The Relationship Between Quality of Life and Clinical Efficacy From a Randomized Trial Comparing Olanzapine and Ziprasidone

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Objective: To examine treatment-specific changes in health-related quality of life (QOL) among patients with schizophrenia and to assess the association between clinical and QOL improvement.

Method: This post hoc analysis used the findings of a 28-week, randomized, multicenter trial of patients with schizophrenia (DSM-IV) treated with olanzapine (10–20 mg/day) or ziprasidone (80–160 mg/day). Data were collected from August 2001 to December 2002. Efficacy was measured using the Positive and Negative Syndrome Scale (PANSS). Quality of life was assessed with the generic health self-administered Medical Outcomes Study Short-Form 36-Item Health Survey (SF-36) and the disease-specific expert-administered Heinrichs-Carpenter Quality of Life Scale (QLS). Mixed-effects-repeated-measures and last-observation-carried-forward approaches were used to assess the effects of treatment on QOL and the association of clinical outcomes to QOL outcomes.

Results: Olanzapine- and ziprasidone-treated patients demonstrated similar improvement from baseline to endpoint on the SF-36 and QLS. All correlations between changes in PANSS scores and the SF-36 were significant ($p < .001$), ranging from –0.159 to –0.400. All correlations between changes in PANSS scores and the QLS were significant ($p < .0001$), ranging from –0.286 to –0.603. The correlations between the 2 QOL measures were generally significant but small to moderate in magnitude.

Conclusions: The results of this study indicate that, in patients with schizophrenia, olanzapine and ziprasidone treatment are associated with significant QOL and clinical improvements. Further, the significant correlation between change scores on the PANSS and QOL measures suggests that treatment-related clinical improvements are associated with improved health-related and disease-specific QOL.

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Second-generation antipsychotics (SGAs) have generally been accepted as effectively reducing positive symptoms associated with schizophrenia. Additionally, SGAs have shown efficacy in reducing negative symptoms, cognitive impairment, and mood disturbance associated with schizophrenia.[1] An added benefit of SGAs is generally better tolerability than first-generation antipsychotics.[1] As it has become more accepted that SGAs positively impact negative symptoms and show improved adverse event profiles, clinicians and researchers have become increasingly interested in broader effects associated with these medications.[2]

There is an increased interest in the differential ability of SGAs to improve quality of life (QOL) for patients who take these medications. However, most publications have focused on the clinical efficacy of SGAs,[1] whereas fewer have examined their relative impact on QOL.[2] Research on QOL of patients undergoing antipsychotic treatment is a relatively recent occurrence compared with research on clinical efficacy. Meltzer and colleagues[3] published the first report of QOL under antipsychotic treatment and reported that, after 6 months of clozapine treatment, patients in their open trial showed significant improvement on a QOL measure. Franz et al.,[4] in an observational trial, examined the QOL of patients with schizophrenia who were being treated with either conventional or atypical antipsychotics. These authors reported that patients treated with atypical antipsychotics had significantly better QOL than patients treated with conventional antipsychotics. Revicki et al.[5] reported results for a randomized clinical trial, finding at both 6 and 52 weeks of treatment that olanzapine-treated

patients showed significantly better QOL outcomes than haloperidol-treated patients.

Despite an overall paucity of studies examining differential effects on QOL among SGAs, there are a few notable exceptions. These studies have sought to distinguish differential impact of SGAs on QOL when possible, or to report QOL outcomes associated with SGAs.Tran et al.[6] reported that both olanzapine- and risperidone-treated groups experienced significant improvement in QOL, but that these benefits did not differ between these 2 treatments. More recently, Voruganti et al.[7] reported no QOL differences between the SGAs included in their study (risperidone, olanzapine, quetiapine, and clozapine). Studied in isolation, olanzapine has been shown to have a significant impact on the QOL of patients with schizophrenia in several studies,[5,8,9] with similar results being observed for risperidone, quetiapine, and clozapine.[10–12] Almost all SGAs have been reported to be clinically effective; however, little QOL information has been published for many SGAs including ziprasidone.[2]

Another issue that has received some attention is the relationship between QOL and clinical efficacy. The association between clinical change and change in QOL has been inconsistent.[13–15] Although it is generally agreed that SGAs positively impact both clinical symptoms and QOL, the relationship of these constructs remains unclear. In their literature review, Pinikahana and colleagues[14] found little evidence for a relationship between positive symptoms and QOL; however, negative symptoms, general pathology, and mood disturbance were all found to have demonstrated relationships to QOL. Additionally, different studies have used different measures of quality of life and little information comparing these measures is available.

Breier et al.[16] report the primary efficacy results for the trial reported on here, including results for the Positive and Negative Syndrome Scale (PANSS) subscales and total scores and Quality of Life Scale (QLS) total. The current study sought to explore 3 related QOL issues. First, to our knowledge, no previously reported study has compared olanzapine and ziprasidone with regard to their impact on patient QOL. To address this gap, in the current report we hypothesized that patients treated with olanzapine would show greater improvements in QOL compared with those treated with ziprasidone. This hypothesis is related to the finding that olanzapine-treated patients showed significantly greater improvement on all PANSS subscales[16] than those treated with ziprasidone, and to the report by Pinikahana et al. of a relationship between negative symptoms and general pathology with QOL.[14] Second, we hypothesized that improvements in symptom severity measures (i.e., clinical improvements) would be associated with improved QOL regardless of the drug. Finally, we were interested in exploring the relationship between the Medical Outcomes Study Short-Form 36-Item Health Survey (SF-36), a self reported generic health assessment, and the QLS, an expert-administered disease-specific assessment, as these measures differ in their focus and method of administration.

METHOD

Our post hoc analysis used the data from the clinical trial of Breier et al.[16] This was a multicenter, randomized, double-blind, parallel, 28-week trial that compared treatment outcomes among both inpatients and outpatients with schizophrenia (DSM-IV).[17] Data were collected from August 2001 to December 2002. A comprehensive detailing of the methods can be found in Breier et al.[16] and is therefore briefly summarized here.

The experimental variable was treatment assignment to either olanzapine (10–20 mg by mouth per day) or ziprasidone (80–160 mg by mouth per day). A treatment period of 28 weeks was chosen to capture ongoing improvement in the primary endpoint (change in PANSS total) beyond the 8-week acute treatment phase and to provide an adequate period of observation to capture potential relapse. Each patient, or their authorized legal representative, signed an informed consent document that fully explained the risks and benefits of study participation. Data on a variety of adverse events were collected in this study, including weight, electrocardiograms, fasting glucose, and lipids. Additionally, extrapyramidal symptoms were measured by the Simpson-Angus Scale,[18] Barnes Akathisia Scale,[19] and Abnormal Involuntary Movement Scale.[20] Details on adverse events data collection and results can be found in Breier et al.[16]

Outcome Measures

Clinical efficacy was measured with the Positive and Negative Syndrome Scale (PANSS),[21] using the subscales and total scores. The scale consists of 30 items, each rated on a scale from 1 (symptom not present) to 7 (symptom extremely severe). The subscales include positive symptoms, negative symptoms, general psychopathology, cognition, and excitability. The PANSS was administered every week for the first 2 months and then 7 times during the rest of the trial.

The QOL measures used in this study were the Medical Outcomes Study Short-Form 36-Item Health Survey (SF-36)[22–24] and the Heinrichs-Carpenter Quality of Life Scale (QLS).[25] The QOL measures were administered at baseline, 8 weeks, 15 weeks, 22 weeks, and the end of the trial. The SF-36 is a self-reported generic measure of health, with 8 dimensions: physical functioning, role physical, bodily pain, general health, energy, social functioning, role emotional, and mental health; and 2 primary-factor analytic components: physical and mental component score (PCS and MCS respectively). To better understand the SF-36, the physical functioning dimen-

sion starts with "The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?"[23(p3:13)] This opening statement is followed by a list of activities such as "lifting or carrying groceries, walking several blocks, walking one block."[23(pp3:13–3:14)] According to Pukrop and colleagues,[24] the reliability for the 8 SF-36 dimensions in a sample of patients diagnosed with schizophrenia ranged from 0.71 for the role emotional and general health dimensions to 0.89 for the physical functioning and bodily pain dimensions (with a median of 0.83). SF-36 dimensions were transformed so that these scores represented the percentage of the total possible scale score; this transformation is described in the SF-36 manual.[23]

The QLS is a schizophrenia-specific QOL scale that has been widely used in clinical trials comparing antipsychotic medications. Unlike the SF-36, the QLS is an interviewer-administered instrument composed of 21 items covering 4 dimensions: instrumental roles, intrapsychic foundations, common objects and activities, and interpersonal relations. Heinrichs and colleagues[25] reported that intraclass correlations between raters for the 4 QLS dimensions and the total score ranged from 0.84 to 0.97. Cramer and colleagues[26] reported that the QLS was sensitive to change over time (effect size 0.35, $p < .001$) and between medications (effect size 0.335, $p < .01$) in a study comparing QOL instruments. Interrater reliability was not assessed for QOL measures in the current study.

Statistical Analysis

For clinical outcomes, we employed the PANSS subscales and total scores. Change scores were then computed to summarize the clinical effects from randomization to study completion. To address the relative drug effect on QOL, change scores were similarly computed for the 8 dimensions of the SF-36 and the QLS total and its 4 dimensions. Postbaseline visitwise scores were analyzed using a mixed-effects model repeated-measures (MMRM) approach (primary data analysis), which included terms for treatment, investigator, visit, treatment-by-visit interaction, baseline value, and baseline-by-visit interaction. Change from baseline to the last observation carried forward (LOCF) was analyzed using a fixed-effects analysis of covariance. This model included terms for treatment, investigator, and baseline value.

Change scores were compared between treatment groups for all measures using analysis of variance, with baseline values as covariates. Pearson product-moment correlations were computed between the measure of clinical efficacy (PANSS total and subscales) and QOL measures for treatment groups. The individual treatment group correlations were compared using the χ^2 test of homogeneity of correlations to ascertain that treatment group did not moderate the clinical/QOL relationship. Pearson product-moment correlations were computed to assess the relationships between changes in the measures of clinical efficacy (PANSS) and changes in QOL measures for the total sample (ignoring treatment group). Pearson product-moment correlations were computed between the SF-36 and the QLS for treatment groups. The individual treatment group correlations were compared using the χ^2 test of homogeneity of correlations to ascertain that treatment group did not moderate the SF-36/QLS relationship. Pearson product-moment correlations were computed to assess the relationship between changes in the QOL measures for the total sample (ignoring treatment group). Also, Pearson product-moment correlations were computed between the QOL measures and various adverse events for the total sample. All analyses were done using SAS software version 8 (SAS Institute Inc.; Carey, N.C.). Statistical significance was set at .05.

RESULTS

Although Breier et al.[16] report complete primary results for this trial, we repeat trial results that pertain to the current study or provide basic trial information. A total of 548 patients were randomly assigned to olanzapine ($N = 277$) or ziprasidone ($N = 271$). The only demographic variable that differed at baseline was mean age, with patients randomly assigned to olanzapine being slightly older than those randomly assigned to ziprasidone (40.1 vs. 38.2 years, $p = .037$). Significantly more olanzapine (59.6%) than ziprasidone (42.4%) patients completed the study ($p < .001$). The mean modal treatment dose was 15.3 mg/day for olanzapine and 116.0 mg/day for ziprasidone. Also, as reported in Breier et al.,[16] on the primary endpoint (PANSS total score), olanzapine-treated patients showed significantly greater improvement than ziprasidone-treated patients on both the LOCF and MMRM analyses ($p < .001$). Olanzapine-treated patients demonstrated significantly greater improvement than ziprasidone-treated patients on 2 dimensions and the total score for the QLS with the LOCF analysis; however, no significantly greater improvement was found with the MMRM analysis (Table 1).

The QOL general health scale, the SF-36, was not reported in Breier et al.[16] and is reported here as new data. Olanzapine-treated patients demonstrated significantly greater improvement when compared with ziprasidone-treated patients on 3 dimensions of the SF-36 with the LOCF analysis; however, only 1 dimension, social functioning, showed significantly greater improvement with the MMRM analysis (Table 2).

To establish that treatment did not have an impact on the relationship between the PANSS and the QOL measures, the individual treatment group correlations between these measures were compared. For each treat-

Table 1. Between-Treatment Changes in Baseline-to-Endpoint QLS Scores (LOCF and MMRM analyses) for 548 Patients Diagnosed With Schizophrenia Randomly Assigned to Olanzapine or Ziprasidone

			QLS Scores					
				LOCF Change to Endpoint		MMRM Endpoint		
QLS Dimension	Treatment[a]	N	Baseline Mean (SD)	Mean (SD)	p Value	N	LS Mean (SE)	p Value
Instrumental roles	Olanzapine	200	6.4 (5.81)	2.9 (5.76)	.088	133	9.80 (0.47)	.352
	Ziprasidone	193	6.1 (5.43)	2.1 (6.22)		89	9.16 (0.56)	
Intrapsychic foundations	Olanzapine	200	17.6 (6.49)	4.9 (9.09)	.041	133	22.88 (0.62)	.612
	Ziprasidone	193	16.6 (7.09)	3.9 (9.68)		89	22.44 (0.73)	
Common objects and activities	Olanzapine	200	5.4 (2.51)	1.5 (2.88)	.009	133	7.07 (0.19)	.202
	Ziprasidone	193	5.3 (2.87)	1.1 (2.69)		89	6.72 (0.23)	
Interpersonal relations	Olanzapine	200	16.3 (8.22)	5.3 (9.45)	.056	133	21.82 (0.77)	.220
	Ziprasidone	193	15.5 (8.37)	3.8 (10.29)		89	20.49 (0.89)	
QLS total score (transformed)	Olanzapine	200	45.8 (19.76)	14.6 (24.16)	.033	133	61.34 (1.81)	.353
	Ziprasidone	193	43.5 (20.26)	10.9 (25.48)		89	58.94 (2.11)	

[a]Olanzapine, 10 to 20 mg/day; ziprasidone, 80 to 160 mg/day.
Abbreviations: LOCF = last observation carried forward, LS = least squares, MMRM = mixed-effects model repeated-measures, QLS = Heinrichs-Carpenter Quality of Life Scale, SD = standard deviation, SE = standard error.

Table 2. Between-Treatment Comparison of Baseline-to-Endpoint SF-36 Scores (LOCF and MMRM analyses)

			SF-36 Scores					
				LOCF Change to Endpoint		MMRM Endpoint		
SF-36 Dimension	Treatment[a]	N	Baseline Mean (SD)	Mean (SD)	p Value	N	LS Mean (SE)	p Value
Bodily pain	Olanzapine	246	76.9 (25.04)	4.7 (27.92)	.249	159	83.20 (1.52)	.672
	Ziprasidone	239	75.5 (27.28)	3.3 (26.36)		109	82.28 (1.79)	
General health	Olanzapine	242	57.6 (22.66)	7.2 (21.50)	.033	156	65.24 (1.48)	.755
	Ziprasidone	237	58.8 (21.00)	2.9 (23.47)		109	64.58 (1.71)	
Mental health	Olanzapine	245	56.8 (23.53)	10.1 (23.79)	.173	158	67.49 (1.51)	.862
	Ziprasidone	237	55.6 (21.29)	8.6 (25.34)		109	67.86 (1.75)	
Physical functioning	Olanzapine	245	75.4 (24.18)	3.5 (25.13)	.775	159	79.44 (1.63)	.285
	Ziprasidone	239	75.5 (24.79)	2.7 (25.18)		109	81.93 (1.91)	
Role emotional	Olanzapine	245	44.4 (42.80)	17.3 (47.39)	.043	158	69.27 (3.20)	.213
	Ziprasidone	239	47.4 (41.47)	7.9 (50.74)		109	63.53 (3.75)	
Role physical	Olanzapine	245	54.5 (41.43)	7.8 (45.17)	.229	158	68.01 (2.98)	.904
	Ziprasidone	239	52.3 (40.48)	5.2 (47.18)		109	67.49 (3.49)	
Social functioning	Olanzapine	246	54.2 (30.29)	15.2 (33.63)	.010	159	73.76 (1.88)	.039
	Ziprasidone	239	55.8 (30.80)	8.4 (32.64)		109	68.19 (2.21)	
Vitality	Olanzapine	245	52.1 (23.53)	9.2 (25.04)	.263	158	60.43 (1.63)	.384
	Ziprasidone	237	52.8 (21.46)	6.9 (26.34)		109	62.46 (1.89)	
Mental component summary	Olanzapine	241	37.8 (13.42)	6.8 (12.93)	.021	156	45.91 (0.82)	.258
	Ziprasidone	236	38.1 (11.99)	4.5 (13.57)		109	44.61 (0.94)	
Physical component summary	Olanzapine	241	48.3 (8.73)	0.6 (8.58)	.657	156	49.36 (0.57)	.340
	Ziprasidone	236	48.0 (8.97)	0.5 (8.97)		109	50.13 (0.66)	

[a]Olanzapine, 10 to 20 mg/day; ziprasidone, 80 to 160 mg/day.
Abbreviations: LOCF = last observation carried forward, LS = least squares, MMRM = mixed-effects model repeated-measures, SD = standard deviation, SE = standard error, SF-36 = Medical Outcomes Study Short-Form 36-Item Health Survey.

ment group there were 90 correlations between the PANSS (subscales and total scores) and the 2 QOL measures; using the χ^2 test of homogeneity 7 pairs of correlations were statistically significantly different between those treated with olanzapine and those treated with ziprasidone. Of the 7 pairs of correlations that were significantly different, 4 were for the SF-36 social functioning scale (data not shown). For the relationship of clinical efficacy to QOL, all inverse correlations between the PANSS (subscales and total scores) and the SF-36 (subscales and component scores) were significant ($p < .001$). The magnitude of the inverse correlations was small to moderate, ranging from –0.159 between PANSS negative and SF-36 physical functioning to –0.400 between PANSS general psychopathology and SF-36 mental component score (data not shown). Similarly, the PANSS and the QLS showed significant inverse correlations on all comparisons ($p < .0001$). For this comparison, though, the magnitude of the inverse correlations was moderate to large, ranging from –0.286 between PANSS excited and QLS instrumental roles (data not shown) to –0.603 between PANSS total and QLS intrapsychic foundations. Table 3 shows baseline scores and percentage improvement in the PANSS total, positive, and negative scores and the dimension scores for both QOL measures; this table also provides the correlation of mean changes between the PANSS scores and the dimension scores for the QOL measures.

Table 3. Correlation of Mean Changes Between PANSS Scores and Dimension Scores for the Quality of Life (QOL) Measures

Measure	Baseline Score	% Improvement	Correlation of Mean Change		
			PANSS Positive	PANSS Negative	PANSS Total
PANSS					
Positive	24.78	36.57	…	…	…
Negative	26.80	27.80	…	…	…
Total	100.62	30.72	…	…	…
QOL measure					
SF-36					
Bodily pain	76.21	5.25	–0.205	–0.176	–0.234
General health	58.22	8.70	–0.198	–0.228	–0.250
Mental health	56.20	16.71	–0.305	–0.260	–0.356
Physical functioning	75.47	4.11	–0.205	–0.159	–0.216
Role emotional	45.87	27.63	–0.226	–0.198	–0.256
Role physical	53.41	12.19	–0.263	–0.201	–0.264
Social functioning	54.97	21.52	–0.319	–0.276	–0.366
Vitality	52.44	15.45	–0.233	–0.259	–0.288
Mental component score	37.91	14.95	–0.315	–0.299	–0.381
Physical component score	48.17	1.09	–0.211	–0.181	–0.224
QLS					
Instrumental roles	6.25	40.07	–0.335	–0.420	–0.417
Intrapsychic foundations	17.14	25.56	–0.493	–0.577	–0.603
Common objects and activities	5.36	24.09	–0.421	–0.449	–0.497
Interpersonal relations	15.88	28.75	–0.400	–0.492	–0.498
QLS total (transformed)	44.63	28.55	–0.473	–0.565	–0.582

Abbreviations: PANSS = Positive and Negative Syndrome Scale, QLS = Heinrichs-Carpenter Quality of Life Scale, SF-36 = Medical Outcomes Study 36-Item Short-Form Health Survey.

To ascertain that treatment did not have an impact on the relationship between the QLS and the SF-36, the individual treatment group correlations between these measures were compared. For each treatment group there were 50 correlations between the QLS and SF-36; using the χ^2 test of homogeneity, 1 pair of correlations was statistically significantly different between those treated with olanzapine and those treated with ziprasidone (SF-36 bodily pain with QLS instrumental role, olanzapine $r = 0.217$, ziprasidone $r = –0.010$; $p = .023$). Nearly all correlations between change from baseline to endpoint on the QLS (interviewer-administered) and SF-36 (self-rated) were significant ($p < .05$) but small to moderate in magnitude. The only nonsignificant correlation was for the relationship between the SF-36 dimension of bodily pain and the QLS dimension of interpersonal relations ($r = 0.088$, $p = .08$). The 2 dimensions with the largest correlation were the SF-36 mental health dimension and the QLS dimension of intrapsychic foundations ($r = 0.408$, $p < .0001$).

To ascertain whether adverse events that may have occurred during this study had an impact on QOL, correlations between adverse events and the QOL measures were calculated. Several of the correlations of adverse events and QOL were significant, though the magnitude of the correlations was very small. The largest correlation was between the SF-36 physical function dimension and fasting glucose ($r = –0.147$, $p = .002$). This translates to a coefficient of determination (r^2) of 0.020, indicating that fasting glucose shares 2.0% of its variance with the SF-36 physical function dimension.

DISCUSSION

With the exception of the SF-36 social functioning scale, QOL measures were statistically comparable across treatments in this trial. The PANSS total and subscale scores were all significantly correlated with the SF-36 dimension and component scores and the QLS total and dimension scores. These significant correlations show that improvement in clinical symptoms is in fact associated with QOL improvement. The interest in QOL in the treatment of patients with schizophrenia is a relatively recent phenomenon.[2–5] This study suggests that greater clinical efficacy may lead to greater QOL and functional outcomes, which may indicate that the impact for more efficacious treatments goes beyond simple symptom relief.

The correlations for the mean change scores between the PANSS and QOL scales were significant; however, their magnitude was generally small to moderate, suggesting that these measures provide unique information. The uniqueness of this information argues for the continued inclusion of QOL measures in studies of patients with schizophrenia. The correlations for the mean change scores between the PANSS and SF-36 were generally lower in magnitude than those between the PANSS and QLS, for perhaps 2 reasons. First, the PANSS[21] and QLS[26] are both specifically designed for use with patients with schizophrenia, whereas the SF-36[22–24] is not. This suggests that when used with patients with schizophrenia, the SF-36 is less than optimal in that it may not assess general health issues specifically relevant to these patients. The second reason may be related to instrument

administration in that both the PANSS and the QLS are clinician- or interviewer-administered and the SF-36 is self-reported. Perhaps the decreased correlations for the PANSS with the SF-36 are simply related to the fact that different people completed the instruments.[27] The mean change correlations between the SF-36 and QLS do provide more data regarding this issue; however, the broad range of correlations between these 2 measures does not lead us to prefer one of these alternatives to the other. The addition of patient-reported measures that are health specific to schizophrenia and that assess both symptoms and QOL would help to elucidate the nature of this relationship. This is consistent with an editorial by Naber,[28] in which he states, "In agreement with other authors, subsequent studies showed that self-ratings by schizophrenic patients are possible, useful and necessary."[28(p82)]

Certainly, the current analysis shows the value of including QOL measures in trials comparing treatments for patients with schizophrenia. To the specific hypotheses in this study we can make the following statements: first, we were unsuccessful at demonstrating that olanzapine-treated patients would show greater improvements in QOL than ziprasidone-treated patients. Olanzapine-treated patients produced better outcomes on one measure of social functioning than ziprasidone-treated patients. However, this result is not conclusive as many comparisons were made, inflating the likelihood of finding a significant result simply by chance. Additionally, the significantly different dropout rates between treatment groups threaten our ability to find accurate treatment differences. For the second hypothesis, that improvements in symptom severity measures would be associated with improved QOL, we found significant correlations between all PANSS scores and QOL dimensions. The magnitude of these correlations was generally small to moderate, providing support for the hypothesis that clinical symptoms are related to QOL but reinforcing that symptom and QOL measures provide unique information. This relationship was also not found to be moderated by treatment, with perhaps one exception being the SF-36 social functioning scale. Finally, we explored the relationship between the SF-36 and QLS and found significant correlations between all SF-36 and QLS, dimensions except 1. Again these correlations were significant but generally small to moderate in magnitude, suggesting unique information is provided by the SF-36 and QLS.

This study has several limitations, perhaps the most important being that it is a secondary analysis of a clinical trial using outcome measures for which the study may not have been adequately powered. Another study design limitation is the length of this study, 28 weeks, is more than adequate for assessing the clinical effects of antipsychotic treatment, however this time frame may be too brief for QOL changes to occur. Finally a limitation of this study is the failure to measure the interrater reliability of the QOL measures used. Despite these and other limitations, the data from this study indicate that there may be a relationship between clinical efficacy and QOL.

From these findings, we argue for the inclusion of more diverse QOL measures in schizophrenia trials to allow for a better understanding of the patients' experience as well as the effect of treatment on QOL. Continued development of measures for this area and a better understanding of the role QOL plays in patient outcomes are vital to the continued improvement of treatment for patients with schizophrenia. Given that this study was not designed to detect such differences, yet treatment differences emerged nonetheless, further research exploring the impact of various treatments on QOL is warranted.

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

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