 15.99	53.87 ± 13.91	43.02 ± 16.91
Age at onset (Mean ± SD)	39.47 ± 18.99	28.21 ± 9.96	44.61 ± 17.03	43.85 ± 24.64	31.64 ± 16.91
Education (Mean ± SD)	11.28 ± 4.17	10.71 ± 3.69	11.23 ± 4.21	10.91 ± 4.37	12.37 ± 4.14
Illness duration (Mean ± SD)	12.32 ± 12.68	16.65 ± 12.54	11.63 ± 13.76	12.87 ± 11	8.95 ± 10.59
CGI-S (Mean ± SD)	4.11 ± 1.06	5.23 ± 0.72	3.38 ± 0.63	4.32 ± 0.80	4.98 ± 0.88
PSP (Mean ± SD)	64.82 ± 11.01	58.11 ± 11.03	66.17 ± 9.29	66.84 ± 11.95	65.31 ± 12.36
DAI-10 (Mean ± SD)	2.03 ± 3.85	3.05 ± 4.56	4.37 ± 1.56	1.09 ± 2.47	2.66 ± 2.37
SAT-P (Mean ± SD)	60.37 ± 18.61	59.36 ± 19.43	67.98 ± 17.33	51.24 ± 16.96	48.24 ± 10.62
Male gender N (%)	189 (36.9)	39 (46.4)	77 (30.4)	35 (38.9)	38 (45.2)
Psych. anamnesis N (%)	392 (76.7)	80 (95.2)	165 (65.2)	79 (87.8)	68 (80.9)
Suicidal attempts N(%)	39 (7.63)	4 (4.7)	17 (6.7)	7 (7.8)	11 (13.1)
Antipsychotics N (%)	166 (32.5)	84 (100)	11 (4.3)	30 (33.3)	41 (48.8)
Mood stabilizers N (%)	157 (30.7)	19 (22.6)	9 (3.6)	87 (96.7)	61 (72.6)
Antidepressants N(%)	283 (55.4)	15 (11.9)	244 (96.4)	31 (34.4)	8 (9.5)
Psychotherapy N (%)	105 (20.5)	0 (0)	51 (20.2)	0 (0)	42 (50)
Diagnosis of schizophrenia N (%)	84 (16.4)	--	--	--	--
Diagnosis of major depression N (%)	253 (49.5)	--	--	--	--
Diagnosis of bipolar disorder N (%)	90 (17.6)	--	--	--	--
Diagnosis of BPD N(%)	84 (16.4)	--	--	--	--

N = number; MDD = Major Depressive Disorder; BP = Bipolar Disorder; BPD = Borderline Personality Disorder; DAI 10 = Drug Attitude Inventory-10; CGI – S = Clinical Global Impression- Severity; SAT- P = Satisfaction Profile; PSP = Personal and Social Performance.

Table 2: Results of multiple regression analysis in the whole sample of 511 patients and in the four subgroups: schizophrenia, major depressive disorder, bipolar disorder, and borderline personality disorder. Dependent variable ΔPSP. P ≤ 0.05 *; P ≤ 0.01 **

Variables	Total sample		Schizophrenia		MDD		BD		BPD	
	β	SE	β	SE	β	SE	β	SE	β	SE
Suicidal attempts	-2.39**	0.91	--	--	-2.04*	1.05	--	--	--	--
Age at onset	0.03**	0.01	--	--	--	--	--	--	--	--
CGI-S	-1.54**	0.24	-1.16*	0.47	-1.27**	0.43	-2.45*	0.86	--	--
SAT-P	0.23**	0.01	0.09**	0.02	0.27**	0.02	0.34**	0.04	--	--
DAI-10	--	--	0.72**	0.09	--	--	--	--	--	--
Psychotherapy	3.88**	0.54	--	--	3.28**	0.59	--	--	9.92**	0.96

MDD = Major Depressive Disorder; BP = Bipolar Disorder; BPD = Borderline Personality Disorder; DAI 10 = Drug Attitude Inventory-10; CGI – S = Clinical Global Impression- Severity; SAT- P = Satisfaction Profile; PSP = Personal and Social Performance, SE = Standard Error.

variables, including psychiatric symptoms, onset and duration of illness, hospitalizations, suicide attempts, attitude to treatments, pharmacotherapy, psychotherapy, and subjective perception of quality of life, are predictive of the change of the global measure of real-world functioning during one year of usual outpatient treatment in a large sample of subjects with a diagnosis of schizophrenia, bipolar disorders, major depression, or borderline personality disorder.

Previous investigations have been performed about the clinical and demographic predictive factors of real-world functioning in a single

evaluation, but to our knowledge this is the first study that evaluated the relationship between these factors and the improvement of real-world functioning over a time span. Thus, our findings are only partially comparable with those of other trials.

The main results of our study showed that improvement of real-world functioning in the whole sample, measured with the change of PSP between baseline and one year of usual management, was directly and independently related to the age of illness onset, the subjective perception of quality of life, and the intervention with psychotherapy. On the other hand, the

severity of psychiatric symptoms and the presence of suicide attempts were inversely related to the change of PSP score and predicted a worse real-world functioning. Concerning age at onset, literature findings are concordant with our data and indicate that patients with early-onset of disease have prominent deficits in functional outcome [30], probably due to the impact of the illness in a critical period of development, when specific social roles (such as independent living, work capacities, and secondary social relationships) and neurocognitive functions are still taking shape [31,32].

Several investigations have shown significant relations between patients' functioning and quality of life, in terms of individual's physical health status, psychological status and well-being, and social interaction [33,34]. In particular, quality of life was found to be an important outcome indicator and predictor of symptomatic and functional improvement in schizophrenia [35]. Some authors, in line with our methodological choice, suggested that self-reporting measures of quality of life are more appropriate than measures reported by clinicians [30,36,37]. Our findings are substantially in agreement with the previous studies outlining that improvement of real-world functional outcomes was significantly related to patients' global life satisfaction [38], and better daily functioning is one of the indicator of recovery and better quality of life [39]. We found that a better subjective perception of quality of life was significantly related to PSP improvement in the whole sample of patients and in each diagnostic category, except for BPD. We can hypothesize that in BPD patients intense feelings of anger and dysphoria and persistent mood instability are likely to impair patients' ability to appreciate and to take advantage in daily functioning from a better quality of life.

In the present study, another important factor that was identified as a predictor of improvement of daily functioning, was a psychotherapeutic intervention. In fact, the two subgroups of patients with major depressive disorder and with borderline personality disorder, that were treated with interpersonal psychotherapy (IPT), showed a larger PSP change. Several previous investigations have shown that psychotherapies had positive effects in improving real-world functioning in psychiatric disorders [40-43]. In particular, interpersonal psychotherapy was found efficacious in improving the community interpersonal functioning in depressed patients

[44,45]. Concerning BPD, limited research has focused on improvement of functional outcomes after psychotherapy. In fact, the majority of studies of specific psychotherapies for BPD patients were aimed to assess the efficacy of interventions in terms of decrease of symptoms severity [46,47]. Nevertheless, BPD patients have a high level of interpersonal reactivity and instability that produce a severe impairment in daily functioning [48]. So, it is not surprising that patients who receive IPT, a psychotherapeutic model specifically aimed at improving interpersonal functioning, present a significant overall improvement of daily functioning after one year.

In our investigation patients with a more severe degree of psychiatric symptoms showed a reduced daily functioning change during one year of usual treatment in the total sample and in each diagnostic category, again except for BPD. This finding is expected and intuitive as individuals with a higher level of symptoms producing a significant functional impairment have fewer resources to achieve and maintain the real-world milestones. Literature confirmed our results reporting significant relationships between severity of symptom domains and functional outcome in schizophrenia and mood disorders [49-57]. The lack of significant relationships between PSP change and severity of global symptoms in BPD patients might depend on the considerable heterogeneity of BPD symptomatology that would produce unstable and unpredictable effects on the real-world functioning.

As for the influence of suicidal behaviors on everyday functioning, a growing number of studies demonstrated that patients with a history of suicide attempts showed impaired functioning abilities [58], but no investigations have yet considered the impact of suicidality on the change of functioning level. In our study, we found that patients, with a higher number of suicide attempts, in particular subjects with a diagnosis of major depressive disorder, showed a lower degree of improvement in the community functioning. An interpretation of this result considers data indicating that patients with a history of suicidal acts present lower abilities in domains of neurocognitive functioning [58]. Thus, they show a reduced cognitive flexibility and a limited opportunity to change their real-world daily-living skills.

In our investigation we also evaluated whether the attitude to pharmacotherapy may predict

the daily functioning improvement. Only in the subgroup of patients with schizophrenia a positive attitude to pharmacological treatment was significantly related to real-world functioning change in one year of observation. So, in the group of patients with schizophrenia a better attitude and adherence to antipsychotic treatment recommended by major guidelines produced a more pronounced effect (that reached the statistical significance) on improvement of real-life functioning. This result is concordant with data from Mohr and colleagues [59], who found that functional performances correlated positively with subjective satisfaction with medications and, in particular, the best level of functioning was linked to treatment with antipsychotics. In another investigation comparing schizophrenic responder, schizophrenic resistant and non-schizophrenic patients, authors concluded that poor adherence to drug therapy may predict poor psychosocial functioning in both subgroups of schizophrenic patients [60]. Adherence to drug therapy, at least in patients with schizophrenia, appears a more important factor to change real-world functioning than drug treatment itself, as administration of different classes of drugs was never found significant in regression analyses.

This study suffered from some limits. A few demographical and clinical data were retrospectively collected due to the naturalistic design of this study. We did not use specific psychopathological rating scales for each diagnostic category, but the same clinical global impression measure for all the diagnoses. So, we cannot determine whether specific clusters of symptoms influenced the real-world functioning change. There may be additional clinical predictors that were not considered in our sample and that may play an important role in patients' long-term functional outcome. Despite

these limitations, there are some strengths of our investigation that should be noticed: the large number of patients and the naturalistic design that avoids the selection biases of randomized controlled designs. Indeed, since data from randomized controlled trials provide outcome measures in a relatively homogenous population under artificial conditions, it is important to verify these results in real-world settings.

In summary, our naturalistic study was aimed to identify in a large sample of outpatients, including subjects with schizophrenia, bipolar disorders, major depressive disorder, and borderline personality disorder, whether demographic and clinical variables predict a change in the real-world functioning. We found that in the whole sample and in each diagnostic category, except for BPD, a higher degree of global symptoms was inversely related to the change of PSP score and predicted a worse community functioning. A history of suicide attempts was also associated to reduce functioning improvement in the total sample and in depressed patients. In each diagnostic category, except in BPD, a better subjective perception of quality of life was related to the change of the dependent variable. Patients with major depressive disorder and with borderline personality disorder that received interpersonal psychotherapy (IPT) showed a higher degree of functional improvement. A positive attitude and adherence to pharmacological treatment was significantly related to the real-world functioning improvement only in schizophrenia, but not in the other subgroups. Further studies aimed to identify predictors of real-world functioning in samples of patients with psychiatric disorders are required to replicate our findings. Data on this topic can be useful to promote a more accurate evaluation of patients in order to obtain a better functional outcome.

References

- Menendez-Miranda I, Garcia-Portilla MP, Garcia-Alvarez L, et al. Predictive factors of functional capacity and real-world functioning in patients with schizophrenia. *Eur. Psychiatry* 30(5), 622-627 (2015).
- Cardenas V, Abel S, Bowie CR, et al. When functional capacity and real-world functioning converge: the role of self-efficacy. *Schizophr. Bull* 39(4), 908-916 (2013).
- Harvey PD. Assessment of everyday functioning in schizophrenia: implications for treatments aimed at negative symptoms. *Schizophr. Res* 150(2-3), 353-355 (2013).
- Robertson BR, Prestia D, Twamley EW, et al. Social competence versus negative symptoms as predictors of real world social functioning in schizophrenia. *Schizophr. Res.* 160(1-3), 136-141 (2014).
- Harvey PD, Strassnig M. Predicting the severity of everyday functional disability in people with schizophrenia: cognitive deficits, functional capacity, symptoms, and health status. *World Psychiatry*. 2012;11(2):73-79.
- Galderisi S, Rossi A, Rocca P, et al. The influence of illness-related variables, personal resources and context-related factors on real-life functioning of people with schizophrenia. *World. Psychiatry* 13(3), 275-287 (2014).
- Olsson AK, Hjärthag F, Hellidin L. Predicting real-world functional milestones in schizophrenia. *Psychiatry Res* 30(1), 1-6 (2016).
- Rocca P, Montemagni C, Mingrone C, et al. A cluster-analytical approach toward real-world outcome in outpatients with stable schizophrenia. *Eur. Psychiatry* 32(1), 48-54 (2016).
- Hirschfeld RM, Lewis L, Vornik LA. Perceptions and impact of bipolar disorder: how far have we really come? Results of the national depressive and manic-depressive association 2000 survey of individuals with bipolar disorder. *J. Clin. Psychiatry* 64(1), 161-174 (2003).

10. Dean BB, Gerner D, Gerner RH. A systematic review evaluating health-related quality of life, work impairment, and healthcare costs and utilization in bipolar disorder. *Curr. Med. Res. Opin* 20(1), 139–154 (2004).
11. Depp CA, Mautsach BT, Harmell AL, et al. Meta-analysis of the association between cognitive abilities and everyday functioning in bipolar disorder. *Bipolar. Disord* 14(3), 217–226 (2012).
12. Henry BL, Minassian A, Perry W. Everyday functional ability across different phases of bipolar disorder. *Psychiatry. Res.* 210(3), 850–856 (2013).
13. Peters AT, Peckham AD, Stange JP, et al. Correlates of real world executive dysfunction in bipolar I disorder. *J. Psychiatr. Res* 53(1), 87–93 (2014).
14. Nitzburg GC, Russo M, Cuesta-Diaz A, et al. Coping strategies and real-world functioning in bipolar disorder. *J. Affect. Disord* 198(1), 185–188 (2016).
15. Langlieb AM, Guico-Pabia CJ. Beyond symptomatic improvement: assessing real-world outcomes in patients with major depressive disorder. *Prim. Care. Companion. J. Clin. Psychiatry* 12(2) (2010).
16. Wang PS, Beck AL, Berglund P, et al. Effects of major depression on moment-in-time work performance. *Am J. Psychiatry* 161(10), 1885–1891 (2004).
17. Kessler RC, Akiskal HS, Ames M, et al. Prevalence and effects of mood disorders on work performance in a nationally representative sample of US workers. *Am. J. Psychiatry* 163(9), 1561–1568 (2006).
18. Zanarini MC, Frankenburg FR, Reich DB, Fitzmaurice G. The 10-year course of psychosocial functioning among patients with borderline personality disorder and axis II comparison subjects. *Acta. Psychiatr. Scand* 122(2), 103–109 (2010).
19. Alvarez-Tomás I, Soler J, Bados A, et al. Long-Term Course of Borderline Personality Disorder: A Prospective 10-Year Follow-Up Study. *J. Pers. Disord* 17(1), 1–16 (2016).
20. First MB, Gibbon M, Spitzer RL. Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II). Washington (DC) American Psychiatric Press, 1997a.
21. First MB, Spitzer RL, Gibbon M. Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I). Washington (DC) American Psychiatric Press, 1997b.
22. Bellino S, Bozzatello P. Interpersonal Psychotherapy Adapted for Borderline Personality Disorder (IPT-BPD): A Review of Available Data and a Proposal of Revision. *J. of Psychol. Psychotherapy* 5(6), 1–5 (2016).
23. Guy W. Clinical global impression (C.G.I.). Ecdeu Assessment Manual for Psychopharmacology. US Dept Health, Education, and Welfare publication (ADM) 76–338. Rockville, Md: National Institute of Mental Health 218–222 (1967).
24. Morosini PL, Magliano L, Brambilla L, et al. Development, reliability and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. *Acta. Psychiatr. Scand* 101(4), 323–329 (2000).
25. Majani G, Callegari S. SAT-P Satisfaction Profile. Soddifazione soggettiva e qualità della vita. Erickson, 1998. Trento (IT).
26. Rossi A, Arduini L, De Cataldo S, et al. Subjective response to neuroleptic medication: a validation study of the Italian version of the Drug Attitude Inventory (DAI). *Epidemiol. Psichiatr Soc* 10(2), 107–114 (2001).
27. Goldman HH, Skodol AE, Lave TR. Revising Axis V for DSM-IV: a review of measures of social functioning. *Am. J. Of. Psychiatry* 149(1), 1148–1156 (1992).
28. Rocca P, Montemagni C, Castagna F, et al. Relative contribution of antipsychotics, negative symptoms and executive functions to social functioning in stable schizophrenia. *Prog. Neuropsychopharmacol. Biol. Psychiatr* 33(2), 373–379 (2009).
29. Velthorst E, Fett AJ, Reichenberg A, et al. The 20-Year Longitudinal Trajectories of Social Functioning in Individuals With Psychotic Disorders. *Am. J. Psychiatry* 2016.
30. Puig O, Penadés R, Baeza I, et al. Assessment of real-world daily-living skills in early-onset schizophrenia through the Life Skills Profile scale. *Schizophr. Res* 145(1–3), 95–100 (2013).
31. Lay B, Blanz B, Hartmann M, et al. The psychosocial outcome of adolescent-onset schizophrenia: a 12-year follow up. *Schizophr. Bull* 26(4), 801–816 (2000).
32. Oie M, Sundet K, Ueland T. Neurocognition and functional outcome in early-onset schizophrenia and attention-deficit/hyperactivity disorder: a 13-year follow-up. *Neuropsychology* 25(1), 25–35 (2011).
33. Karadayı G, Emiroğlu B, Üçok A. Relationship of symptomatic remission with quality of life and functionality in patients with schizophrenia. *Compr. Psychiatry* 52(1), 701–707 (2011).
34. Kokacya MH, Virit O, Copoglu US, et al. Symptomatic Remission Determines Functional Improvement and Quality of Life in Schizophrenia. *Noro. Psikiyat. Ars* 53(4), 328–333 (2016).
35. Cohen C, Vengassery A, Garcia Aracena EF. A Longitudinal Analysis of Quality of Life and Associated Factors in Older Adults with Schizophrenia Spectrum Disorder. *Am. J. Geriatr. Psychiatry* 25(7), 755–765 (2017).
36. Voruganti L, Heslegrave R, Awad AG, et al. Quality of life measurement in schizophrenia: reconciling the quest for subjectivity with the question of reliability. *Psychol. Med* 28(1), 165–170 (1998).
37. Harvey PD, Velligan DI, Bellack AS. Performance-based measures of functional skills: usefulness in clinical treatment studies. *Schizophr. Bull* 33(5), 1138–1148 (2007).
38. Edmondson M, Pahwa R, Lee KK, et al. A dual change model of life satisfaction and functioning for individuals with schizophrenia. *Schizophr. Res* 139(1–3), 110–115 (2012).
39. Charzyńska K, Kucharska K, Mortimer A. Does employment promote the process of recovery from schizophrenia? A review of the existing evidence. *Int. J. Occup. Med. Environ. Health* 28(3), 407–418 (2015).
40. Gamble SA, Smith PN, Polshuck EL, et al. Domain-specific social functioning improvements during treatment of depressed women with histories of childhood sexual abuse. *J. Affect. Disord* 130(3), 478–482 (2011).
41. Pascual JC, Palomares N, Ibáñez Á. Efficacy of cognitive rehabilitation on psychosocial functioning in Borderline Personality Disorder: a randomized controlled trial. *BMC. Psychia* 21(15), 255 (2015).
42. Young S, Emilsson B, Sigurdsson JF, et al. A randomized controlled trial reporting functional outcomes of cognitive-behavioural therapy in medication-treated adults with ADHD and comorbid psychopathology. *Eur Arch. Psychiatry. Clin. Neurosci* 267(3), 267–276 (2017).
43. Driessen E, Van HL, Peen J et al. Cognitive-behavioral versus psychodynamic therapy for major depression: Secondary outcomes of a randomized clinical trial. *J. Consult. Clin. Psychol* 85(7), 653–663 (2017). Brakemeier EL, Frase L. Interpersonal psychotherapy (IPT) in major depressive disorder. *Eur. Arch. Psychiatry Clin. Neurosci* 262(1), 117–121 (2012).
44. Brakemeier EL, Frase L. Interpersonal psychotherapy (IPT) in major depressive disorder. *Eur. Arch. Psychiatry Clin. Neurosci* 262(1), 117–121 (2012).
45. Lemmens LHJ, Galindo-Garre F, Arntz A, et al. Exploring mechanisms of change in cognitive therapy and interpersonal psychotherapy for adult depression. *Behav. Res. Ther* 94(1), 81–92 (2017).
46. Stoffers JM, Völlm BA, Rucker G, et al. Psychological therapies for people with borderline personality disorder. *Cochrane. Database. Syst. Rev* 15(8), CD005652 (2012).
47. Links PS, Shah R, Eynan R. Psychotherapy for Borderline Personality Disorder: Progress and Remaining Challenges. *Curr.*

- Psychiatry. Rep* 19(3), 16 (2017).
48. Sinnave R, van den Bosch LM, van Steenbergen-Weijenburg KM. Change in interpersonal functioning during psychological interventions for borderline personality disorder—a systematic review of measures and efficacy. *Personal. Ment. Health* 9(3), 173-194 (2015).
 49. Bowie CR, Reichenberg A, Patterson TL, et al. Determinants of real-world functional performance in schizophrenia subjects: correlations with cognition, functional capacity, and symptoms. *Am. J. Psychiatry* 163(3), 418-425 (2006).
 50. Bowie CR, Twamley EW, Anderson H, et al. Self-assessment of functional status in schizophrenia. *J. Psychiatr. Res* 41(12), 1012-1018 (2007).
 51. Bowie CR, Depp C, McGrath JA, et al. Prediction of real-world functional disability in chronic mental disorders: a comparison of schizophrenia and bipolar disorder. *Am. J. Psychiatry* 167(9), 1116-1124 (2010).
 52. Leifker FR, Bowie CR, Harvey PD. Determinants of everyday outcomes in schizophrenia: the influences of cognitive impairment, functional capacity, and symptoms. *Schizophr. Res* 115(1), 82-87 (2009).
 53. Stefanopoulou E, Lafuente AR, Saez Fonseca JA, Huxley A. Insight, global functioning and psychopathology amongst in-patient clients with schizophrenia. *Psychiatr. Q* 80(3), 155-165 (2009).
 54. Galderisi S, Bucci P, Mucci A, et al. Categorical and dimensional approaches to negative symptoms of schizophrenia: focus on long-term stability and functional outcome. *Schizophr. Res* 147(1), 157-162 (2013).
 55. van der Voort TY, Seldenrijk A, van Meijel B, et al. Functional versus syndromal recovery in patients with major depressive disorder and bipolar disorder. *J. Clin. Psychiatry* 76(6), 809-814 (2015).
 56. Tan EJ, Rossell SL. Comparing how co-morbid depression affects individual domains of functioning and life satisfaction in schizophrenia. *Compr. Psychiatry* 66(1), 53-58 (2016).
 57. Vancampfort D, Stubbs B, Sienaert P, et al. Depressive symptoms and muscular fitness contribute independently to the ability to perform daily life activities in people with bipolar disorder. *Nord. J. Psychiatry* 70(6), 477-482 (2016).
 58. Saffer BY, Klonsky ED. The Relationship of Self-reported Executive Functioning to Suicide Ideation and Attempts: Findings from a Large U.S.-based Online Sample. *Arch. Suicide. Res* 20(1), 1-18 (2016).
 59. Mohr P, Rodriguez M, Bravermanová A, et al. Social and functional capacity of schizophrenia patients: A cross-sectional study. *Int. J. Soc. Psychiatry* 60(4), 352-358 (2014).
 60. Iasevoli F, Giordano S, Balletta R, et al. Treatment resistant schizophrenia is associated with the worst community functioning among severely-ill highly-disabling psychiatric conditions and is the most relevant predictor of poorer achievements in functional milestones. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 65(1), 34-48 (2014).