

## Psychiatric Symptoms and Quality of Life in Schizophrenia: A Meta-Analysis

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**Quality of life (QoL) has been recognized as an important outcome of schizophrenia treatment, yet the determinants of QoL for individuals with schizophrenia are not well known. Research has consistently found psychiatric symptoms to be negatively related to QoL, however, findings concerning the strength of these relationships have been mixed, making it difficult to determine the degree to which such symptoms are related to poor QoL. This research presents a systematic meta-analysis of studies examining the relationship between psychiatric symptoms and QoL in schizophrenia, in an effort to elucidate the determinants of QoL for this population. A total of 56 studies were extracted from literature searches of relevant databases for empirical reports published between 1966 and 2005 examining the relationship between positive, negative, and/or general psychiatric symptoms and QoL. Weighted effect size analyses revealed small relationships between psychiatric symptoms and QoL, with general psychopathology showing the strongest negative associations across all QoL indicators. Moderator analyses indicated that variation in effect sizes could be accounted for by differing operationalizations of QoL, study design, sample, and participant treatment setting. In particular, positive and negative symptoms were more strongly related to poor QoL among studies of schizophrenia outpatients, whereas general psychopathology showed a consistent negative relationship with QoL across all study samples and treatment settings. Implications for future research and treatment development are discussed.**

*Key words:* functional outcome/psychopathology/wellbeing/well-being

### Introduction

The development of a range of antipsychotic medications has provided individuals with schizophrenia some relief from the cardinal symptoms of the illness<sup>1</sup> that has allowed treatment developers to focus on improving

broader and more functional outcomes.<sup>2,3</sup> One key outcome addressed by this research is quality of life (QoL). Broadly, QoL may be defined as a person's sense of well-being and satisfaction with his/her life circumstances, as well as a person's health status and access to resources and opportunities.<sup>4</sup> Clearly, such an outcome is of particular importance to researchers aiming to develop treatments to help individuals with schizophrenia lead more fulfilling and satisfying lives. Unfortunately, the factors that influence QoL in schizophrenia are not well known. One factor consistently shown to be negatively associated with QoL is psychiatric symptoms.<sup>5</sup> However, due to wide variations in measurement strategies and definitions of QoL, it has been difficult to identify which psychiatric symptoms are most strongly associated with poor QoL in individuals with schizophrenia. Furthermore, the strength of these associations has also been difficult to discern, with some studies finding small to moderate relationships between psychiatric symptoms and QoL<sup>6,7</sup> and others presenting findings that suggest that certain aspects of these concepts may be indistinguishable.<sup>8,9</sup>

Clarifying the relationship between psychiatric symptoms and QoL represents an important step both in elucidating the factors that affect QoL for individuals with schizophrenia and in understanding the utility of the concept of QoL for guiding future treatment development efforts. For example, if indicators of QoL share only a modest amount variance with psychiatric symptoms, such findings would suggest that measures of QoL not only possess some discriminant validity but would also point to the importance of looking beyond symptom-reduction strategies for improving QoL in schizophrenia. Additionally, because certain psychiatric symptoms likely share more variance with QoL than other symptoms clarifying the differential relationships among various patterns of symptomatology and QoL could point to important constraints regarding the use of QoL assessments in schizophrenia research, as well as suggest fruitful directions toward improving QoL for individuals living with the illness. While these issues have been the focus of much research over the past several decades<sup>5,10</sup> and are of particular importance if measures of QoL are to be the benchmarks for novel treatments aimed at improving functional outcomes in schizophrenia, to date, findings across studies have been mixed. The research reported here attempts to account for this variation and

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provide clarification about the nature of the relationship between psychiatric symptoms and QoL in schizophrenia, through the systematic use of meta-analytic techniques, in an effort to identify the symptomatic determinants of QoL in schizophrenia and the utility of the concept in schizophrenia research.

### What Is QoL?

The QoL literature in addressing schizophrenia has been particularly difficult to summarize because of the disparities in the definitions researchers have used to operationalize the concept.<sup>11,12</sup> Some researchers have conceptualized QoL largely as a subjective affair that only the patient can report,<sup>13–16</sup> whereas others have argued for the importance of including more “objective” indicators of QoL,<sup>17,18</sup> such as housing and health status, or frequency of social interactions. Both sides of this argument are equally compelling. Proponents of subjective indicators of QoL point to the importance of understanding and acknowledging the unique perspectives individuals with schizophrenia have about their lives,<sup>19</sup> and proponents of objective indicators emphasize the need for measures uncontaminated by mood states and cognitive disturbances.<sup>12,17</sup> Researchers have also differed with regard to how broadly they consider the concept of QoL to be. Some investigators define QoL as a global evaluation of one’s total life experiences,<sup>20</sup> others focus more narrowly on the absence of disease and health-related symptoms,<sup>21</sup> and still others focus on discrete indicators of social and material wellbeing.<sup>4,22</sup> Each of these definitions appears to have face validity, but the range of differences encompassed in these definitions has resulted in some investigators questioning the utility and distinctiveness of the concept.<sup>23,24</sup>

Recent reviews of the QoL literature have helped provide some perspective with regard to what exactly is meant by QoL, and how the concept is being used in mental health outcomes research. For example, Gladis et al<sup>10</sup> identify 2 predominant models of QoL that have guided, either implicitly or explicitly, research in this area. The first model focuses on the individual’s satisfaction with his/her current life circumstances and is almost exclusively measured by subjective evaluations. The second model focuses on health (eg, functional impairment) and social and material wellbeing (eg, number of close friends, adequacy of financial resources) and is often measured by objective evaluations. Lehman’s<sup>4</sup> review of the measurement literature suggests a similar multidimensional model of QoL incorporating an overall sense of well-being, functional status, and access to resources and opportunities. Other reviews of the literature, including some of the early sociological models, conceptualize QoL in a similar fashion.<sup>12,25,26</sup>

What can be concluded from these varying conceptualizations of QoL is that although the concept is indeed broad, specific parameters do exist. QoL can be thought of

as a multidimensional set of components consisting of a person’s (1) satisfaction with his/her life as a whole, or *general wellbeing*; (2) observable social and material wellbeing, or *objective QoL*; (3) satisfaction with his/her social and material wellbeing, or *subjective QoL*; and (4) health and functional status, or *health-related QoL*. Although comprehensive factor-analytic investigations have yet to be conducted to empirically establish these 4 dimensions of QoL, each dimension is supported by a considerable body of literature, both in psychiatry and other disciplines, and unique measurement techniques. General wellbeing and subjective QoL are usually assessed with self-report instruments, such as the Gurin single-item wellbeing measure<sup>20</sup> or the Quality of Life Enjoyment and Satisfaction Questionnaire<sup>27</sup> that ask participants to indicate either their overall satisfaction with life or their satisfaction with specific life domains (eg, social, material). Objective QoL is usually measured either by self-report or by structured interview, such as in Lehman’s Quality of Life Interview,<sup>28</sup> and attempts to amass specific observable indicators of social and material wellbeing (eg, monthly income, number of close friends). Health-related QoL is measured in a similar fashion but restricts its content to the areas of symptomatology, disability, and functional status related to physical and/or mental health. For the purpose of this meta-analysis, we used this broad conceptualization of QoL to guide our survey of the literature surrounding the relationship between psychiatric symptoms and QoL among individuals with schizophrenia.

### Are Psychiatric Symptoms Important to QoL?

Studies addressing QoL for individuals with schizophrenia and other severe mental illnesses have identified a number of important influential factors, such as social support,<sup>29</sup> unmet need,<sup>30</sup> and medication side effects.<sup>13</sup> However, most of the research examining factors affecting QoL has primarily focused on the impact of psychiatric symptoms. These studies consistently indicate that negative symptoms and general psychopathology (eg, anxiety, depression) have a significant negative relationship with QoL. Findings concerning positive symptoms have been mixed (see Lambert and Naber<sup>5</sup> for a recent review), and the magnitude of the relationships among negative symptoms, general psychopathology, and QoL have shown substantial variation, with some studies finding large relationships among these measures,<sup>8,9</sup> and others revealing small to moderate relationships.<sup>6,7</sup> These variations appear to be at least partially due to differences in the conceptualization and measurement of QoL. For example, some studies examining the influences of subjective QoL have found the relationship with general psychopathology to be so large, that the utility of subjective measurements have been questioned,<sup>12</sup> whereas other studies examining the influences of objective QoL have found its relationship with psychiatric symptoms to be negligible.<sup>31</sup>

Furthermore, measures of health-related QoL often include some assessment of mental health that may inflate the relationship between psychiatric symptoms and QoL. Few studies have examined the differential impact of psychiatric symptoms on the various dimensions of QoL.

Variation among studies examining the relationship between psychiatric symptoms and QoL may also be due to the sample differences. Psychiatric symptoms may have less of an impact for individuals living on psychiatric inpatient units because most of these units are secure settings where florid psychiatric symptoms are expected and, thus, are often less disruptive to a person's ability to meet his/her needs. Indeed, in the only study to examine the differential relations among psychiatric symptoms and the QoL of inpatients and outpatients with schizophrenia, Kasckow et al<sup>32</sup> found that negative symptoms and general psychopathology had a markedly stronger relationship with the health-related QoL of elderly outpatients with schizophrenia. Furthermore, research on psychosocial influences of QoL among inpatients with schizophrenia suggests that, besides symptoms, factors such as social support and self-esteem may also have a significant influence on QoL for these individuals.<sup>29,33</sup>

Recent research examining the QoL of individuals in the early course of schizophrenia has also indicated that psychiatric symptoms may be more influential to the QoL of such individuals, compared with more chronic populations. For example, a number of studies have found particularly strong relationships among negative symptoms, general psychopathology, and QoL for individuals in the early course of the illness.<sup>34-36</sup> Although no studies have compared the relations between psychiatric symptoms and QoL for individuals with chronic vs first-episode psychosis, it seems plausible that the recent onset of such a debilitating illness may enhance the impact of the symptoms of this illness on QoL. Unfortunately, studies have yet to examine how the relationship between psychiatric symptoms and QoL changes throughout the course of schizophrenia and fully elucidate whether such symptoms pose increased threats to the QoL of individuals living in the community.

What can be seen from this brief review of the literature addressing the relations between psychiatric symptoms and QoL among individuals with schizophrenia is that evidence concerning the importance psychiatric symptoms to QoL has been substantially mixed, and it remains unclear which specific symptoms are most important to which dimensions of QoL, and for whom these symptoms hold the greatest impact. Answers to these questions hold marked importance for treatment developers aiming to improve the QoL of individuals with this illness.

### How Can a Meta-Analysis Help?

A meta-analytic approach to understanding the relations between psychiatric symptoms and QoL in schizophrenia

has a number of advantages over any single study of this relationship. First, because meta-analysis is usually intended to answer general questions about how a set of constructs are related, estimates of these relationships across studies using diverse measurement strategies can be pooled and summarized to provide an overall understanding of the relationship among a set of constructs.<sup>37</sup> This holds a particular advantage to summarizing the QoL literature because we have found over 50 different instruments that putatively tap into this concept, few of which are consistently used throughout the literature. Meta-analytic techniques help to ensure that all measurement strategies are represented in effect size estimates, thereby providing a more general understanding of the relationship between psychiatric symptoms and QoL than studies employing any single measure of the concept. Second, because the emphasis in meta-analysis is on the size of relationships rather than on their statistical significance,<sup>38</sup> the approach lends itself well to identifying which psychiatric symptoms are the most influential to QoL, by estimating the overall magnitude of these effects over a large, accumulated body of literature. Finally, because any single study often does not include multiple measurement approaches and sampling techniques, meta-analysis becomes a key method for understanding how and why relationships among constructs vary across methodological characteristics.<sup>39</sup> As discussed above, the relationship between psychiatric symptoms and QoL in schizophrenia has shown marked variation in the literature, but no single study has been able to identify why such variation occurs. By pooling studies with different methodological characteristics, meta-analytic techniques allow for a systematic investigation of sources of this variation that can ultimately lead to an understanding of the conditions under which psychiatric symptoms hold the largest impact to individuals with schizophrenia.

The purpose of this research was to conduct a systematic and comprehensive meta-analysis of all existing studies, both published and unpublished, examining the relations between psychiatric symptoms and QoL in schizophrenia, in order to arrive at a clearer understanding of the symptomatic determinants of QoL in schizophrenia and utility of this concept for guiding future treatment development efforts. Specifically, we aimed to (1) identify the types of psychiatric symptoms that are most strongly related to QoL, (2) estimate the overall magnitude of these relationships, and (3) identify systematic moderators of the relationship between psychiatric symptoms and QoL.

### Methods

#### *Literature Search*

An extensive literature search was conducted to locate both published and unpublished studies documenting

the relationship between psychiatric symptoms and QoL in schizophrenia. This was accomplished by performing keyword searches of PsycINFO and Medline databases from January 1966 (when the concept of QoL was first introduced to the medical literature by Elkinton<sup>40</sup>) to December 2005, using the search strings “QoL,” “wellbeing,” or “well-being” combined with “schizophrenia.” These database searches yielded 492 published and 10 unpublished reports. Abstracts retrieved from these searches were then examined, and studies were included for further consideration if they reported empirical quantitative findings on either the relationship between psychiatric symptoms and QoL or the psychometric evaluation of a measure of QoL. The latter were included because early in the search process, it was noted that although psychometric studies of QoL instruments often did not have the examination of the relationship between psychiatric symptoms and QoL as their primary goal, these studies routinely included analyses assessing the relationships between these measures. From these abstract searches, studies were then examined and included in this research if they (1) initially validated or used a previously validated measure of QoL, (2) used a previously validated measure to assess positive, negative, and/or general psychopathology, (3) reported some statistic on the relationship between these measures, (4) distinguished between positive, negative, and/or general psychopathology in their measurement of symptomatology, and (5) included a sample containing only individuals with schizophrenia, schizoaffective, or schizophreniform disorder. Validated measures of QoL (eg, the Quality of Life Enjoyment and Satisfaction Questionnaire,<sup>27</sup> Lehman’s Quality of Life Interview<sup>28</sup>) and psychiatric symptoms (eg, the Brief Psychiatric Rating Scale,<sup>41</sup> the Positive and Negative Syndrome Scale<sup>42</sup>) consisted of those instruments that have been subjected to at least one psychometric evaluation in the published literature. Additionally, references of relevant studies were examined for additional studies to be included in this research, and several QoL researchers were queried for relevant unpublished studies. In total, 56 studies (52 published and 4 unpublished) assessing the relationship between psychiatric symptoms and QoL in schizophrenia were found and included in this research.

### *Study Coding Procedures*

After assembling the studies that were to be included in this research, theoretically and/or methodologically relevant characteristics of each study that may moderate the relationship between psychiatric symptoms and QoL were systematically coded by 2 raters (S.M.E. and C.E.N.). Relevant characteristics included the type of population under study (ie, first-episode or chronic schizophrenia), the treatment setting in which the study was conducted (ie, inpatient, outpatient, or mixed), and

the design of each study (ie, cross-sectional vs longitudinal). Studies were categorized by population type because psychiatric symptoms may differentially affect the QoL of first-episode vs chronic patients. Likewise, treatment setting was recorded because there is evidence that different factors may influence the QoL of psychiatric inpatients vs outpatients.<sup>32</sup> Finally, the design of each study was recorded to explore the attenuating effects of temporal examinations of the relationship between psychiatric symptoms on QoL. Raters for each of these study characteristics were generally in high agreement (range of  $\kappa = 0.56$ – $0.83$ ). Disagreements between raters were resolved by consensus. Additionally, type of QoL measure (ie, health related, subjective, objective, or general wellbeing) was coded to examine the separate relations between psychiatric symptoms and different indicators of QoL. The indicators that are putatively assessed by each measure were extracted from the developer’s description of the instrument.

### *Data Analysis*

After coding the different characteristics of each study, effect sizes representing the relationship between psychiatric symptoms and QoL were extracted. The majority of studies presented these effect sizes using Pearson’s  $r$ , however, if other statistics were reported (eg,  $t$  or  $F$ ), these were converted to  $r$  using procedures outlined by Rosenthal.<sup>43</sup> In order to avoid the overestimation of effect sizes, if relationship statistics were not presented, but only discussed as not significant,  $r$  was assumed to be zero. If a study only reported regression coefficients to represent the relationship between psychiatric symptoms and QoL, the study authors were contacted to obtain zero-order correlations among the variables of interest. This was necessary because, although a recent simulation study has suggested that including regression coefficients in meta-analyses does not markedly influence estimated effects,<sup>44</sup> many of the regression analyses in our sample of studies were performed in a stepwise manner, and thus the size of nonsignificant effects were not reported. Studies that used stepwise regression and whose authors could not be contacted to obtain zero-order correlations were excluded. Only one study was included that used multiple ordinary least squares regression and, therefore, required us to estimate  $r$  from  $\beta$  using methods outlined by Peterson and Brown, because the author could not be contacted to provide zero-order correlations.

For studies reporting relationships between QoL subscale scores and symptomatology, these effect sizes were averaged using Fisher’s  $r$ -to- $z$  transformation procedure to produce a single effect size. However, for studies reporting relationships between symptomatology and multiple indicators of QoL (eg, subjective and objective QoL), the relationships between each indicator and psychiatric symptoms were included in our analysis. As such,

studies could, and frequently did, contribute more than one effect size. Strictly speaking, this would preclude us from performing statistical tests on these effect sizes because they are not all orthogonal.<sup>38</sup> To address this issue, the majority of moderator analyses were conducted on general or composite QoL effects. These were computed by averaging across within-study indicators of QoL to produce a single effect size per study, the results of which are statistically independent and amenable to statistical testing. As such, composite effects consist of an amalgamation of independent effect sizes of different indicators of QoL and, therefore, can be thought of as effects representing the general domain of QoL. Because we were particularly interested in examining the relations between psychiatric symptoms and domain-specific indicators of QoL, effect sizes were also computed for each QoL indicator. If a single study yielded multiple measures of the same QoL indicator, these were averaged to produce a single estimate of that indicator per study. As such, within each domain-specific indicator of QoL, studies only yielded a single effect size that allowed for the application of significance tests on a within-indicator basis. Additionally, to reduce the number of studies that yielded multiple effect sizes, only longitudinal effects were retained from studies presenting both cross-sectional and longitudinal relationships between psychiatric symptoms and QoL. In total, 190 effect sizes were extracted from 56 studies (see table 1); 61 examining relations between QoL and positive symptoms, 62 examining relations with negative symptoms, and 67 examining relations with general psychopathology.

After extracting effect sizes from each study, an average effect size ( $r$ ), weighted by its degrees of freedom, and 95% confidence interval were computed within each symptom domain using methods outlined by Rosenthal,<sup>43</sup> to estimate the relationship between positive, negative, and general psychiatric symptoms and QoL. Confidence intervals that did not include zero were considered to be statistically significant. The homogeneity statistic,  $Q$  was used to examine heterogeneity among these estimated effect sizes. This statistic tests the hypothesis that the effect sizes included in the analysis are from multiple populations of effects and has a chi-square distribution with  $k - 1$  degrees of freedom, where  $k$  is the number of effect sizes included in the analysis.<sup>39</sup> Potential study moderators of the relationship between psychiatric symptoms and QoL were investigated by calculating a between-group homogeneity statistic,  $Q_B$ , for each moderator. In meta-analysis, this statistic is analogous to the analysis of variance, where  $Q_B$  represents between-group differences in the variation of the effect sizes being estimated. Significant results from this analysis suggest that a proportion of the variance in heterogeneous effects is being explained by the study moderator.<sup>39</sup> However, Hunter and Schmidt<sup>38</sup> caution that over-reliance on this method can be misleading because legitimate heterogeneity of

**Table 1.** Stem and Leaf Plots of Effect Sizes of Relationships Between Psychiatric Symptoms and Quality of Life

Stem	Leaf
Positive symptoms ( $n = 61$ )	
-5	3
-4	88644310
-3	875554442
-2	9988665532100
-1	988553311
-0	9988642220
0	0000011699
1	0
Negative symptoms ( $n = 62$ )	
-7	750
-6	7
-5	997321
-4	54411
-3	87664420
-2	877744100
-1	9777644432100
-0	9997543100
0	00002
1	12
General psychopathology ( $n = 67$ )	
-7	6
-6	20
-5	975542
-4	8777544444111
-3	998877664321111100
-2	987765221111
-1	97766431
-0	773
0	007

Note: Includes studies.<sup>6-9,31,32,34-36,46,58-103</sup>

effect sizes can occur without systematic moderators (eg, due to different sources of random error). As such, we restricted our moderator analyses to a small number of theoretically and methodologically relevant moderators of the relationship between psychiatric symptoms and QoL.

## Results

### *Are Psychiatric Symptoms Related to QoL in Schizophrenia?*

We began our analysis of the relationship between psychiatric symptoms and QoL in schizophrenia, by first examining the size of these relationships within and across different indicators of QoL. As can be seen in table 2, positive and negative symptoms were significantly negatively related to both composite and domain-specific indicators of QoL. Positive symptoms had the strongest negative relationship with health-related QoL and had the smallest association with subjective QoL and general wellbeing. Furthermore, the relationships between positive symptoms and QoL were not particularly strong, with small

**Table 2.** Estimated Effect Sizes of the Relationships Between Psychiatric Symptoms and Quality of Life (QoL)

Indicator	Total Studies	<i>n</i>	<i>r</i>	95% CI	Heterogeneity <sup>a</sup>
Positive symptoms					
Composite QoL	43	3998	-0.20	-0.23 to -0.17	<i>Q</i> = 97.21**
Subjective QoL	19	2256	-0.15	-0.19 to -0.11	<i>Q</i> = 42.90**
Objective QoL	15	1150	-0.18	-0.24 to -0.13	<i>Q</i> = 36.60**
General wellbeing	12	1198	-0.08	-0.14 to -0.03	<i>Q</i> = 23.09*
Health-related QoL	15	1256	-0.26	-0.31 to -0.21	<i>Q</i> = 37.87**
Negative symptoms					
Composite QoL	44	4114	-0.25	-0.28 to -0.22	<i>Q</i> = 170.14**
Subjective QoL	20	2359	-0.12	-0.16 to -0.08	<i>Q</i> = 29.54
Objective QoL	16	1207	-0.47	-0.51 to -0.42	<i>Q</i> = 97.26**
General wellbeing	11	1154	-0.14	-0.20 to -0.08	<i>Q</i> = 23.86**
Health-related QoL	15	1256	-0.29	-0.34 to -0.24	<i>Q</i> = 51.36**
General psychopathology					
Composite QoL	50	5106	-0.34	-0.36 to -0.31	<i>Q</i> = 121.41**
Subjective QoL	25	2997	-0.29	-0.33 to -0.26	<i>Q</i> = 74.89**
Objective QoL	13	1019	-0.26	-0.32 to -0.20	<i>Q</i> = 41.81**
General wellbeing	13	1434	-0.27	-0.31 to -0.22	<i>Q</i> = 16.91
Health-related QoL	15	1389	-0.42	-0.46 to -0.37	<i>Q</i> = 32.45**

Note: Confidence intervals (CIs) that do not include zero are statistically significant.

<sup>a</sup>Significant results indicate heterogeneity among studies.

\**P* < .05

\*\**P* < .01.

effect sizes observed between positive symptoms and all indicators of QoL, except for health-related QoL. This is not surprising given the inconsistency of findings from previous research examining the relationship between positive symptoms with QoL. Similarly, negative symptoms were also moderately negatively associated with health-related QoL, although again, small effect sizes were observed between negative symptoms and general wellbeing and subjective QoL. In contrast to positive symptoms, negative symptoms were also strongly negatively related to objective QoL. However, this large effect size appeared to be primarily due to the strong relationship between the Quality of Life Scale<sup>45</sup> (QLS) and negative symptoms that has been reported in a number of previous studies.<sup>9,46</sup> Indeed, focused contrasts of the differences in the effects of negative symptoms on objective QoL indicated that studies employing the QLS exhibited relationships with objective QoL over twice the size ( $r = -0.52$ ) of studies employing other measures ( $r = -0.22$ ),  $Q_B(1) = 23.60$ ,  $P < .0001$ . Taken together, these findings suggest that only a small amount of variance in QoL can be accounted for by positive and negative symptoms, with the strongest relationships existing between these symptom clusters and health-related QoL.

Also presented in table 2 are estimated effect sizes of the relationship between general psychopathology and QoL. These results broadly indicate that not only is general psychopathology significantly negatively related to QoL but that, consistent with previous research,<sup>5</sup>

general psychopathology tends to be more strongly associated with QoL than either positive or negative symptoms. Similar to negative symptoms, general psychopathology was most strongly related to health-related QoL, although relationships with objective and subjective QoL were moderate. Again, general wellbeing continued to be somewhat less associated with psychiatric symptoms than other indicators of QoL, although its association was not weak and markedly close in size to relationships between symptoms and subjective and objective indicators. Such findings suggest that general psychopathology is moderately associated with all areas of QoL in schizophrenia, even more so than positive and negative symptoms.

#### *What Accounts for Variability Among the Relations Between Psychiatric Symptoms and QoL?*

While we found evidence that positive, negative, and general psychiatric symptoms were negatively related to a variety of indicators of QoL, there was substantial heterogeneity among these effects. Decomposing these effects by the type of QoL indicator examined (eg, health-related QoL) did account for a significant amount of variability among the relationships between negative,  $Q_B(3) = 54.08$ ,  $P < .0001$ , and general psychiatric symptoms,  $Q_B(3) = 18.88$ ,  $P < .001$ , and QoL, but not between positive symptoms,  $Q_B(3) = 1.15$ , ns, and QoL. (These analyses were restricted to studies that provided effect

sizes for only a single indicator of QoL, to avoid violating statistical assumptions of independence. Repeating these analyses with all studies yielded the same pattern of results, with the exception of the relationship between positive symptoms and QoL. With all studies included, different indicators of QoL significantly moderated this relationship,  $Q_B(3) = 21.80$ ,  $P < .001$ , suggesting that (1) limiting this analysis to studies only containing a single effect size may have biased its results and (2) positive symptoms may in fact affect dimensions of QoL differently in schizophrenia. However, violations of statistical independence confound these results and make them speculative at best.) However, nearly all these “decomposed” effects continued to exhibit some significant heterogeneity (see table 2). This suggested that factors in addition to the type of indicator of QoL may be accounting for variability among these effect sizes. As such, we conducted a series of moderator analyses to examine the degree to which different study attributes moderated the relationship between psychiatric symptoms and QoL. These analyses focused on the aforementioned moderator variables with which we used to classify each study (ie, study design, length of illness, and treatment setting) and were performed on the composite index of QoL to ensure both statistical independence and adequate cell sizes to conduct reliable statistical analyses.

We began our investigation of potential moderators by conducting a series of moderator analyses to examine whether studies that employed longitudinal designs showed different relationships between psychiatric symptoms and QoL than studies employing cross-sectional designs. Results indicated that the relationship between general psychiatric symptoms and QoL was significantly attenuated in longitudinal ( $r = -0.28$ ) compared with cross-sectional studies ( $r = -0.35$ ),  $Q_B(1) = 4.57$ ,  $P < .05$ . Relations with negative symptoms were also attenuated in longitudinal ( $r = -0.20$ ) vs cross-sectional ( $r = -0.27$ ) studies, although only marginally,  $Q_B(1) = 3.90$ ,  $P = .05$ . No significant differences were found in the relationship between positive symptoms and QoL among longitudinal vs cross-sectional studies,  $Q_B(1) = 0.15$ , *ns*. Such findings indicate that the longitudinal contribution of psychiatric symptoms to QoL, particularly negative symptoms and general psychopathology, may be much less than cross-sectional reports of these associations.

After finding that longitudinal studies tended to show smaller relationships between psychiatric symptoms and QoL than cross-sectional examinations, we then conducted a similar series of moderator analyses to investigate whether these relationships differed systematically for studies including individuals with first-episode vs chronic schizophrenia, and studies of individuals in inpatient vs outpatient treatment settings. (Analyses comparing inpatient vs outpatient studies were restricted to a subsample of studies because some [ $n = 10$ ] commingled these samples in their analysis). Results from

these analyses indicated that although the relationships between negative and general psychiatric symptoms and QoL did not differ systematically between studies including individuals with first-episode vs chronic schizophrenia, all  $Q_B(1) < 0.76$ , all  $P > .38$ , the relationship between positive symptoms and QoL was substantially reduced among studies examining first-episode ( $r = -0.08$ ,  $P = .13$ ) vs chronic patients ( $r = -0.21$ ,  $P < .0001$ ),  $Q_B(1) = 4.51$ ,  $P < .05$ . Such findings suggest, contrary to our expectations, that positive symptoms may be less influential to the QoL of individuals who recently developed schizophrenia than those who have had the illness for some time.

Regarding differences in the relationships among psychiatric symptoms and QoL between treatment settings, both positive and negative symptoms showed a significantly stronger relationship with QoL among studies of individuals treated in outpatient ( $r = -0.28$  and  $-0.32$ , respectively) vs inpatient settings ( $r = -0.12$  and  $-0.22$ , respectively), all  $Q_B(1) > 7.87$ , all  $P < .01$ . However, general psychopathology was related to QoL equally among studies of both outpatients and inpatients,  $Q_B(1) = 0.62$ , *ns*. These findings suggest that positive and negative symptoms may be more influential to the QoL of individuals with schizophrenia receiving treatment in the community, but that general psychopathology has a moderate negative relationship with QoL regardless of treatment setting.

#### *How Big Is the File-Drawer Problem?*

Having found that psychiatric symptoms were significantly negatively related to QoL in schizophrenia, we conducted a series of file-drawer analyses to determine the extent to which our findings could be influenced by unpublished studies of nonsignificant effects. These analyses were conducted because of the consistent finding that studies reporting negative or nonsignificant effects tend not to be published<sup>43</sup> and thus are relegated to the file drawer. This is a potentially serious issue in any systematic meta-analysis because only surveying studies of significant effects can lead to an overestimation of effect sizes. Fortunately, a file-drawer analysis can provide some idea of the magnitude of this problem by estimating the number of unpublished studies containing null findings that would be needed to render the results of a meta-analysis nonsignificant.<sup>39</sup> File-drawer analyses of the estimated effect sizes between psychiatric symptoms and composite QoL indicated that there would need to be 54, 82, and 131 unpublished studies finding nonsignificant effects between positive, negative, and general psychiatric symptoms and composite QoL, respectively, in order to reduce the unweighted effect sizes of these relationships to 0.10. To reduce the unweighted effect sizes to 0.05, 151, 207, and 311 unpublished studies finding nonsignificant effects between positive, negative,

and general psychiatric symptoms and QoL, respectively, would need to exist. Such findings suggest that it is unlikely enough unpublished studies of null effects exist to render the findings of this meta-analysis non-significant.

## Discussion

QoL is emerging as an important outcome of the treatment of schizophrenia, yet relatively little is known about the factors that influence the QoL of individuals who suffer from this illness. The relationship between psychiatric symptoms and QoL among individuals with schizophrenia has been studied most extensively. However, this research has yet to elucidate how important psychiatric symptoms are to QoL, and which symptoms hold the strongest relations to QoL. To our knowledge, this is the first systematic meta-analysis to examine the effects of any potential contributor to QoL in schizophrenia. The results of this analysis suggest that psychiatric symptoms have a significant, but small, negative relationship with QoL in schizophrenia, with general psychopathology consistently emerging as the strongest contributor to poor QoL. In addition, findings suggest that positive and negative symptoms are not related to the QoL of all groups of individuals with schizophrenia equally, but that such symptoms may be particularly detrimental to QoL in studies of individuals receiving treatment in the community, and that positive symptoms are only weakly related to QoL in studies of individuals in the early course of the illness. Such findings hold several important implications for treatment development and future QoL studies in schizophrenia research.

First, given that general psychopathology shows the strongest relationship with QoL, this suggests that non-psychotic signs and symptoms are important targets for treatments aiming to improve QoL for individuals with schizophrenia. Previous research has suggested that the strong correlations observed between measures of general psychopathology and QoL might be the result of subjective ratings being unduly influenced by mood.<sup>17,47</sup> As such, it has not been clear whether such symptoms simply contaminate some forms of QoL measurement or should, in fact, be legitimate targets for QoL treatments. This research lends support to the latter, because both subjective and objective indicators of QoL were similarly and consistently most strongly related to general psychopathology. Unfortunately, while considerable progress has been made over the past 2 decades in developing effective pharmacological and/or psychosocial treatments for non-psychotic psychopathology, principally anxiety and depressive symptoms, their optimal methods of use for individuals with schizophrenia have not been clearly identified.<sup>48</sup> Further, much less attention has been paid to treatment of the secondary psychological effects of living with a chronic disability, such as schizophrenia.<sup>49</sup>

While our research does not identify a causal link between symptoms of general psychopathology and poor QoL in schizophrenia, it does suggest that identifying optimal methods of managing co-occurring nonpsychotic signs and symptoms, as well as the secondary effects of schizophrenia on psychological health may be particularly fruitful avenues for improving QoL among this population.

Additionally, this research points to the need for any QoL treatment to attend to both the patient's environment and stage of illness, because the relationships between some psychiatric symptoms and QoL varied significantly across these patient characteristics. In this research, we found that studies of individuals receiving treatment in the community showed significantly stronger negative relationships between positive and negative symptoms and QoL, compared with studies of individuals in inpatient settings. This pattern is congruent with the only known study to examine the moderating influence of the patient's environment on the effects of psychiatric symptoms on QoL<sup>32</sup> and suggests that positive and negative symptoms may be most disabling for those living in the community. This is not surprising, given that most inpatient units are specifically designed to accommodate such symptoms, whereas in the community these symptoms pose substantial threats to social adjustment and functioning.<sup>50,51</sup> The functional threats these symptoms present to individuals attempting to build a life in the community could substantially stifle progress on social, work, and life goals that would result in poorer QoL.

It is interesting that length of illness also moderated the relationship between positive symptoms and QoL, but that contrary to our expectations, studies of individuals in the early course of schizophrenia showed no significant relationship between positive symptoms and QoL. There may be a number of different reasons for this finding that concern how individuals who develop schizophrenia adjust to the onset of positive symptoms; however, because individuals experiencing a first episode of schizophrenia usually present in inpatient settings, the attenuated relationship between positive symptoms and QoL may simply reflect the diminished influence these symptoms hold to the QoL of individuals living on inpatient units. Unfortunately, because first-episode and inpatient studies were completely collinear in this research, we are unable to conclude whether the reduced relationship between positive symptoms and QoL in first-episode schizophrenia is due to treatment setting or the recent onset of the illness. Future research is needed to disentangle this issue by focusing on the determinants of QoL among individuals in the early course of schizophrenia living in the community.

Further, although this research indicates that psychiatric symptoms have a significant negative relationship with QoL in schizophrenia, the magnitude of this relationship is not large. For example, even general



psychopathology that was most strongly related to QoL, explained no more than 12% of the variance in composite QoL scores. When only longitudinal studies were considered, general psychopathology explained less than 8% of the variance in QoL. Although this finding supports the discriminant validity of the concept of QoL in schizophrenia research, it underscores the need for further investigation into the psychosocial influences of QoL in schizophrenia and points to the importance of developing psychosocial approaches to help these individuals achieve more satisfying lives. An emerging literature of these influences suggests that helping individuals with schizophrenia build broader networks of support and meet their basic needs are promising starting points for treatments targeting QoL.<sup>29</sup> Although pharmacological therapies that result in symptom reduction can produce important improvements in health-related QoL,<sup>52</sup> psychosocial treatments are likely to be particularly well-suited to help improve the broader dimensions of QoL through enhancing a person's social support system or assisting in the meeting of basic needs. This is reflected in the broad improvements in QoL that have been found to result from some trials of psychosocial treatments that target these outcomes, such as case management services<sup>53-55</sup> and peer support programs.<sup>56</sup> While there is a clear need for future research to continue elucidating the effects of psychosocial treatments on the different domains of QoL, such findings suggest an important role for psychosocial approaches in improving QoL in schizophrenia. Consequently, as future research clarifies the prominent psychosocial influences of QoL, it will be important to direct these findings toward the development of psychosocial treatments targeted specifically at improving QoL for this population.

Finally, this research points to the relevance of several methodological characteristics that need to be attended to when designing and reporting on future studies of QoL in schizophrenia research. To begin, given that general psychopathology shares a modest amount of variance with all indicators of QoL, it will be important for future QoL studies to account for this overlap during study design and analysis. This is particularly important for future treatment studies, as before treatment effects can be interpreted as improvements in QoL, they need to be distinguished from improvements in general psychopathology. Further, there is a clear need for future longitudinal studies of the determinants of QoL in schizophrenia, because we found that cross-sectional studies tended to significantly overestimate the predictive utility of symptomatology. Unfortunately, to date, few longitudinal studies have examined the determinants of QoL in schizophrenia, particularly with regard to psychosocial determinants. Such studies are vital to the identification of the key determinants of QoL in schizophrenia and the mechanisms by which such determinants influence QoL, as well as the development of targeted approaches to im-

prove QoL among this population. Lastly, future QoL studies will need to ensure that their samples are homogeneous with regard to stage of illness and treatment setting or specifically account for the differential relationships that are likely to occur across these factors between QoL and other constructs under investigation. In our review of the literature, we found that it was not uncommon for studies to contain mixed samples of inpatients and outpatients or early course and chronic patients. However, as our results show, there are systematic differences in how the dimensions of QoL interact with psychiatric symptoms among these samples, and ignoring these differences would obscure results. Consequently, future studies of the relationship between psychiatric symptoms and QoL will need to gather homogeneous samples, block on treatment setting and course of illness, or statistically account for these factors in moderator analyses, in order to accurately represent their results.

It is important to note that although these findings hold implications for treatment development efforts and future QoL research, this research also has a number of limitations that need to be recognized and addressed in future studies. First, it is important to remember that the unit of analysis in a meta-analytic study is research results and not individuals.<sup>37</sup> As such, moderators of the effects of psychiatric symptoms on QoL cannot be interpreted at an individual level, rather such moderators must be understood as explaining variation among studies. Consequently, implications derived from moderator analyses need to be tested within studies of individuals in order to confirm these findings. Second, because of the relatively small number of studies that examined specific indicators of QoL (eg, subjective QoL) within certain moderator cells (eg, outpatient samples), it was necessary to conduct moderator analyses on composite QoL scores. This precluded us from examining how different indicators of QoL are moderated by different study characteristics. Such an analysis is likely to further clarify for whom psychiatric symptoms hold the largest threat to QoL, because these indicators are conceptually distinct and may react differently to symptoms among various patient populations. Future research will need to explicitly examine this issue by utilizing measures of QoL that contain multiple indicators, such as the Lehman Quality of Life Interview.<sup>28</sup> Third, it is important to remember that many measures of health-related QoL include symptom measures as well, which may explain why psychiatric symptoms were most strongly related to health-related QoL. As such, effects regarding the relationship between psychiatric symptoms and health-related QoL need to be interpreted with caution, and future research will need to control for shared variance between psychiatric symptoms and symptom components of health-related QoL when examining these effects. Unfortunately, to date, most health-related QoL measures commingle mental

and physical health symptoms in their measurement and scoring strategies that precludes meta-analytic techniques from disaggregating these effects. Fourth, it should be recognized that although the 4 dimensions of QoL examined in this research were derived from an extensive review of the literature, this 4-factor structure has yet to be subjected to empirical examination. Consequently, the distinctiveness of these dimensions of QoL continues to remain unclear, and future factor-analytic investigations are needed to elucidate the latent structure of the QoL construct. Finally, although general psychopathology appears to have the strongest relationship with QoL, because the heterogeneity of symptoms that fall within the omnibus “general psychopathology” category, the relative contribution of different nonpsychotic symptom domains to QoL is not clear from this research. Some research has suggested that symptoms of anxiety may be the most important to QoL,<sup>57</sup> although few investigations have examined the independent influence of anxiety and other forms of general psychopathology on QoL within a single study. Additionally, while it is clear that general psychopathology is negatively related to QoL, this relationship cannot be assumed to be unidirectional (as having a poorer QoL is likely to have negative psychological consequences) and the reasons why such symptoms pose a larger threat to QoL in schizophrenia than the cardinal symptoms of the illness are not clear. Future longitudinal research is needed to clarify the relative predictive importance and reciprocal influence of different components of general psychopathology on QoL in schizophrenia, as well as to understand the mechanisms by which such symptoms influence QoL. Addressing these issues will provide important information about the determinants of QoL in schizophrenia and point to the methods that can be employed to help these individuals lead fuller and more satisfying lives.

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