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Patient versus rater evaluation of symptom severity in treatment resistant schizophrenia receiving clozapine

Jianmeng Song[a], Carol Borlido[a], Vincenzo De Luca[a,b], Leah Burton[a], Gary Remington[a,b,*]

[a] Schizophrenia Division, Centre for Addiction and Mental Health, Toronto, ON, Canada
[b] Department of Psychiatry, University of Toronto, Toronto, ON, Canada

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ABSTRACT

Patient input as part of health care has taken on increased importance recently. To look at whether patients with treatment resistant schizophrenia (TRS) are able to provide a valid self-assessment of symptoms, the present study investigated patient versus rater evaluation of clinical symptoms. Ninety-three patients diagnosed with TRS and treated with clozapine were recruited. Both patients and raters completed the 7-point Clinical Global Impression – Schizophrenia Version (CGI-SCH) scale, thereby providing evaluations for positive, negative, depressive, and cognitive symptoms as well as overall illness severity. Patients rated their clinical symptoms significantly lower than raters. A positive correlation was found between patients and raters for all symptom domains, while the strength of correlation varied. Age, gender and years of education did not impact the relationship between patient and rater scores. The conclusion is that patients provided valid information in self-assessments of symptoms when compared to raters, and this was consistent over time. In addition, the greatest heterogeneity between rater and patient ratings occurred with regard to cognitive symptoms. Patient assessments may help further engage individuals in their care and permit clinicians to identify where discrepancies exist. Addressing these issues offers opportunities for improved therapeutic alliance, education, and shared decision-making within treatment.

1. Introduction

In medicine, including psychiatry, there is increased interest regarding engagement of patients in their own care (Hamann et al., 2008; Johansson and Eklund, 2003; McCabe et al., 2013; Jo Anne et al., 2001; Angermeyer et al., 2001; Strupp and Hadley, 1977); this includes not only treatment options but also knowledge of the illness (Estroff, 1989). With disorders such as schizophrenia, though, where psychosis represents a core domain, there are obvious concerns with such an approach given the lack of insight that can be observed in conjunction with these symptoms (Amador et al., 1993).

It remains, however, that thinking regarding this topic has shifted over the years. The literature related to self-experience, at least historically, focused largely on narrative descriptions of the experience (Davidson and Strauss, 1992) and the negative impact of illness on self-concept (Thompson, 1988). More recently, it has been proposed that patients' perceptions of symptoms are important in their own right (Flanagan et al., 2010). However, doubt remains as to whether patients with schizophrenia are capable of providing valid self-assessments with regard to their illness (Bobes et al., 2005).

To this last point, more recent evidence would suggest otherwise. A variety of studies have focused on self-assessment and patient involvement as important variables when discussing treatment optimization and personal well-being (Levander et al., 2007; Karow and Pajonk, 2006; Gould et al., 2015). For example, a 5-year study assessing antipsychotic treatment concluded that more active patient involvement in monitoring their own treatment (e.g., structured patient, as well as clinician, rating scales) can prove beneficial in both clinical decision-making and treatment adherence (Levander et al., 2007). Other work has shown that self-assessments predict subjective quality of life (Karow and Pajonk, 2006), as well as objective real life functioning (Gould et al., 2015). Arguably, this is not the same, though, as evaluation of specific symptoms.

Regarding symptoms, previous research by our group has suggested a middle ground in this regard. Specifically, clinician and patient symptom ratings demonstrated moderate overlap, leading to the conclusion that patient-reported outcomes provide complimentary, but not redundant, information related to clinical status (Fervaha et al., 2015). Notably, the population for this study was drawn from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE)

* Corresponding author at: University of Toronto, 250 College St., Toronto, ON M5T 1R8, Canada.
E-mail address: gary.remington@camh.ca (G. Remington).

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schizophrenia study (Lieberman et al., 2005).

As an academic tertiary care psychiatric setting, these findings beg the question of whether the same results would also hold true in a more selective population, specifically those with treatment-resistant schizophrenia (TRS). With a clozapine clinic that follows over 700 such patients, this question had significant clinical relevance. More specifically, this population represents the most ill population, in particular from the standpoint of positive symptoms. One might therefore assume that in this group there would be substantial differences between patient and rater. This said, if the information is complimentary, it could prove valuable in better engaging this population through a more informed understanding of their perceptions regarding treatment response. Accordingly, this study set out to a) assess a population meeting criteria for TRS and treated with clozapine; b) evaluate different symptom domains; and c) evaluate a limited number of variables that might possibly impact ratings, in this case age, gender, and years of education.

2. Methods

2.1. Setting

This study was carried out at the Centre for Addiction and Mental Health (CAMH), an urban tertiary care psychiatric centre associated with the University of Toronto. The Schizophrenia Division has as part of its infrastructure a clozapine clinic serving those with TRS. At any given time, approximately 700–750 individuals are being monitored as they start or are maintained on clozapine.

2.2. Participants

The present data were collected as part of an externally funded grant evaluating clozapine therapeutic drug monitoring. Participants met the following inclusion criteria: age 18 or older; a confirmed diagnosis of TRS (Lee et al., 2015); clozapine monotherapy; administration for a minimum of 3 months, and stable clozapine dose for at least 1 week. Exclusion criteria included: depot antipsychotic or electroconvulsive therapy within 3 months. Participants were all registered at CAMH and recruited either through our outpatient schizophrenia clinics, research registry, clinician or research staff referrals, or locally distributed flyers.

This study evaluating clozapine therapeutic drug monitoring was approved by the local research ethics board at CAMH, and all participants provided written informed consent.

2.3. Instruments and procedures

The primary outcome measure, the Clinical Global Impression scale – Schizophrenia Version (CGI-SCH) (Haro et al., 2003), was used for the purpose of clinical assessment. It incorporates 5 domains related to schizophrenia symptoms: positive, negative, depressive, cognitive, and overall severity. A user's guide accompanying the scale provides anchor points for scale items. CGI-SCH ratings from raters drew upon other scales being used as part of assessments, including the Brief Psychiatric Rating Scale – Anchored (BPRS-A; Woerner et al., 1988) which assesses various symptoms, both psychotic and not psychotic, as well as the Brief Neurocognitive Assessment (BNA; Fervaha et al., 2015), used to measure patients' global neurocognitive impairment. CGI-SCH ratings were also formulated based on a medical chart review of current symptoms. Scores involve a 7-point rating: 1 = normal, not at all ill; 2 = borderline mentally ill; 3 = mildly ill; 4 = moderately ill; 5 = markedly ill; 6 = severely ill; and 7 = very severely ill. A self-report version of this same scale was used for subjective ratings; patients were instructed to report their perceived severity of illness for each of the 5 symptoms domains on the same 7-point scale after each item was explained by the raters. Specifically, the raters explained the definition of each item according to the user's guide. Raters were permitted to rephrase symptom terminology according to patients' own description of their illness. Unlike raters, patients were prompted to rate the symptoms based on their own perception without access to clinical scales or medical records.

Five raters as three sets received inter-rater training before conducting interviews independently. During the final training meeting, interclass correlation (ICC) estimates and their 95% confidence intervals were calculated using SPSS statistical package version 24 (SPSS Inc, Chicago, IL) based on a mean-rating (k = 2 or 3), absolute-agreement, 2-way mixed-effects model. A high degree of reliability was found among the three sets; the ICC estimates were 0.90 (0.71–0.96), 0.96 (0.85–0.99), 0.92 (0.80–0.91), suggesting good inter-rater reliability (Koo and Li, 2016).

2.4. Statistical analysis

Statistical analyses were conducted using SPSS statistical package version 24 (SPSS Inc, Chicago, IL). Internal consistency of the CGI-SCH patient version was calculated using reliability analysis. Spearman's correlation coefficients were calculated to evaluate the convergent validity between CGI-SCH and BPRS-A, the correlation between age and CGI-SCH, the relationship between rater and patient ratings for the CGI-SCH, and the correlation between CGI-SCH cognitive symptoms and BNA global standardized scores. Wilcoxon signed rank tests examined differences between rater and patient ratings on the CGI-SCH and rating differences across baseline and last observation. Independent sample t tests were used to compare group differences related to gender, and education; each of these variables has been linked to illness insight (Cobo et al., 2016; Cernovsky et al., 1994; Gerretsen et al., 2014).

3. Results

3.1. Demographics

A summary of demographic and clinical variables is shown in Table 1. Ninety-three patients consented to participate in the study (M (age) = 43.04, SD = 13.09), with one failing to complete the interview. Most patients received clozapine monotherapy and had at least three months' exposure (six were on a second antipsychotic at baseline and one had been on clozapine for less than 3 months). All patients completed at least one visit, while 69 completed two visits, and 56 completed all three visits. Visit one was designated as the baseline visit, while the final visit for each patient represented last observation. The average length between baseline visit and last observation was 121.78 days (SD = 40.51 days).

3.2. Reliability and validity of CGI-SCH patient version

3.2.1. Internal consistency

Only internal consistency at baseline was calculated for CGI-SCH rater and patient versions. Both scales showed high internal consistency (Cronbach's α (rater) = 0.754, Cronbach's α (patient) = 0.845). The CGI-SCH rater version has been validated by Haro et al. (2003), and the high internal consistency of the CGI-SCH patient compared to CGI-SCH rater version confirmed validity of this measure; this supports use of a patient-rating scale to measure patients' perception of symptom severity.

3.2.2. Convergent validity with BPRS-A

Spearman's rho was calculated between CGI-SCH and BPRS-A total score for both rater and patient version at baseline and last observation. Results showed that BPRS-A, as a validated measurement of schizophrenia symptoms, is significantly correlated with both versions of CGI-SCH, while the strength varied (Table 2). Specifically, the correlation between CGI-SCH item 5 – Overall Severity and BPRS-A total score is

Table 1
Patient demographics and clinical characteristics during the baseline visit.

Categories	*N* or Mean (± SD or%)
Gender	
Male	66 (71.7%)
Female	26 (28.3%)
Age (years)	43.04 (± 13.09)
Minimum	21
Maximum	72
Education (years)	12.88(± 3.24)
Minimum	4
Maximum	22
Diagnosis	
Schizophrenia	71 (77.4%)
Schizoaffective	21 (22.6%)
Clozapine dose (mg/day)	379.62(± 146.147)
Minimum	75
Maximum	900
Clozapine levels	
Clozapine level in blood (nmol/L)	1586.41 (range 210–4795)
Norclozapine level in blood (nmol/L)	996.9 (range 200–2344)
Clozapine & Norclozapine level in blood (nmol/L)	2605.53 (range 427–7139)
Average length of clozapine monotherapy (year)	8.7 (± 7.1)
Maximum	26.2
Minimum	0.2
Self-reported clozapine adherence in the past seven days	
100%	86 (93.5%)
75%	6 (6.5%)
50%	0
≤ 25%	0
Using other psychotropic medication	51 (55.4%)
BPRS	35.32(± 8.66)
Minimum	20
Maximum	58
BPRS factor scores	
Reality distortion	10.39 (± 5.25)
Negative symptoms	4.35 (± 1.74)
Disorganization	5.5 (± 2.6)
Anxiety/depression	6.72 (± 2.87)
Average duration between baseline and the last observation (days)	121.78(± 40.51)
Maximum	286
Minimum	57

Table 2
Convergent validity of rater and patient CGI-SCH relating to BPRS-A.

Symptom domains	Baseline Rater	Baseline Patient	Last observation Rater	Last observation Patient
Positive	0.784 **	0.635**	0.710**	0.622**
Negative	0.515**	0.437**	0.501**	0.594**
Depressive	0.543**	0.581**	0.525**	0.493**
Cognitive	0.316**	0.453**	0.392**	0.590**
Overall severity	0.762**	0.564**	0.707**	0.628**

*Note:***Correlation is significant at the 0.01 level (2-tailed).

strong for rater version versus moderate for patient version (Table 3). Overall, the CGI-SCH patient version has good convergent validity related to BPRS.

3.3. Comparison between rater and patient Ratings: CGI-SCH

At baseline, there was a significant difference between rater and patient scores for positive ($z = -4.975$, $p = 0.000$), negative ($z = -4.047$, $p = 0.000$), and cognitive symptoms ($z = -4.074$, $p = 0.000$), in addition to overall severity ($z = -5.279$, $p = 0.000$) (Table 3). More specifically, raters reported higher scores than patients, at baseline as well as last observation (Table 3), significantly so on the following measures: positive symptoms ($z = -2.691$, $p = 0.007$), negative symptoms ($z = -3.235$, $p = 0.001$), and overall severity ($z = -3.026$, $p = 0.002$).

This said, rater and patient evaluations for each measure were significantly and positively correlated at both baseline and last observation (Table 3).

Table 3
Wilcoxon signed rank test and Spearman's correlation evaluating the relationship between rater and patient CGI-SCH scores.

Symptom domains	Rater *M*	Rater SD	Patients *M*	Patients SD	*z*	*Sig.(2-tailed)*	*Correlation*
Baseline							
Positive	3.48	1.641	2.70	1.608	−4.975	0.000*	0.744**
Negative	3.17	1.228	2.47	1.438	−4.047	0.000*	0.375**
Depressive	2.17	1.192	2.26	1.385	−0.988	0.323	0.853**
Cognitive	3.40	1.367	2.65	1.486	−4.074	0.000*	0.313**
Overall Severity	3.78	1.209	2.83	1.374	−5.279	0.000*	0.506**
Last observation							
Positive	3.32	1.597	2.87	1.946	−2.691	0.007*	0.797**
Negative	3.07	1.375	2.47	1.588	−3.235	0.001*	0.547**
Depressive	2.35	1.194	2.26	1.492	−0.810	0.418	0.793**
Cognitive	3.06	1.314	2.60	1.437	−2.103	0.036	0.269***
Overall severity	3.46	1.159	3.01	1.532	−3.026	0.002*	0.669**

Notes: **p* value ≤ 0.025 **Correlation is significant at the 0.01 level (2-tailed) ***Correlation is significant at the 0.05 level (2-tailed).

3.4. Comparison between baseline and last observation: CGI-SCH

The paired sample *t*-test indicated that raters' evaluation of cognitive symptoms ($z = -2.831$, $p = 0.005$) was significantly different between baseline and last observation. In contrast, evaluation of all clinical symptoms and outcomes was stable from the patients' perspective i.e., no significant differences between baseline and last observation.

3.5. Comparison between age, gender, and CGI-SCH items

3.5.1. Age

To better understand the possible impact of age, Spearman's rho was calculated to examine the correlation between CGI-SCH items and patient age. Results indicated that age is significantly, but weakly, correlated with raters' scores on the following CGI-SCH items: negative symptoms and overall severity at baseline, as well as depressive symptoms and cognitive symptoms at both baseline and endpoint. On the other hand, patient age was only significantly correlated with patients' rating for depressive symptoms at baseline; no significant correlation was found for other patient rated CGI-SCH items (Table 4).

3.5.2. Gender

Based on results of an independent group *t*-test, males and females did not differ on any of the CGI-SCH scores, either from rater or patient

Table 4
Spearman's correlation results: Rater versus Patient CGI-SCH scores as a function of age.

Symptom domains	Baseline Rater	Baseline Patient	Last observation Rater	Last observation Patient
Positive	0.146	0.097	0.167	0.119
Negative	0.238*	0.105	0.206	0.081
Depressive	0.252*	0.249*	0.257*	0.229
Cognitive	0.358*	0.175	0.351**	0.220
Overall Severity	0.320**	0.125	0.202	0.084

Notes: *Correlation is significant at the 0.05 level (2-tailed). **Correlation is significant at the 0.01 level (2-tailed).

Table 5
Spearman's rho evaluating the Correlation between CGI-SCH Cognitive Symptoms and BNA.

Symptom domains	Baseline Rater	Patient	Last observation Rater	Patient
Cognitive	−0.685**	−0.058	−0.791**	−0.136

Note: **Correlation is significant at the 0.01 level (2-tailed).

perspective.

3.6. Effect of age and years of education on CGI-SCH score differences (Raters vs. Patients)

Before analyzing the regression analysis, scores were corrected to represent the score difference between raters and patients; this was done by using the raters' rating minus the patients' rating of the same items. A single linear regression was calculated to predict score differences based on years of education and age, respectively. Results indicated that years of education and age did not influence the agreement of each CGI-SCH item between raters and patients.

3.7. Correlation between CGI-SCH – cognitive symptoms and BNA

Spearman's rho was calculated to test the correlation between CGI-SCH item 4 – cognitive symptoms and BNA global cognition score, which was standardized according to specific age ranges (Table 5). Results indicated that while raters' scoring of cognitive symptoms was strongly correlated with BNA standardized scores, this was not the case for patients' rating.

4. Discussion

The purpose of this study was to assess rater versus patient ratings of clinical symptoms in a specific population, specifically patients with TRS treated with clozapine. We were interested in symptom domains beyond psychosis, as well as variables that might impact ratings (in this case age, gender, and years of education).

Our results indicated that patients often rate their own symptoms lower on clinical scales, in line with earlier work by our group (Fervaha et al., 2014). Indeed, patients' ratings were significantly lower compared to raters' during both baseline and final visit for positive and negative symptoms, as well as overall severity. Patient ratings with regard to cognitive symptoms were significantly lower than raters only at the baseline visit. It must also be noted, though, that self-ratings positively correlated with raters' evaluations. This was particularly true for depressive symptoms, where the difference with raters was non-significant, suggesting patients might better understand this domain. Notably, positive symptoms also showed a strong correlation between raters and patients, while negative symptoms showed a modest but significant correlation. In contrast, the relationship for cognitive symptoms was weak, with patients underestimating the extent of deficits.

There may be several explanations for this last finding. It is possible, for example, that individuals with schizophrenia have less insight regarding cognitive symptoms than other features of the illness, such as positive symptoms (Medalia and Thysen, 2010). It may also be the case that more attention has been given to the positive and negative symptoms; many clinicians do not formally assess cognition on a routine basis. As a result, patients are not well informed about their neurocognitive symptoms and may be less aware of such deficits or how these manifest themselves. We are reminded that insight is multidimensional and may vary across domains (Konsztowicz et al., 2018). It is interesting that patients rated themselves as stable in terms of cognition across visits, while raters rated their cognitive symptoms, as well as overall severity, differently across visits. More specifically, raters reported both as improved across time. The stable ratings on the part of patients may reflect their adaptation to the illness; living with these symptoms daily, patients may come to see them as a 'normal' part of their day. Conversely, it is possible that perceived improvement noted by raters reflected, at least in part, increased comfort and disclosure on the part of patients over visits.

The present findings must also be viewed in the context of other reports assessing this issue. At least to some extent, they argue against the notion that individuals with schizophrenia lack the insight required to provide valid information through self-report (Bobes et al., 2005). Scores differed with the rater, at least for some domains, but this was more a function of severity. Generally speaking, scores between rater and patient were positively correlated; however, the strength of correlation varied between symptoms. The strong correlation with respect to positive symptoms aligned with other work in this area, although our findings contrasted somewhat with their finding of a lack of correlation for negative symptoms (Hamera et al., 1996). Instead, our findings demonstrated a modest, but significant, correlation; it is also worth pointing out that they employed the BPRS (Hamera et al., 1996). We do agree with their argument that patients may find it more difficult to self-rate negative symptoms due to the behavioral, versus experiential, nature of negative symptoms (Hamera et al., 1996). As with others, we too found that age and gender did not seem to impact scores (Bradshaw and Brekke, 1999). More globally, our results also align with previous work that individuals with schizophrenia are capable of appreciating their symptoms as well as their impact (Liddle and Barnes, 1988), and are capable of reliable self-reporting using a scale such as the CGI-SCH (Lindstrom et al., 2007).

There are limitations that warrant comments. First of all, patients' insight into illness was not collected as part of the study, which would have proved valuable in better understanding the precise nature of this relationship. Although the rater explained questions at the time of assessment, it is possible that patients varied in their understanding, thereby impacting responses. In addition, patients' everyday functioning was not measured as part of the study. Going forward, it would be useful to investigate rater versus patient evaluations of functioning and the relationship, if any, to specific symptom ratings. The assessment tool used for self-report drew upon the CGI-SCH, which has advantages in terms of simplicity and ease of administration; however, reliability and validity data specific to the instrument used here are limited. Finally, our patient population was homogeneous in terms of meeting criteria for TRS, a strength of the investigation in one regard. At the same time, all patients were also receiving clozapine and this must also be taken into consideration. Clozapine is the only antipsychotic with an indication for use in this population (Remington et al., 2017), which could impact the present findings; arguably, these individuals represent a group that was being optimally treated. This may well be the case, with several caveats. First, we had access to results from clozapine therapeutic drug monitoring, and reported values indicate that at least a subgroup of these individuals had sub-therapeutic levels (see Table 1) (Remington et al., 2012). Further, reported scores for both the CGI-SCH and BPRS reported mean total scores that would place this population in the moderate range of illness despite clozapine treatment (Haro et al., 2003; Leucht et al., 2005).

In summary, the present findings support use of self-report measures in clinical assessments of individuals with schizophrenia; however, they also suggest heterogeneity across symptom domains. Going forward, it will be important to look at this more closely given that we now routinely conceptualize this illness as a disorder of multiple symptom domains. For example, the present study highlights cognition as a potential point of discrepancy, and further work should be sensitive to this issue. There is evidence that insight is heterogeneous across symptom domains (Medalia and Thysen, 2010), but whether the present findings reflect insight per se was not formally evaluated here. This line of investigation, though, takes on increased importance as psychiatry, and

medicine in general, give greater attention to the input of those being treated. Models of care have moved to greater education and shared decision-making, underscoring the importance of patient input (Alguera-Lara et al., 2017; Levander et al., 2007). Findings from the present study encourage the use of structured patient rating scales to involve patients in the education and treatment process.

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Declarations of interest

None

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2019.02.050.

References

Alguera-Lara, V., Dowsey, M.M., Ride, J., Kinder, S., Castle, D., 2017. Shared decision making in mental health: the importance for current clinical practice. Australas. Psychiatry 25 (6), 578–582.
Amador, X.F., Strauss, D.H., Yale, S.A., Flaum, M.M., Endicott, J., Gorman, J.M., 1993. Assessment of insight in psychosis. Am. J. Psychiatry 150 (6), 873–879.
Angermeyer, M.C., Loffler, W., Muller, P., Schulze, B., Priebe, S., 2001. Patients' and relatives' assessments of clozapine treatment. Psychol. Med. 31 (3), 509–517.
Bobes, J., Garcia-Portilla, P., Saiz, P.A., Bascaran, T., Bousono, M., 2005. Quality of life measures in schizophrenia. Eur. Psychiatry 20 (Suppl. 3), S313–S317.
Bradshaw, W., Brekke, J.S., 1999. Subjective experience in schizophrenia: factors influencing self-esteem, satisfaction with life, and subjective distress. Am. J. Orthopsychiatr. 69 (2), 254–260.
Cernovsky, Z.Z., Landmark, J., Helmes, E., 1994. Are schizophrenic symptoms different in patients with higher education? Psychol. Rep. 75 (3 Pt 2), 1552–1554.
Cobo, J., Nieto, L., Ochoa, S., Pousa, E., Usall, J., Banos, I., et al., 2016. Insight and gender in schizophrenia and other psychoses. Psychiatry Res. 243, 268–277.
Davidson, L., Strauss, J.S., 1992. Sense of self in recovery from severe mental illness. Br. J. Med. Psychol. 65 (2), 131–145.
Estroff, S.E., 1989. Self, identity, and subjective experiences of schizophrenia: in search of the subject. Schizophr. Bull. 15 (2), 189–196.
Fervaha, G., Hill, C., Agid, O., Takeuchi, H., Foussias, G., Siddiqui, I., et al., 2015. Examination of the validity of the Brief Neurocognitive Assessment (BNA) for schizophrenia. Schizophr. Res. 166 (1–3), 304–309.
Fervaha, G., Takeuchi, H., Agid, O., Lee, J., Foussias, G., Remington, G., 2014. Determinants of patient-rated and clinician-rated illness severity in schizophrenia. J. Clin. Psychiatry 924–930.
Flanagan, E.H., Davidson, L., Strauss, J.S., 2010. The need for patient-subjective data in the DSM and the ICD. Psychiatry 73 (4), 297–307.
Gerretsen, P., Plitman, E., Rajji, T.K., Graff-Guerrero, A., 2014. The effects of aging on insight into illness in schizophrenia: a review. Int. J. Geriatr. Psychiatry 29 (11), 1145–1161.
Gould, F., McGuire, L.S., Durand, D., Sabbag, S., Larrauri, C., Patterson, T.L., et al., 2015. Self-assessment in schizophrenia: accuracy of evaluation of cognition and everyday functioning. Neuropsychology 29 (5), 675–682.
Hamann, J., Mendel, R.T., Fink, B., Pfeiffer, H., Cohen, R., Kissling, W., 2008. Patients' and psychiatrists' perceptions of clinical decisions during schizophrenia treatment. J. Nerv. Ment. Dis. 196 (4), 329–332.
Hamera, E.K., Kraenzle Schneider, J., Potocky, M., Casebeer, M.A., 1996. Validity of self-administered symptom scales in clients with schizophrenia and schizoaffective disorders. Schizophr. Res. 19 (2–3), 213–219.
Haro, J.M., Kamath, S.A., Ochoa, S., Novick, D., Rele, K., Fargas, A., et al., 2003. The Clinical Global Impression-Schizophrenia scale: a simple instrument to measure the diversity of symptoms present in schizophrenia. Acta Psychiatr. Scand. 107 (s416), 16–23.
Sirey, J.A., Bruce, M.L., Alexopoulos, G.S., Perlick, D.A., Friedman, S.J., Meyers, B.S., 2001. Stigma as a barrier to recovery: perceived stigma and patient-rated severity of illness as predictors of antidepressant drug adherence. Psychiatr. Serv. 52 (12), 1615–1620.
Johansson, H., Eklund, M., 2003. Patients' opinion on what constitutes good psychiatric care. Scand. J. Caring Sci. 17 (4), 339–346.
Karow, A., Pajonk, F.G., 2006. Insight and quality of life in schizophrenia: recent findings and treatment implications. Curr. Opin. Psychiatry 19 (6), 637–641.
Konsztowicz, S., Schmitz, N., Lepage, M., 2018. Dimensions of insight in schizophrenia: exploratory factor analysis of items from multiple self- and interviewer-rated measures of insight. Schizophr. Res. 199, 319–325.
Koo, T.K., Li, M.Y., 2016. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J. Chiropr. Med. 15 (2), 155–163.
Lee, J., Takeuchi, H., Fervaha, G., Sin, G.L., Foussias, G., Agid, O., et al., 2015. Subtyping schizophrenia by treatment response: antipsychotic development and the central role of positive symptoms. Can. J. Psychiatry 60 (11), 515–522.
Leucht, S., Kane, J.M., Kissling, W., Hamann, J., Etschel, E., Engel, R., 2005. Clinical implications of Brief Psychiatric Rating Scale scores. Br. J. Psychiatry 187, 366–371.
Levander, S., Eberhard, J., Lindström, E., 2007. Clinical decision-making during 5 years of antipsychotic treatment. Acta Psychiatr. Scand. 116 (s435), 17–26.
Liddle, P.F., Barnes, T.R.E., 1988. The subjective experience of deficits in schizophrenia. Compr. Psychiatry 29 (2), 157–164.
Lieberman, J.A., Stroup, T.S., McEvoy, J.P., Swartz, M.S., Rosenheck, R.A., Perkins, D.O., et al., 2005. Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators, Effectiveness of antipsychotic drugs in schizophrenia. N. Engl. J. Med. 22 (353), 1209–1223.
Lindström, E., Eberhard, J., Levander, S., 2007. Five-year follow-up during antipsychotic treatment: efficacy, safety, functional and social outcome. Acta Psychiatr. Scand. 116 (s435), 5–16.
Medalia, A., Thysen, J., 2010. A comparison of insight into clinical symptoms versus insight into neuro-cognitive symptoms in schizophrenia. Schizophr. Res. 118 (1–3), 134–139.
McCabe, R., Khanom, H., Bailey, P., Priebe, S., 2013. Shared decision-making in ongoing outpatient psychiatric treatment. Patient Educ. Couns. 91 (3), 326–328.
Remington, G., Addington, D., Honer, W., Ismail, Z., Raedler, T., Teehan, M., 2017. Guidelines for the pharmacotherapy of schizophrenia in adults. Can. J. Psychiatry 62 (9), 604–616.
Remington, G., Agid, O., Foussias, G., Ferguson, L., McDonald, K., Powell, V., 2012. Clozapine and therapeutic drug monitoring: is there sufficient evidence for an upper threshold? Psychopharmacology (Berl.) 225 (3), 505–518.
Strupp, H.H., Hadley, S.W., 1977. A tripartite model of mental health and therapeutic outcomes: with special reference to negative effects in psychotherapy. Am. Psychol. 32 (3), 187–196.
Thompson, E.H., 1988. Variation in the self-concept of young adult chronic patients: chronicity reconsidered. Psychiatr. Serv. 39 (7), 771–775.
Woerner, M.G., Mannuzza, S., Kane, J.M., 1988. Anchoring the BPRS: an aid to improved reliability. Psychopharmacol. Bull. 24 (1), 112–117.