## Determinants of Patient-Rated and Clinician-Rated Illness Severity in Schizophrenia

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#### ABSTRACT

**Objective:** The contribution of specific symptoms on ratings of global illness severity in patients with schizophrenia is not well understood. The present study examined the clinical determinants of clinician and patient ratings of overall illness severity.

**Method:** This study included 1,010 patients with a *DSM-IV* diagnosis of schizophrenia who participated in the baseline visit of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study conducted between January 2001 and December 2004 and who had available symptom severity, side effect burden, cognition, and community functioning data. Both clinicians and patients completed the 7-point Clinical Global Impressions–Severity of Illness scale (CGI-S), the primary measure of interest in the present study. Symptoms were rated using the Positive and Negative Syndrome Scale and the Calgary Depression Scale for Schizophrenia, and functional status with the Quality of Life Scale. Neurocognition, insight, and medication-related side effects were also evaluated.

**Results:** Clinicians rated illness severity significantly higher than patients (P < .001). There was moderate overlap between CGI-S ratings made by clinicians and patients, with almost one third of patients showing substantial (ie, greater than 1 point) discrepancies with clinician ratings. Clinician-rated CGI-S scores were most strongly associated with positive symptoms, with additional independent contributions made by negative, disorganized, and depressive symptoms, as well as functional outcome (all *P* values < .01). Patient-rated CGI-S scores, on the other hand, were most closely related to depressive symptoms, with additional independent contributions made by positive and anxiety symptoms, clinical insight, and neurocognition (all *P* values < .01). Depressive symptoms were the strongest predictor of patient-rated CGI-S scores even in patients with good clinical insight (P < .001).

**Conclusions:** Patient and clinician views of overall illness severity are not necessarily interchangeable and differ in their clinical correlates. Taking these differences into account may enhance patient engagement in care and improve outcomes.

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The Clinical Global Impressions–Severity of Illness scale (CGI-S) is a widely used measure of illness severity in psychotic disorders,<sup>1,2</sup> often used in complement to other more comprehensive psychopathology rating scales such as the Brief Psychiatric Rating Scale (BPRS)<sup>3</sup> or the Positive and Negative Syndrome Scale (PANSS).<sup>4</sup> It is, though, CGI scores that are used as the benchmark for clinical utility.<sup>5–7</sup> Despite the widespread use of the CGI-S, the basis of severity ratings on this measure remains uncertain; more specifically, the differential contribution of specific symptoms to severity ratings on the CGI-S is relatively unknown.

Numerous studies have demonstrated that total scores derived from the BPRS or PANSS are highly correlated with CGI-S scores,<sup>5–11</sup> but only a few studies have examined the impact of specific symptom clusters on CGI-S ratings. One study using the BPRS found that positive, negative, and agitation symptoms were each independently related to CGI-S ratings, with depressive symptoms being unrelated to illness severity ratings.<sup>12</sup> Another study using the PANSS found positive and disorganized symptoms to be most highly associated with CGI-S scores, followed by more modest associations with negative and excitement symptoms, with anxiety/depressive symptoms having little to no association<sup>8</sup>; notably, this study examined only correlations and did not shed light on independent associations. Another study also found that CGI-S ratings were related to positive, disorganized, and negative symptoms, whereas only a small association was noted for depressive symptoms<sup>11</sup>; however, here, too, independent relationships were not delineated. Beyond the BPRS and PANSS, a few studies have examined the relationship between other domains of schizophrenia psychopathology and CGI-S ratings. For example, CGI-S ratings have been found to be related to clinical insight,<sup>13</sup> neurocognition,<sup>14</sup> and functional outcome,<sup>15</sup> to name a few. There has not, however, been an investigation that includes multiple indicators of psychopathology (eg, symptoms, cognition, functioning) and examines their independent explanatory power for predicting CGI-S scores.

The CGI-S is a clinician- (or observer-) rated instrument.<sup>1</sup> Given the increasing importance accorded patient-reported outcomes in schizophrenia research,<sup>16</sup> it is imperative that we also understand illness severity as defined by the patient, as well as possible discrepancies between clinician and patient ratings of overall illness severity. One previous study examined the relationship between clinician and patient ratings of illness severity in a sample of 225 patients with schizophrenia spectrum disorders who responded well to antipsychotic therapy.<sup>17</sup> This study found that clinician-rated and patient-rated CGI-S scores did not significantly differ and moreover that the 2

- Patient self-reported outcomes are increasingly embraced as important clinical endpoints.
- The views of patients with schizophrenia with regard to illness severity are not necessarily equivalent with those of clinicians, and important differences exist in terms of clinical correlates of clinicians and patients: patients' views of illness severity align more closely with depressive symptoms rather than classic psychotic symptoms.

ratings were found to be correlated but, importantly, not redundant.<sup>17</sup> However, the sample was largely responsive to medication and therefore illness severity ratings were relatively low (mean ratings of approximately 2.4–2.5; range not provided<sup>17</sup>). Another study also found a link between clinician- and patient-rated CGI scores and that clinical insight was associated with the discrepancy between the two.<sup>18</sup> Interestingly, clinician-rated and patient-rated CGI-S scores have been found to link with slightly different PANSS total score values<sup>19</sup> and are associated with different genomic markers.<sup>20</sup> No study, to date, has explored the independent association between various clinical variables and CGI-S scores self-reported by patients with schizophrenia.

The present study set out to examine the association between selected clinical variables, including symptom severity, functional status, neurocognitive impairment, and medication-related side effects, with both clinician-rated and patient-rated CGI-S scores. On the basis of previous work, we hypothesized that clinician-rated CGI-S scores would be highly associated with positive psychotic symptoms and that the predictors of patient-rated CGI-S scores would differ from those of CGI-S scores rated by the clinician. Furthermore, we hypothesized that the 2 ratings of illness severity would be significantly, but not highly, related.

#### **METHOD**

#### **Study Design and Participants**

Data were drawn from the baseline visit of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia study. Details of the study design and rationale,<sup>21</sup> as well as primary findings,<sup>22</sup> have been presented elsewhere. The primary purpose of the CATIE study was to compare the effectiveness of atypical and conventional antipsychotic medications through a randomized controlled trial conducted between January 2001 and December 2004 at 57 sites in the United States (16 university clinics, 10 state mental health agencies, 7 Veterans Affairs medical centers, 6 private nonprofit agencies, 4 private-practice sites, and 14 mixed-system sites). One thousand four hundred ninety-three patients were initially randomized to receive olanzapine (7.5-30 mg/d), perphenazine (8-32 mg/d), quetiapine (200-800 mg/d), risperidone (1.5-6 mg/d), or ziprasidone (40-160 mg/d) under double-blind conditions and were followed up to 18 months or until treatment was

discontinued for any reason.<sup>21</sup> Data reported in the present study are from the pre-randomization baseline visit before initiation of any experimental treatment.

The study inclusion criteria have been reported previously.<sup>21</sup> Briefly, participants were eligible if they were between the ages of 18 and 65 years and had a diagnosis of schizophrenia confirmed using the Structured Clinical Interview for *DSM-IV* Axis I Disorders.<sup>23</sup> Participants were excluded from the study if they had a diagnosis of schizoaffective disorder, mental retardation, or other cognitive disorders or if they had only 1 episode of schizophrenia, were pregnant or breast-feeding, or had a serious and unstable medical condition.

The study was approved by the institutional ethics review board at each site, and written informed consent was obtained from the patients or their legal guardians. All participants demonstrated adequate decision-making capacity in regard to participating in the study as determined by the MacArthur Competence Assessment Tool.<sup>24</sup>

#### Measures

The primary measure in the present study was the CGI-S.<sup>1</sup> Two variations of the scale were employed in the CATIE study, one rated by the clinician and the other by the patient.<sup>21</sup> For the clinician-rated CGI-S, the clinician was asked to rate how mentally ill the patient is based on his or her "total clinical experience with the particular population." The following scores can be given: 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. For the patient-rated CGI-S, the patient was asked, "On a scale of '1' to '7,' where '1' is not at all ill, and '7' is the worst that your illness has ever been, how would you rate the severity of your symptoms of schizophrenia (or patient equivalent)?" Importantly, the patient-rated CGI-S had an identical 7-point anchored scoring system to the clinician-rated CGI-S (ie, 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).

Other measures of interest included the PANSS to assess discrete aspects of psychopathology using derived factor scores,<sup>4,25</sup> the Calgary Depression Scale for Schizophrenia (CDSS) to assess depressive symptoms,<sup>26,27</sup> the Heinrichs-Carpenter Quality of Life Scale (QLS) excluding the intrapsychic foundations subdomain to evaluate community functioning,<sup>28</sup> the Insight into Treatment Attitude Questionnaire (ITAQ) to assess clinical insight,<sup>29</sup> the Drug Attitude Inventory (DAI) to assess patient attitudes toward medication and subjective experience,<sup>30</sup> the Simpson-Angus Scale (SAS) to assess extrapyramidal symptoms,<sup>31,32</sup> the Barnes Akathisia Rating Scale (BARS) to assess akathisia,<sup>33</sup> and the Abnormal Involuntary Movement Scale (AIMS) to assess dyskinesia.<sup>1</sup> Neurocognition was also assessed using a battery of assessments, as described in previous reports,<sup>34</sup> which were converted into standardized scores and combined to construct 5 domain scores: verbal memory, vigilance, processing speed, reasoning and problem solving, and working memory.<sup>14</sup> These domain scores were standardized and averaged to create a neurocognitive composite score, which was used in the present analysis.

#### **Statistical Analyses**

First, potential differences in ratings on the clinicianrated versus patient-rated CGI-S scales were examined using a paired-samples *t* test. Discrepancy scores were also computed by subtracting the patient-rated CGI-S scores from the clinician-rated CGI-S scores. Potential differences in clinical insight between patients who were poor estimators of their illness severity (ie, patients who evidenced a difference score greater than 1 point of clinician ratings) were compared to patients who evidenced a difference score within 1 point of clinician ratings using an independent-samples *t* test.

Next, Spearman rank-order correlations were computed to examine the bivariate relationship between various clinical variables and each of the 2 CGI-S scales. Stepwise multiple regression modeling with forward selection was undertaken to examine independent predictors of both the clinician-rated and the patient-rated CGI-S scales separately. To ensure that the independent predictors of patient-rated CGI-S scores were not a consequence of impaired clinical insight, the multiple regression analysis with patient-rated CGI-S scores was repeated while excluding patients with moderate-to-severe lack of insight (as defined by a PANSS clinical insight [G12] score greater than 3). A 2-sided *P* value of less than .05 was considered statistically significant. Statistical analyses were carried out using SPSS version 20 (IBM Corporation, Armonk, New York).

### RESULTS

#### **Patient Characteristics**

Baseline demographic and clinical characteristics of the sample are presented in Table 1. The study sample includes 1,010 individuals with schizophrenia for whom both patient-rated and clinician-rated CGI-S as well as symptom severity, side effect burden, community functioning, and neurocognitive data were available.

#### Clinician-Rated Versus Patient-Rated CGI-S Scores

The clinician-rated CGI-S scores were significantly and positively correlated with the patient-rated CGI-S scores ( $r_s = 0.34$ , P < .001); however, the effect size of this relationship was in the "medium" range,<sup>35</sup> suggesting only a moderate overlap between the scores on these 2 scales. We next examined whether insight moderated this relationship, by examining the concordance between CGI-S ratings in patients with relatively preserved insight and those with a moderate-to-severe lack of illness awareness. Clinician-rated CGI-S scores were significantly and positively correlated with patient-rated CGI-S scores in both patients with good clinical insight (n = 686,  $r_s = 0.45$ , P < .001) and those with impairments in insight (n = 324,  $r_s = 0.17$ , P = .002); however, these scores were more closely linked in patients with good insight (Fisher *r*-to-*z*; *z* = 4.65, *P* < .001).

## Table 1. Sociodemographic and Clinical Characteristics of the Study Sample (N = 1,010)

Variable	Value <sup>a</sup>	Range
Age, y	39.8 (10.9)	18 to 67
Male, %	74.6	
White, %	62.5	
Unemployed, %	83.8	
Patient's education, y	12.2 (2.1)	1 to 21
Illness duration (time since first prescribed antipsychotic medication), y	13.6 (10.3)	0 to 56
CGI-S score		
Clinician-rated	3.9 (0.9)	1 to 7
Patient-rated	3.5 (1.5)	1 to 7
PANSS score		
Total	75.1 (17.7)	31 to 140
Positive factor	21.9 (6.8)	8 to 45
Negative factor	19.0 (6.7)	7 to 40
Disorganization factor	16.4 (5.2)	7 to 34
Excitement factor	7.1 (2.9)	4 to 21
Anxiety/depression factor	10.7 (3.8)	4 to 22
CDSS total score	4.8 (4.5)	0 to 22
QLS total score (excluding the intrapsychic foundations subdomain)	2.5 (1.1)	0.0 to 5.9
DAI total score	5.0 (4.0)	-10 to 10
ITAQ total score	18.2 (5.0)	1 to 22
SAS EPS average score	0.2 (0.3)	0 to 2.2
BARS global clinical severity score	0.5 (0.9)	0 to 5
AIMS sum score	1.6 (3.0)	0 to 23
BMI, kg/m <sup>2</sup>	29.8 (7.0)	16.9 to 61.0
<sup>a</sup> Values shown as mean (SD) unless otherwise Abbreviations: AIMS = Abnormal Involuntary	e noted. Movement Scal	<u></u>

Abbreviations: AIMS = Abnormal Involuntary Movement Scale, BARS = Barnes Akathisia Rating Scale, BMI = body mass index, CDSS = Calgary Depression Scale for Schizophrenia, CGI-S = Clinical Global Impressions-Severity of Illness scale, DAI = Drug Attitude Inventory, EPS = extrapyramidal symptoms, ITAQ = Insight into Treatment Attitude Questionnaire, PANSS = Positive and Negative Syndrome Scale, QLS = Heinrichs-Carpenter Quality of Life Scale, SAS = Simpson-Angus Scale.

Symbol: ... = not applicable.

The clinician-rated illness severity scores were significantly higher than those rated by patients (estimated mean difference [ESD] = 0.40, standard deviation [SD] = 1.51,  $t_{1009}$  = 8.43, P < .001). Discrepancy scores on the CGI-S rated by the clinician versus the patient are shown in Figure 1. Scores on the 2 scales did not differ for 35.1% of the sample and were within 1 point for 70.5% of the participants. The 29.5% of patients who were poor estimators of illness severity (ie, those who evidenced a difference in score of greater than 1 point) had significantly poorer clinical insight than the patients who scored within 1 point of clinician ratings ( $t_{1008}$  = 4.78, P < .001).

Clinician-rated CGI-S scores were also significantly higher than patient-rated scores in patients with good illness awareness (ESD = 0.21, SD = 1.34,  $t_{685}$  = 4.12, P < .001). For these patients with good insight, scores on the 2 scales did not differ for 38.5% of the sample and were within 1 point for 76.1% of the participants.

### **Correlates of CGI-S Scores**

Bivariate correlations between the 2 CGI-S scales and selected clinical variables are shown in Table 2. Greater symptom severity, worse community functioning, and more severe neurocognitive impairments were associated with more severe ratings of illness severity by both clinicians



## Figure 1. Discrepancy Scores Between the Clinician-Rated CGI-S and the Patient-Rated CGI-S<sup>a</sup>

# Table 2. Bivariate Correlations Between Clinical Variables and Scores on the Clinician-Rated and Patient-Rated CGI-S<sup>a</sup>

	Clinician-Rated	Patient-Rated
Clinical Variable	CGI-S Score (r <sub>s</sub> )	CGI-S Score (r <sub>s</sub> )
PANSS score		
Total	0.55***	0.29***
Positive factor	0.57***	0.25***
Negative factor	0.31***	0.16***
Disorganization factor	0.38***	0.11***
Excitement factor	0.30***	0.16***
Anxiety/depression factor	0.25***	0.36***
Depression (CDSS score)	0.18***	0.38***
Functioning (QLS score)	-0.26***	-0.17***
Neurocognition	-0.09**	-0.07*
Clinical insight (ITAQ score)	-0.16**	0.13***
DAI score	-0.14***	-0.06*
EPS Severity (SAS score)	0.10**	0.10**
Akathisia (BARS score)	0.05	0.12***
Dyskinesia (AIMS score)	0.06	0.08*
BMI	-0.10**	-0.02

<sup>a</sup>Reported correlations are statistically significant at \**P*<.05, \*\**P*<.01, or \*\*\**P*<.001.

Abbreviations: AIMS = Abnormal Involuntary Movement Scale; BARS = Barnes Akathisia Rating Scale; BMI = body mass index; CDSS = Calgary Depression Scale for Schizophrenia; DAI = Drug Attitude Inventory; EPS = extrapyramidal symptoms; ITAQ = Insight into Treatment Attitude Questionnaire; PANSS = Positive and Negative Syndrome Scale; QLS = Heinrichs-Carpenter Quality of Life Scale, excluding the intrapsychic foundations subscale;  $r_s$  = Spearman correlation coefficient; SAS = Simpson-Angus Scale.

and patients. Interestingly, poor clinical insight was related to higher clinician-rated illness severity scores, but lower patient-rated illness severity scores. PANSS total scores were significantly related to CGI-S scores, though this relationship was stronger for clinician ratings than those made by patients. The largest correlation with clinician-rated CGI-S scores was with positive symptoms, whereas the largest correlation with patient-rated CGI-S scores was with depressive symptoms.

### **Determinants of Clinician-Rated CGI-S Scores**

We constructed a multiple regression model to examine the independent predictors of clinician-rated CGI-S scores. This model revealed that positive psychotic symptoms were the strongest predictor of clinician-rated illness severity scores (Table 3), with additional contributions made by negative, disorganized, and depressive symptoms as well as community functioning.

### **Determinants of Patient-Rated CGI-S Scores**

Depressive symptoms were found to be the strongest predictor of patient-rated illness severity (Table 4). Additional variables that also independently predicted patient-rated CGI-S scores were positive psychotic symptoms, clinical insight, cognitive functioning, and other depression/anxiety symptoms. This analysis was repeated in 686 patients who demonstrated only mild lack of clinical insight or less, and the results were consistent with the analysis in the larger population; depressive symptoms remained the strongest predictor of patient-rated CGI-S scores, and the same 4 variables explained an additional portion of the variance (Table 4).

## DISCUSSION

The present investigation examined the differences in illness severity ratings made by clinicians and patients, as well as their independent clinical predictors. Scores on the 2

Table 3. Stepwise Multiple Regression Model With Clinician-Rated CGI-S Score as Dependent Variable<sup>a,b</sup>

					$R^2$
Step	Variable Added	β	t	Р	Change
1	Positive symptoms (PANSS)	0.45	15.17	<.001	0.326
2	Negative symptoms (PANSS)	0.09	2.74	.006	0.027
3	Disorganized symptoms (PANSS)	0.12	3.58	<.001	0.006
4	Depression (CDSS)	0.08	2.94	.003	0.007
5	Functioning (QLS)	-0.08	-2.79	.005	0.005

<sup>a</sup>Model statistics: R<sup>2</sup> = 0.371, F<sub>5,991</sub> = 117.02, P < .001.

<sup>b</sup>For ease of presentation, only statistics from the final model are presented. All variables except PANSS total score were examined for entry into the regression model.

Abbreviations: CDSS = Calgary Depression Scale for Schizophrenia, PANSS = Positive and Negative Syndrome Scale, QLS = Heinrichs-Carpenter Quality of Life Scale, excluding the intrapsychic foundations subdomain.

Table 4. Stepwise Multiple Regression Model With Patient-Rated CGI-S Score as Dependent Variable<sup>a</sup>

Sample/					R <sup>2</sup>
Step	Variable Added	β	t	Р	Change
Full sample (N=1,010) <sup>b</sup>					
1	Depression (CDSS)	0.25	6.78	<.001	0.149
2	Positive symptoms (PANSS)	0.21	6.78	<.001	0.033
3	Insight (ITAQ)	0.19	6.60	<.001	0.035
4	Neurocognition	-0.11	-3.81	<.001	0.010
5	Anxiety/depressive symptoms (PANSS)	0.13	3.49	.001	0.009
Subsample with good clinical insight (n=686) <sup>c</sup>					
1	Depression (CDSS)	0.24	5.39	<.001	0.147
2	Insight (ITAQ)	0.13	3.77	<.001	0.041
3	Anxiety/depressive symptoms (PANSS)	0.10	2.08	.04	0.022
4	Neurocognition	-0.09	-2.72	.007	0.017
5	Positive symptoms (PANSS)	0.28	7.72	<.001	0.010

<sup>a</sup>For ease of presentation, only statistics from the final model are presented. All

variables except PANSS total score were examined for entry into the regression model.

<sup>b</sup>Model statistics: R<sup>2</sup> = 0.236, F<sub>5,991</sub> = 61.22, P < .001.

<sup>c</sup>Model statistics: R<sup>2</sup>=0.258, F<sub>5,672</sub>=46.79, P<.001.

Abbreviations: CDSS = Calgary Depression Scale for Schizophrenia, ITAQ = Insight into Treatment Attitude Questionnaire, PANSS = Positive and Negative Syndrome Scale.

scales were found to be significantly, albeit only moderately, correlated with one another. As a very large overlap was not found between these 2 measures, the 2 scores should not be interpreted as interchangeable. Patient-reported outcomes therefore provide additional complementary, not redundant, information on clinical status. Further to this point, we found that for almost one third of cases, a discrepancy of greater than 1 point between clinician and patient ratings was found, and, as expected, level illness awareness was significantly poorer in these patients. Although only a moderate amount of overlap was observed between the clinician and patient ratings of illness severity, it is worth mentioning that both measures improved over the course of the CATIE study.<sup>19</sup> Intervention studies in other populations have also found similar prospective changes in scores on both the clinicianand patient-rated CGI-S.36,37

In contrast to one previous study,<sup>17</sup> we found that, in this large and heterogeneous sample of schizophrenia patients, clinicians' ratings of illness severity were significantly higher than ratings made by patients. Moreover, and also in contrast to previous work,<sup>17</sup> there was only moderate concordance between patient and clinician ratings of illness severity. There are several possible explanations for this, including construct variance, information variance, or observation variance to name a few.<sup>38</sup> Construct variance reflects potential differences in the criteria used by raters in determining an appropriate score, information variance reflects possible differences in information available to different raters, and observation variance reflects a scenario in which raters given identical information differ in their specific focus.<sup>38,39</sup> Construct variance may explain these results, although the anchors employed for both scales were identical; however, the prompts did differ. The patient version of the CGI-S was based on patients' knowledge of their own past illness severity, whereas the clinician version included the ambiguous prompt to base ratings on "total clinical experience,"<sup>1</sup> a feature that has been criticized elsewhere. 40-42 However, this ambiguous prompt would increase variance between clinicians, and not necessarily between clinicians and patients. Information variance could potentially explain the discrepant ratings, especially when one considers the blinding effect of impaired insight. Though multiple sources of variance may exist, a much more likely explanation involves observation variance. It seems plausible that given all sources of information, patients and clinicians accord differential weight to symptoms and associated impairments. It appears that clinicians' ratings of illness severity focus on positive psychotic symptoms, whereas patient ratings are more focused on depressive symptoms. This latter finding is consistent with studies demonstrating the important role of depressive symptoms in predicting other self-report outcomes<sup>43</sup> and underscores the need to recognize and treat these subjectively debilitating symptoms.

One interesting finding that emerged in the present study was that better clinical insight was related to greater illness severity as rated by the patient. This finding is consistent with previous work linking better insight with more severe depressive symptoms in patients with schizophrenia.44-46 Importantly, when restricting the analysis to individuals with good clinical insight, the results remained unchanged, suggesting that the determinants of patient-rated CGI-S scores are not secondary to lack of illness awareness. The association between clinician and patient ratings of illness severity were also found to be moderated by level of insight, with those with relatively good illness awareness evidencing a stronger relationship between the 2 ratings. Greater neurocognitive impairment was also related to higher patient ratings of illness severity; however, such impairments were not independently predictive of clinician-rated CGI-S scores.

It is noteworthy that negative symptoms and functional status were independently associated with clinicians' ratings of illness severity, but did not figure into patients' ratings. This finding is in line with previous work showing that patients underreport negative symptoms<sup>39,47</sup> as well as other evidence suggesting that patients are satisfied with

life despite experiencing functional impairments.<sup>48,49</sup> This finding has important implications for the treatment of negative symptoms, as our data suggest that severity of these symptoms is not incorporated into patient ratings of their illness severity. Accordingly, they may neither recognize nor seek out treatment for these debilitating symptoms. It will be important going forward to replicate these findings in a sample of patients with predominant negative symptoms.

Medication-related side effects demonstrated little to no association with clinician-rated CGI-S scores. This is to be expected, as ratings on the CGI-S are taken on the basis of "mental illness severity" and do not, at least directly, incorporate side effects.<sup>1,2</sup> Previous work has demonstrated that clinicians rate illness severity differently based on adverse event profiles in patients with mood disorders,<sup>50–52</sup> a finding that is not directly extended here to patients with schizophrenia. Although neurologic side effects did not have an independent impact on patient-rated CGI-S scores, once other symptoms had been accounted for, these side effects did demonstrate a small bivariate association, underscoring the burden of these motor symptoms.

The present study has several strengths, including the large sample of schizophrenia patients as well as the numerous assessments used to evaluate symptoms, side effects, cognition, and functioning. Conversely, there are limitations that warrant comment. First, prompts for the 2 versions of the CGI-S differed between clinicians and patients; preferably, ratings should be based on identical prompts and anchors. There is, in fact, evidence suggesting (at least some) schizophrenia patients fail to acknowledge certain symptoms (eg, hallucinations) as signs of mental illness.<sup>47</sup> Second, given the self-report nature of the patient-rated CGI-S assessment, it is possible that patients intentionally misrepresented themselves and rated the severity of their illness more favorably. Third, although many facets of schizophrenia psychopathology were assessed, some were not (eg, obsessive-compulsive symptoms), leaving open the possibility that factors not included in our models account for variance in CGI-S scores. Fourth, symptom severity ratings were made by clinicians. It would be interesting to explore whether patients also differed in the assessment of their own symptoms and whether self-rated symptom severity would more closely align with patient ratings of overall illness severity. Fifth, this study included patients whose illness was largely chronic; hence, these findings may not be generalizable to first-episode populations. Lastly, the patient sample was quite heterogeneous, and all patients were included in each analysis together. This may have masked cultural or racial differences in ratings of illness severity for both clinicians and patients.

The findings from the present study suggest that clinician and patient ratings of illness severity are not interchangeable and that meaningful differences exist between them. Moreover, each is associated with a different set of predictors. Clinician ratings of global illness severity are more closely associated with severity of positive psychotic symptoms, whereas patient ratings are more closely related to depressive symptom severity. Those involved in care should be aware that the views of patients regarding their illness are not synonymous with those of the clinician. Taking this distinction into account may enhance therapeutic alliance and, ultimately, measures of outcome.

**Drug names:** olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal and others), ziprasidone (Geodon).

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This is a multisite, clinical trial of persons with schizophrenia comparing the effectiveness of randomly assigned medication treatment.

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#### Patient- and Clinician-Rated Severity of Schizophrenia