

Adherence, self-stigma and discontinuation of pharmacotherapy in patients with anxiety disorders – cross-sectional study

Andrea CINCULOVA^{1,2}, Jan PRASKO^{1,2}, Dana KAMARADOVA^{1,2}, Marie OCISKOVA^{1,2}, Klara LATALOVA^{1,2}, Kristyna VRBOVA^{1,2}, Radim KUBINEK^{1,2}, Barbora MAINEROVA^{1,2}, Ales GRAMBAL^{1,2}, Anezka TICHACKOVA^{1,2}

¹ Department of Psychiatry, Faculty of Medicine and Dentistry, Palacky University Olomouc, University Hospital Olomouc, Czech Republic

² Department of Psychology, Philosophical Faculty, Palacky University Olomouc, Czech Republic

Correspondence to: prof. MUDr. Jan Prasko, PhD.
Department of Psychiatry, Faculty of Medicine and Dentistry
Palacky University Olomouc, University Hospital Olomouc
I.P. Pavlova 6, Olomouc, Czech Republic.
E-MAIL: prasko.jan@seznam.cz

Submitted: 2017-07-07 Accepted: 2017-08-02 Published online: 2017-12-10

Key words: self-stigma; adherence; discontinuation of medication; anxiety disorders

Neuroendocrinol Lett 2017; **38**(6):429–436 PMID: 29298284 NEL380617A05 © 2017 Neuroendocrinology Letters • www.nel.edu

Abstract

INTRODUCTION: Treatment adherence is one of the main factors affecting the success of treatment and, secondarily, the quality of life and social adaptation of the patients. The aim of this study was to investigate the association between self-stigmatization, treatment adherence and history of discontinuation of drug treatment.

METHODS: The cross-sectional study was conducted on 120 (98 completed all the questionnaires) neurotic outpatients treated in the University Hospital Olomouc. The following variables were evaluated: the objective and subjective Clinical Global Impression (CGI) scale, Drug Attitude Inventory (DAI-10) questionnaire measuring adherence, Internalized Stigma of Mental Illness (ISMI) scale measuring self-stigma, and a demographic data questionnaire.

RESULTS: Data analysis showed no correlation between self-stigmatization and age, age of onset or length of the post-hospitalization phase. However, there were significant correlations between self-stigmatization and the severity of the disorder (assessed by both objective and subjective CGI), number of previous hospitalizations, total number of psychiatrists visited by the patient, the arbitrary discontinuation of medication in the past, and the dose of an antidepressant. Furthermore, self-stigma was significantly negatively correlated with the current treatment adherence. The rate of adherence was negatively correlated with both objective and subjective CGI only.

CONCLUSIONS: Self-stigma significantly affects the current adherence to the treatment of neurotic spectrum disorders.

INTRODUCTION

There is no single definition of adherence. Previously, the terms adherence and compliance were used interchangeably to refer to a patient's effort to follow treatment advice. Compliance suggests that the patient will obey or conform to treatment instructions. In adherence, more attention is paid to the patient's right to choose whether he/she will or will not follow the instruction. Adherence to the treatment of mental disorders is one of the main factors affecting the success of treatment and, secondarily, the patient's quality of life and social adaptation (Lysaker *et al.* 2007, Ustündağ & Kesebir 2013). In psychiatric patients, partial adherence or non-adherence was related to poorer clinical outcomes including greater use of emergency care, more hospitalizations and suicides (Gilmer *et al.* 2004, Livingston & Boyd 2010). Factors involved in adherence may be divided as follows:

1. factors associated with the illness itself, especially its symptoms (severity of depression, psychotic symptoms, odds ratio, cognitive deficit, prognosis, etc.);
2. factors related to the patient's personality (values, prejudices, intelligence, education, attitude to drugs, preview, expectations from treatment, self-stigma, etc.);
3. factors related to the environment (negative attitudes about the treatment in the patient's family, stigma, loneliness, lack of social support, etc.); and
4. factors associated with the treatment and doctor (availability, doctor-patient relationship, physician's erudition) or the drug alone (efficacy, side effects, onset, ease of use, number of daily doses, etc.).

Patients' attitudes towards medication were assessed with the Drug Attitude Inventory. This questionnaire can measure attitudes and rate of adherence towards pharmacotherapy (Brook *et al.* 2003, Tay 2007). The patients also completed a short questionnaire asking if they had ever discontinued medication by their own decision. Prediction of patients' adherence to the treatment based only on clinical judgment seems to be insufficient (Vermeire *et al.* 2001).

Another important factor that may significantly affect the treatment adherence is the degree of stigmatization and self-stigma. Patients' attempts to avoid stigma may lead to denying that they are mentally ill, delay and avoidance of the treatment, and may be the most significant barrier to seeking help (Camp *et al.* 2002, Barney *et al.* 2009). Although they have not yet experienced any signs of stigmatization, patients suffering from anxiety disorders are often afraid of being stigmatized as they anticipate it.

The anticipatory anxiety may then prevent the patients from seeking adequate help from a psychiatrist. Self-stigma is a gradual process during which a person adopts the negative evaluations of the social environment which are connected to the presumed features

that are socially evaluated as inferior (Brook *et al.* 2003, Corrigan *et al.* 2011). Self-stigma is associated with lower adherence to medical procedures (Ustündağ & Kesebir 2013, Sirey *et al.* 2001, Fung *et al.* 2008, Tsang *et al.* 2010, Padurariu 2011). Patients who agree with societal prejudices about psychiatric patients believe less in the improvement of their mental state, they are more depressed and suffer from negative self-esteem.

The main goals of this study were to evaluate the rate of adherence and self-stigma, and to investigate the relationships between adherence, self-stigma and discontinuation of medication in stabilized neurotic outpatients. The following hypotheses were proposed: (1) rate of self-stigma and non-adherence is related to demographic data such as age, marital status, family psychiatric load and education; (2) higher rates of self-stigma are associated with lower adherence to the treatment and frequent administration of psychotropic drugs in the past; and (3) patients who previously arbitrarily discontinued drugs have lower adherence to treatment and higher self-stigma.

METHOD

The participation in this study was offered to well-stabilized outpatients already diagnosed as suffering from neurotic spectrum disorders (anxiety disorders, somatoform disorders, post-traumatic stress disorder, obsessive-compulsive disorder [OCD], and dissociative disorders) who were treated in a university hospital psychiatric outpatient department between 1 July and 30 September 2013.

The inclusion criteria were: (a) a diagnosis of neurotic spectrum disorder (F4X) according to the ICD-10 criteria (MKN-10 1996); (b) willingness to participate in the study; and (c) age between 18 and 75 years.

Excluded were patients with mental retardation, organic mental disorders, severe physical illness, and those with mental health requiring hospitalization, change in medication or crisis intervention. The patients were treated with standard drugs used for the diagnostic group according to the best practices and principles of good clinical practice.

Assessment instruments

Internalized Stigma of Mental Illness (ISMI) – This scale consists of 29 items with a four-point scale and measures 5 areas of internalized stigma. These areas include feelings of alienation and exclusion from society, the degree of consent to the stereotypes about people with mental illness, perception of how others have behaved toward them since they were diagnosed as mentally ill, rate of withdrawal from society, and the degree of resistance to the stigma (Boyd *et al.* 2014). The Czech version of the scale was standardized by Ociskova *et al.* (2014).

Drug Attitude Inventory (DAI-10) – This questionnaire was designed to assess patients' attitude to

medication. The patient checks each statement as true or false. The statements are concerned with the effects of the medication, its necessity and voluntary use. It assesses the current level of adherence.

Clinical Global Impression (CGI; Guy 1976) – This is a scale for an overall assessment of the severity of psychopathology. The source of evaluation is a comprehensive assessment of the patient’s physician with the objective version (CGI-O). In its subjective version (CGI-S), the patient evaluates the overall condition by himself/herself on a 1–7 scale, wherein each of the degrees of severity has described features.

Demographic questionnaire – It contains basic information – gender, age, employment status, pension income, education, age of illness onset, overall time of attending the outpatient department, number of hospitalizations, time elapsed since the last hospitalization, number of visited psychiatrists, current medication, and information about discontinuing medication in the past (either on recommendation of a psychiatrist or willingly).

Statistical evaluation and ethics

The statistical software Prism3 and SPSS-17 were used for statistical evaluation. Demographic data and mean total scores in the individual questionnaires and CGI were assessed using descriptive statistics to identify the mean, median, standard deviation, and the character of the data distribution. The relationships between categories were assessed by correlation coefficients and linear regression. The relationships between alternative variables (gender, marital status, discontinuation of medication) were assessed by the Fisher test. The meanings of the correlations of the individual factors was analyzed using backward stepwise regression. A 5% level of significance was considered acceptable for all statistical tests.

The study was approved by the local ethics committee. The research was conducted in accordance with the latest version of the Helsinki Declaration and recommendations for good clinical practice (EMEA 2002).

RESULTS

Description of the participants

A total of 120 patients (39 men and 81 women) participated in this study. Table 1 provides summary characteristics of the probands.

Out of all participants, 98 patients (81.7%) completed all the questionnaires. The reasons for not com-

pleting the questionnaires were lack of time, loss of motivation, inability to concentrate on the task in the waiting room, and absence of corrective appliances

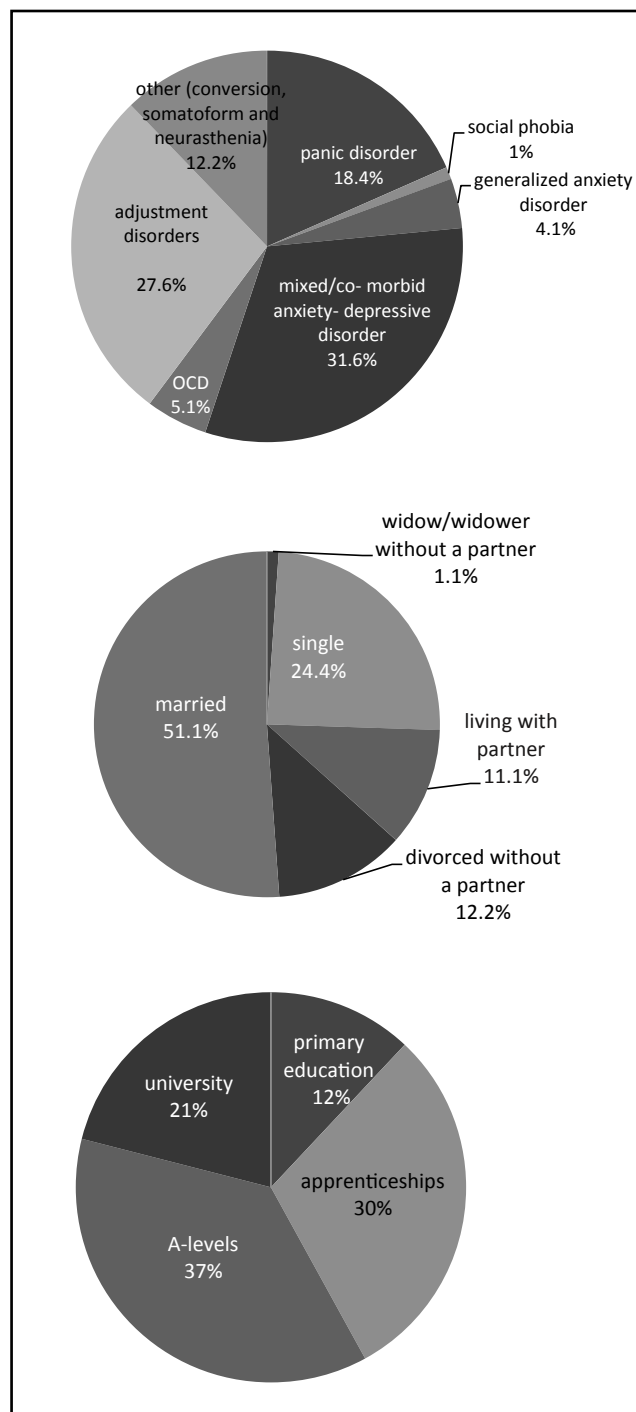


Fig. 1. Distribution of the diagnoses, marital status and education.

Tab. 1. Demographic and clinical data.

	age	CGI-S	CGI-O	Onset of illness	Number of hospitalizations	Psychiatrists	Adherence	ISMI
All patients	43.13±14.08	3.40±1.57	2.73±1.31	34.96±14.28	1.14±1.82	1.68±1.04	4.57±4.30	59.40±14.60
Those who filled out questionnaires	41.86±13.86	3.33±1.53	2.72±1.31	34.51±13.86	1.18±1.94	1.70±1.07	4.11±4.25	59.50±14.84

(glasses). The group of patients who did not fill in all the required questionnaires did not differ statistically significantly from the investigated group. The most common diagnoses were mixed or comorbid anxiety-depressive disorder and adjustment disorder (Figure 1).

Most patients were married (Figure 1). A positive family psychiatric history was found in 43 patients (43.9%). Most frequently, the participants had secondary education (Figure 1).

Treatment

Eighty-nine out of 98 patients (90.8%) were treated with antidepressants, twenty (20.4%) were treated with anxiolytics, and 18 (18.4%) with antipsychotics. The mean dose of antidepressants was 37.1 ± 21.4 mg (paroxetine index), anxiolytics 9.4 ± 6.9 mg (diazepam index), and antipsychotics 0.9 ± 0.6 mg (risperidone index). A total of 45.9% of the patients discontinued medication on the recommendation of their psychiatrist and 30.4% admitted discontinuing medication by their own will.

Self-stigma, adherence and discontinuation of drugs in the whole group: relation to demographic and clinical variables

Family history of psychiatric illnesses. The mean self-stigma rate in patients without a family history of psychiatric illness was lower than in patients with the

familial predisposition. The result was not statistically significant; only a trend was discovered. Adherence to treatment was significantly higher in patients with no family history of psychiatric illness. There was no statistically significant difference between groups in discontinuation of medication (Table 2).

Gender. The mean self-stigma rate was 59.50 ± 14.84 points. There was no statistically significant difference in self-stigma rates between men and women. The difference in adherence between women and men was not statistically significant either. The proportion of patients discontinuing their medication in the past by their own will was 28.57% of the whole group, once again with no significant gender difference (Table 2). It may be concluded that gender plays no role in the rates of self-stigma and adherence or discontinuation of medication in the past.

Education. Although the self-stigma rate decreases with the education level, the differences between the groups did not reach statistical significance (one-way ANOVA: $F=1.61$ $df=97$; n.s.) (Figure 2).

The mean rate of current adherence in patients with different education levels showed the opposite trend, being higher in case of secondary education and even higher in university-educated patients. But the differences did not reach statistical significance (one-way ANOVA: $F=0.9511$ $df=97$; n.s.) (Figure 3).

The frequency of medicine discontinuation in the past varied in patients with different education levels (Figure 4). Patients with primary education discontinued drugs more frequently than those with higher education levels. This difference did not reach statistical significance (chi-square: $p=0.0521$).

Partnership status. Table 2 shows differences between groups of patients with and without partners. There was no statistical difference in the measured variables.

When comparing self-stigma rates in patients who discontinued medication in the past and those who did not, a statistically significant difference was found.

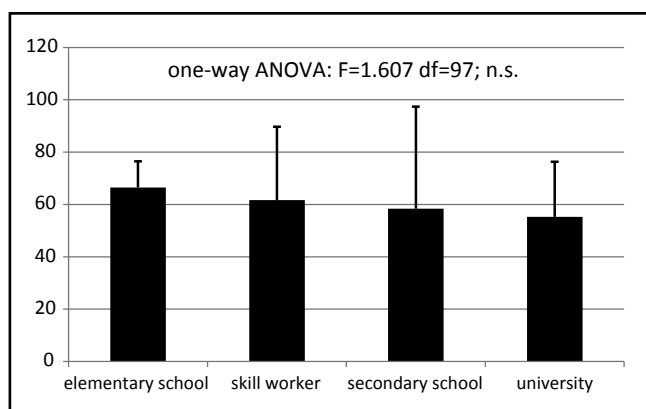


Fig. 2. Total ISMI scores according to the level of education.

Tab. 2. Self-stigma, adherence and discontinuation of medication in relation to heredity, gender and partnership.

	Rate of stigmatization (value±SD)	Statistics – group comparison	Treatment adherence (value±SD)	Statistics – group comparison	Frequency of discontinued medication	Statistics – group comparison
Patients with heredity	62.59±13.76	unpaired t-test: $t=1.885$ $df=96$; $p=0.0624$	2.71±4.01	unpaired t-test: $t=3.084$ $df=96$; $p<0.0027$	41.94	Fisher’s exact test: n.s.
Patients without heredity	56.98±15.33		5.26±4.14		27.78%	
Men	59.00±16.34	unpaired t-test: $t=0.2311$ $df=96$; n.s.	3.63±3.82	unpaired t-test: $t=0.7879$ $df=96$; n.s.	34.38%	Fisher’s exact test: n.s.
Women	59.74±14.18		4.35±4.46		25.76%	
With a partner	58.38±14.98	unpaired t-test: $t=1.141$ $df=88$; n.s.	4.18±4.13	unpaired t-test: $t=0.098$ $df=88$; n.s.	28.6%	Fisher’s exact test: n.s.
Without a partner	62.09±14.96		4.27±3.87		35.3%	

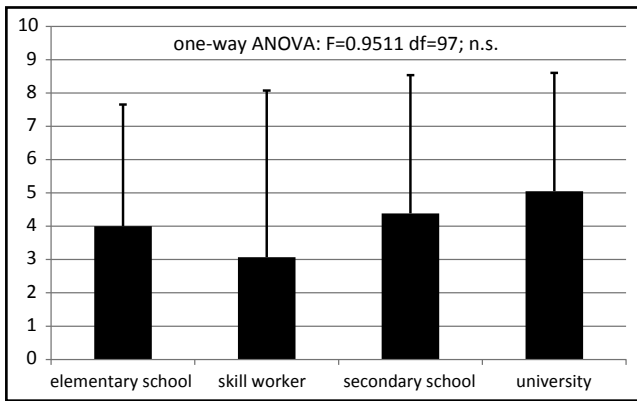


Fig. 3. DAI-10 according to the level of education.

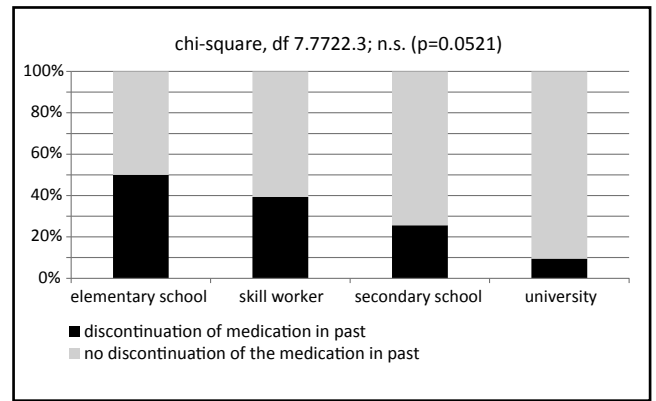


Fig. 4. Medication discontinuation in the past and education.

Tab. 3. Self-stigma, adherence and CGI in relation to discontinuation of medication in the past.

	Rate of stigmatization	Statistics - group comparison	Treatment adherence	Statistics - group comparison	CGI-O	Statistics - group comparison	CGI-S	Statistics - group comparison
Patients who discontinued	65.82±12.98	unpaired t-test, t=2.756 df=96; p<0.01	4.18±4.13	unpaired t-test t=0.098 df=88; n.s	2.69±1.29	Mann-Whitney test: n.s.	3.20±1.6	Mann-Whitney test: n.s.
Patients who did not discontinue	56.97±12.98		4.27±3.87		2.82±1.36		3.64 ±1.28	

The patients who discontinued their drugs in the past showed a higher level of self-stigma (Figure 5).

There was no statistically significant difference in the current level of adherence between the group of patients who discontinued medication and those who did not. Moreover, when comparing the current severity of the disorder measured by both objective and subjective CGI, there were no statistically significant differences between the two groups (Table 3).

Correlation between self-stigma rates and demographic and clinical data. Self-stigma rates did not

correlate significantly with age, age of onset of the disease, or the time elapsed since the last hospitalization. However, there were statistically significant positive correlations between self-stigma rates and the severity of the disorder as measured by subjective (Spearman $r=0.4687$, $p<0.0001$) and objective CGI (Spearman $r=0.5156$, $p<0.0001$), number of previous hospitalizations (Spearman $r=0.4466$, $p<0.0001$), number of different outpatient psychiatrists visited (Spearman $r=0.1995$, $p<0.05$), discontinuation of medication in the past by one's own will (Spearman $r=0.2859$, $p<0.005$), and the dose of antidepressants (Spearman $r=0.2532$, $p<0.05$).

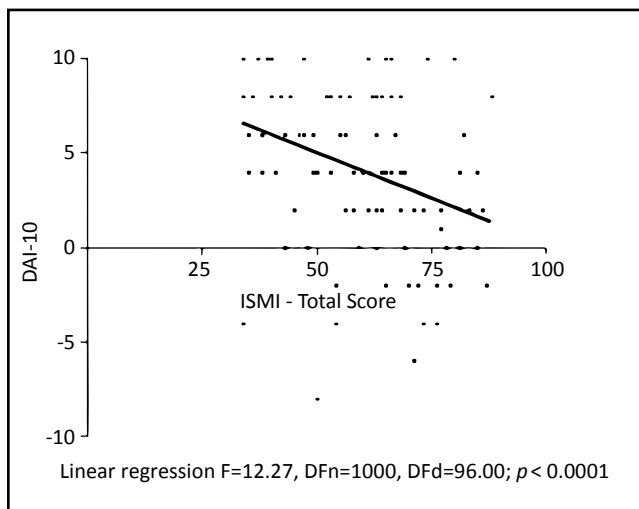


Fig. 5. Self-stigma and discontinuation of medication in the past.

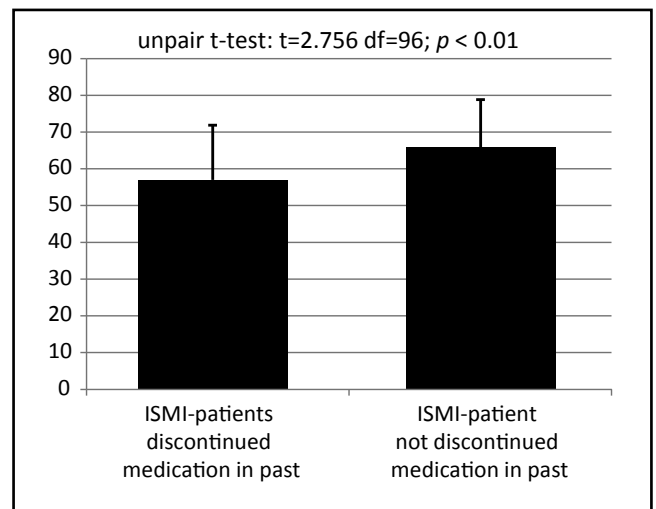


Fig. 6. Linear regression between total ISMI scores and adherence.

Self-stigma was significantly correlated with the current treatment adherence (Pearson $r=-0.3366$, $p<0.001$). This means that higher rates of self-stigma were associated with lower treatment adherence (Figure 6).

Correlation of the current rate of adherence with demographic and clinical data. The rate of adherence was significantly negatively correlated with subjective CGI (Spearman $r=-0.2855$, $p<0.005$) and objective CGI scores (Spearman $r=-0.2724$, $p<0.005$). However, it did not correlate with age, age of onset of illness, duration of the illness, number of hospitalizations, number of psychiatrists visited, or the doses of medication.

Results of stepwise regression analysis

If the rate of self-stigma was identified as a dependent variable and independent variables were DAI-10, objective CGI, heredity, employment, education (primary, secondary and tertiary), marital status (with / without partner), age, gender, discontinuing or not discontinuing medication in the past, successive steps of stepwise regression identified two most significant independent factors – DAI-10 and objective CGI. These factors explained 27% of the self-stigma variance ($p<0.0001$).

When adherence was set as a dependent variable and ISMI, heredity, objective CGI, education, gender, marital status, discontinuation of medication in the past, age, and occupation were independent variables entering the regression, the stepwise analysis identified two most significant independent factors – ISMI and family psychiatric burden. These explained 16.4% of the variance of adherence ($p<0.0001$). A family history of psychiatric illness as a single independent variable explained 9% of the variance of adherence ($p<0.005$).

DISCUSSION

The study evaluated relationships between self-stigma, treatment adherence, discontinuation of medication in the past by patients' own decision, and demographic and clinical data.

In the first analysis, a relationship between self-stigma and demographic data was evaluated. The findings showed that gender played no role in the negative perception of self as a psychiatric patient. Similarly, there was no relationship with the educational level and presence or absence of a partner. These findings do not correspond with the results of other studies. In a study by Girma *et al.* (2013), there was a significantly higher self-stigma rate in women than in men and the rate of self-stigma decreased with increasing levels of education. On the other hand, Yen *et al.* (2005) did not confirm the relationship between gender, age and self-stigma. Mosanya *et al.* (2014) found an inverse relationship between the level of education and the degree of self-stigma. This could be due to different rating scales in self-stigma, but also by different socio-economic and cultural factors. Our findings are compatible with

a systematic review and meta-analysis of 127 articles focused on stigma and self-stigma mostly in developed countries⁴ which found no significant relationship between demographic factors and self-stigma.

In the present study, self-stigma rates were statistically different between patients who had discontinued medication in the past and those who had not. It may be concluded that the higher level of self-stigma is associated with less willingness to use psychotropic drugs as this may be understood as confirmation of the mental disorder and of being different. The correlation analysis showed no relationship between self-stigma and demographic factors like the patient's age and the age of onset of the disorder. But the level of self-stigma is related to current adherence to treatment, the subjective evaluation of the current severity of the disorder and the objective clinical impression. In their study of inpatients, Ociskova *et al.* (2014) identified a statistically significant relationship between the degree of anxiety symptoms and self-stigma. The exact causal relationship between the rate of self-stigma and the severity of anxiety symptoms could not be obtained. We also found higher levels of self-stigma in patients with higher doses of antidepressants, higher numbers of hospitalizations and more severe disorders. The explanation may be as follows: if the patient is severely ill, he/she usually uses higher doses of antidepressants and is more frequently hospitalized. All these factors can lead to higher rates of self-stigma. On the other hand, higher self-stigma rates at the beginning of the treatment may contribute to a smaller effect of pharmacotherapy. High levels of self-stigmatization also correlated with a higher number of changed outpatient psychiatrists. Patients with high self-stigmatization may be more sensitive to possible negative reactions from psychiatrists or may expect more such reactions. An important question is whether the self-stigma rate is stable over time, and the variance depends on the compensation of mental health. These questions, however, could not be answered by our cross-sectional study.

In the present study, current treatment adherence was not associated with gender, age, duration of the disorder, number of hospitalizations, number of visited psychiatrist, doses of medication, education (although there was a statistical trend), or presence of a relationship. This is in contrast with findings by other authors. In a study of patients suffering from panic disorder by Grilo *et al.* (1998), an effect of education on adherence was discovered. Patients with lower education were less adherent. Conversely, Santana *et al.* (2010) found that OCD patients with lower education stayed longer in therapy. The differences between our results and the results of these studies can be explained by the strict focus on a particular diagnostic group and the use of other assessment tools. However, the small numbers of subjects in all these studies may distort the results.

In the present study, the significant correlation between adherence and self-stigma was found by both

correlation analysis and stepwise regression. These findings are consistent with results of Sirey *et al.* (2001) who examined adherence to antidepressants treatment in depressed patients and found lower perceived stigma and lower internalized stigma to be better predictors of adherence. Matas *et al.* (1992) demonstrated better adherence in patients living in a relationship. In our study, the correlation between adherence and relationship was not present. The difference can be explained by a different study population. While Matas *et al.* (1992) studied also patients with schizophrenia and bipolar disorder, our study focused only on neurotic patients.

On the other hand, the severity of self-stigma and current treatment adherence did not differ in patients who had previously discontinued medication and those who had not. However, current adherence rates correlated negatively with the subjective and objective evaluation of disorder severity. According to Ociskova *et al.* (2014), there was a significant negative correlation between subjective and objective measure of the improvement in the treatment and self-stigma rate at the beginning of the treatment.

There was no difference in discontinuation of medication between men and women. According to our data, the trend to discontinue medication was less frequently observed in patients with higher education. It also seems that having a stable relationship may not protect against it. In their meta-analysis, Taylor *et al.* (2012) found that only about half of patients with anxiety disorders completed treatment without discontinuation of medication. The highest proportion of discontinuation was due to prejudices in the family environment, low motivation to treat the patient and the presence of personality disorder. Discontinuation of medication in the past in our group was not associated with the current severity of the disorder or current treatment adherence. Conversely, Grilo *et al.* (1998) found that patients with higher perceived severity of anxiety interrupted therapy more often. Results reported by Toni *et al.* (2004) showed opposite results, with higher frequency of interruption of treatment with antidepressants being associated with a lower severity of panic disorder.

Limitations of the study

One of the limitations of the study is the use of self-administered questionnaires. Over 18% of patients did not fill out the questionnaire or they filled it out incompletely and thus information on their degree of self-stigma, adherence, and discontinuation of drugs in the past was inadequate and could not be calculated. Despite the fact that demographic or clinical data of the patients who dropped out of the study did not differ from those of participants who fully cooperated in the study, it may be just a subset of patients who have significant problems with adherence and discontinuation of medication.

Another limitation of the study appears to be the number of diagnoses, with the disorders being represented unevenly. The study also did not take into account the diversity of medication. Important limitations are the small size of the group and the absence of a standard diagnostic interview.

The results are cross-sectional and cannot capture possible changes in the dynamics of mental health. There is no information on stability of self-stigma in time where adherence may vary within the changes of the patients' condition.

CONCLUSION

Adherence to treatment has become a repeatedly mentioned factor of the treatment success. Adherence may be increased through motivation, proper instructions to patients about the necessity of compliance with the recommended treatment regimen, and explaining the consequences of the non-adherent behavior. Important factors influencing the adherence seem to be stigma and self-stigma. Self-stigmatization was negatively correlated with the degree of adherence and was lower in patients living in a relationship, less frequently hospitalized patients, those receiving lower doses of antidepressants, and those with a lower number of changed psychiatrists. If these results are confirmed by further studies, increased adherence may be an important strategy for reducing self-stigma. This can be done using systematic psychoeducation of patients or within the psychotherapeutic management.

REFERENCES

- 1 Barney LJ, Griffiths KM, Christensen H, Jorm AF (2009). Exploring the nature of stigmatising beliefs about depression and help-seeking: implications for reducing stigma. *BMC Public Health*. **9**: 61.
- 2 Boyd JE, Adler EP, Otilingam PG, Peters T (2014). Internalized Stigma of Mental Illness (ISMI) Scale: a multinational review. *Compr Psychiatry*. **55**(1): 221–231.
- 3 Brook OH, van Hout HPJ, Nieuwenhuysea H, de Haan M (2003). Effects of coaching by community pharmacists on psychological symptoms of antidepressant users; a randomised controlled trial. *European Neuropsychopharmacology*. **13** (5): 334–354.
- 4 Bulloch AGM, Patten SB (2010). Non-adherence with psychotropic medications in the general population. *Soc Psychiatry Psychiatr Epidemiol*. **45**(1): 47–56.
- 5 Camp DL, Finlay WML, Lyons E (2011). Is low self-esteem an inevitable consequence of stigma? An example from women with chronic mental health problems. *Social Science & Medicine*. **55**: 823–834
- 6 Corrigan PW, Rafacz J, Rüsche N (2011). Examining a progressive model of self-stigma and its impact on people with serious mental illness. *Psychiatry Res*. **189**(3): 339–343.
- 7 EMEA, 2002: <http://www.ema.europa.eu/pdfs/human/ich/013595en.pdf>. 20.3.2009
- 8 Fung KMT, Tsang HWH, Corrigan PW (2008). Self-stigma of people with schizophrenia as predictor of their adherence to psychosocial treatment. *Psychiatric Rehabilitation Journal*. **32**: 485–495.

- 9 Gilmer TP, Dolder CR, Lacro JP, Folsom DP, Lindamer L, Garcia P, Jeste DV (2004). Adherence to treatment with antipsychotic medication and health care costs among Medicaid beneficiaries with schizophrenia. *Am J Psychiatry*. **161**: 692–699.
- 10 Girma E, Tesfaye M, Froeschl G, Möller-Leimkühler AM, Dehning S, Müller N (2013). Facility based cross-sectional study of self stigma among people with mental illness: towards patient empowerment approach. *Int J Ment Health Syst*. **7**(1): 21. doi: 10.1186/1752-4458-7-21.
- 11 Grilo CM, Money R, Barlow DH, oddard AW, Gorman JM, Hofmann SG, Papp LA, Shear MK, Woods SW (1998). Pretreatment patient factors predicting attrition from a multicenter randomized controlled treatment study for panic disorder. *Compr Psychiatry*. **39**(6): 323–332.
- 12 Guy W (1978) ECDEU Assessment Manual for Psychopharmacology. Rockville, U.S. DHEW.
- 13 Livingston JD, Boyd JE (2010). Correlates and consequences of internalized stigma for people living with mental illness: a systematic review and meta-analysis. *Social Science & Medicine*. **71**: 2150–2161.
- 14 Lysaker PH, Roe D, Yanos PT (2007). Toward understanding the insight paradox: internalized stigma moderates the association between insight and social functioning, hope, and self-esteem among people with schizophrenia spectrum disorders. *Schizophr Bull*. **33**(1): 192–199.
- 15 Matas M, Staley D, Griffin W (1992). A profile of the noncompliant patient: a thirty-month review of outpatient psychiatry referrals. *General Hospital Psychiatry*. **14**: 124–130.
- 16 Mezinárodní klasifikace nemocí – 10. revize (1996) MKN-10; Maxdorf Praha.
- 17 Ocisková M, Praško J, Kamarádová D, Látalová K, Kurfürst P, Dostálová L, Cinculová A, Kubínek R, Mainerová B, Vrbová K, Ticháčková A (2014). Self-stigma in psychiatric patients--standardization of the ISMI scale. *Neuro Endocrinol Lett*. **35**(7): 624–632.
- 18 Ociskova M, Prasko J, Kamaradova D, Grambal A, Latalova K, Sigmundova Z (2014). Relationship between internalized stigma and treatment efficacy in mixed neurotic spectrum and depressive disorders. *Neuro Endocrinol Lett*. **35**(8): 711–717.
- 19 Padurariu M, Ciobica A, Persson C, Stefanescu C (2011). Self-stigma in psychiatry: ethical and bio-psycho-social perspectives. *Romanian Journal of Bioethics*. **9**(1): 76–82.
- 20 Santana L, Versiani M, Mendlowicz MV, Fontenelle LF (2010). Predictors of adherence among patients with obsessive-compulsive disorder undergoing naturalistic pharmacotherapy. *J Clin Psychopharmacol*. **30**(1): 86–88.
- 21 Sirey JA, Bruce ML, Alexopoulos GS, Perlick DA, Raue P, Friedman SJ, Meyers BS (2001). Perceived stigma as a predictor of treatment discontinuation in young and older outpatients with depression. *Am J Psychiatry*. **158**: 479–481.
- 22 Tay SE (2007). Compliance therapy: an intervention to improve inpatients' attitudes toward treatment. *J Psychosoc Nurs Ment Health Serv*. **45**(6): 29–37.
- 23 Taylor S, Abramowitz JS, McKay D (2012). Non-adherence and non-response in the treatment of anxiety disorders. *J Anxiety Disord*. **26**(5): 583–589.
- 24 Mosanya TJ, Adelufosi AO, Adebowale OT, Ogunwale A, Adebayo OK (2014). Self-stigma, quality of life and schizophrenia: An outpatient clinic survey in Nigeria. *Int J Soc Psychiatry*. **60**(4): 377–386.
- 25 Toni C, Perugi G, Frare F, Mata B, Akiskal HS (2004). Spontaneous treatment discontinuation in panic disorder patients treated with antidepressants. *Acta Psychiatr Scand*. **110**(2): 130–137.
- 26 Tsang HW, Fung KM, Chung RC (2010). Self-stigma and stages of change as predictors of treatment adherence of individuals with schizophrenia. *Psychiatry Res*. **180**(1): 10–15.
- 27 Ustündağ MF, Kesebir S (2013). Internalized stigmatization in bipolar patients: relationship with clinical properties, quality of life and treatment compliance. *Turk Psikiyatri Derg*. **24**(4): 231–239.
- 28 Vermeire E, Hearnshaw H, Van Royen P, Denekens J (2001). Patient adherence to treatment: three decades of research. A comprehensive review. *J Clin Pharm Ther*. **26**(5): 331–342.
- 29 Yen CF, Chen CC, Lee Y, Tang TC, Yen JY, Ko CH (2005). Self-stigma and its correlates among outpatients with depressive disorders. *Psychiatric Services*., doi: 10.1176/appi.ps.56.5.599