Quality of Life Measurement during Antipsychotic Drug Therapy of Schizophrenia

Lakshmi NP Voruganti, MD[1], Ronald J Heslegrave, PhD[2], A George Awad, MD, PhD[3]

[1]Department of Psychiatry, University of Western Ontario; London Health Sciences Centre (Victoria Campus), London, Ontario, Canada

[2]Department of Psychiatry, University of Toronto; The Wellesley Central Hospital, Toronto, Ontario, Canada

[3]Department of Psychiatry, University of Toronto; Clarke Institute of Psychiatry, Toronto, Ontario, Canada

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The strategy for measuring quality of life and the choice of a rating scale should follow a rational scheme aimed at capturing the key components of quality of life of a specified clinical population. This is achieved through defining the purpose of the study, identifying the clinical population and its needs, developing a situation-specific quality of life model, and choosing a battery of psychometrically sound and user-friendly rating scales based on the model. Patients' self-reports and subjective feelings should be central to quality of life measurement, which should also monitor symptom severity, drug side effects, and psychosocial adjustment. This article describes the application of these principles in the context of antipsychotic drug therapy of schizophrenia and identifies potential problems that may arise from the conceptual, psychometric, clinical, and other feasibility issues. The highly subjective nature of the disorder, together with the poor insight, lack of motivation, and neurocognitive deficits of those who are afflicted, poses special difficulties for obtaining and interpreting patients' quality of life appraisals in schizophrenia.

Key Words: quality of life, schizophrenia, antipsychotic drugs, clinical trials, pharmacoeconomics

INTRODUCTION

Measurement, the process of quantification, has been an ancient and integral part of human evolution. The purpose of measurement is to understand and to monitor a phenomenon, often with an intent to modify it. Health, in terms of its quantity and quality, has been a focus of measurement for these same reasons. Measuring quality of life has become a preoccupation of health researchers over the past 3 decades, and it has proved especially challenging for those working in clinical psychopharmacology in recent years. This article provides an overview of contemporary issues surrounding the measurement of quality of life of individuals receiving antipsychotic drug treatment for schizophrenia and discusses

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Address for correspondence: Dr LNP Voruganti, London Health Sciences Centre (Victoria Campus), 392 South Street, London, ON N6A 4G5.

Table 1

List of selected generic quality of life scales[a]

Scale (source)	Description	Comments
Sickness Impact Profile (Bergner and others 1981)	Self-administered scale with 136 items grouped into 12 categories (3 physical, 4 psychosocial, and 5 independent)	Most thoroughly designed, widely used, psychometrically sound, flexible measure; employed in schizophrenia and depression
Nottingham Health Profile (Hunt and others 1985)	Self-administered scale with 38 items grouped into 6 sections (physical mobility, pain, sleep, social isolation, emotions, and energy level)	Simple to use, psychometrically sound, with focus on subjective distress; content skewed towards very sick; not used in schizophrenia
Quality of Well-Being Scale (Patrick and others 1973)	Classifies functioning and prognosis of a person by assessing mobility, physical and social activities based on a 10- to 15-min structured interview	Conceptually thorough, technically complex, psychometrically sound, and useful in health economics, but item content irrelevant for schizophrenia
Short Form Health Survey (Ware 1996)	36-item, self-administered scale; contains subjective measures of well-being and physical, social, and role functioning scales	Popular among clinical researchers; widely tested; used in various psychosomatic studies
Health Utilities Index (Torrance and others 1995)	Classification system based on certain attributes (hearing, memory, pain) and functional levels; weights attached to each; interview-based	Developed from a health-economic perspective; tested rigorously; content fails to capture psychiatric problems

[a]Adapted from McDowell and Newell (1996) and Patrick and Erickson (1993).

the implications for clinical practice, drug trials, and research.

The scope of quality of life measurement in clinical research

One of the striking aspects of quality of life research is that it has been largely driven by market forces, which included demands from patients, clinicians, pharmaceutical firms, and regulatory authorities (Spilker 1996). Even from such diverse perspectives, quality of life is an intuitively familiar and appealing concept that has several advantages. It is global, all inclusive, and subjective, which compels the inclusion of the patient's feelings, attitudes, and opinions in medical decision making and clinical care. Because the concept is understandable and easy to communicate, it has generated widespread enthusiasm and has come to be used as a measure in a variety of clinical, research, and administrative contexts.

The primary functions of a quality of life measure are screening and evaluation. When used for screening purposes, the measure helps to identify the needs of a clinical population and facilitate program planning. Its more important function, however, is as an evaluative measure, monitoring clinical progress and establishing outcome. Quality of life as an outcome measure has been applied in a variety of settings including clinical decision making, outcome research, drug trials, approval of new drugs, program evaluation, and resource allocation. In psychopharmacology, quality of life has come to be identified as an outcome measure in clinical trials involving the study of new antipsychotic drugs (Meltzer and others 1990; Awad 1992). Recently, quality of life measurements have also become the basis of health economic evaluations such as cost-effectiveness analysis and cost-utility analysis, and regulatory authorities (for example, the Food and Drug Administration) have begun to view quality of life data as a requirement for the approval of new drugs (Anonymous 1995). Considering their widespread use and the high stakes involved, the current approaches to and techniques for measuring quality of life require a critical examination.

Current approaches to quality of life measurement

The current approaches to quality of life measurement are of 2 types, direct and indirect. Direct approaches employ psychometric principles and involve various methods of measuring quality of life with the help of questionnaires or rating scales. As the name suggests, these methods have traditionally been developed by clinical psychologists and social scientists. These scales can be either global or multidimensional, generic or disease-specific, and self-administered or interviewer-administered, depending on their length, content, design, and mode of administration (McDowell and Newell 1996).

Generic quality of life scales are designed to be broadly applicable across various types and severities of disease,

Table 2

List of some disease-specific scales available for assessing quality of life in schizophrenia[a]

Scale (source)	Description	Comments
Standardized Social Schedule (Claire and Cairns 1978)	Semistructured interviewer-administered scale with 17 to 48 items probing physical, economic, social, psychological, and other domains	Designed for use with chronic patients, but never tested in schizophrenic population. Measures maladaptation.
Community Adjustment Form (Stein and Test 1980)	Semistructured, 140-item self-report interview exploring physical, economic, social, psychological, and other areas; requires about 45 min	Used in assessing chronic schizophrenia in 2 studies. Psychometric data not available.
Quality of Life Checklist (Malm and others 1981)	Semistructured, interviewer-administered scale with 93 items; requires about 1 h; explores physical, economic, social, psychological, and other functioning	Designed to identify patients' needs. No psychometric data available. Not useful for clinical trials.
Satisfaction with Life Domains Scale (Baker and Intagliata 1982)	Self-report scale, administered by a 10-min interview; contains 15 items on physical social, economic, and psychological functioning	Designed for use as outcome measure. Format and validity acceptable; reliability data unavailable.
Oregon Quality of Life Questionnaire (Bigelow and others 1982)	Structured rating scale containing 246 items, requiring 45 to 90 min; explores physical, economic, social, psychological, and other aspects of life	Tested across a variety of samples: psychometrically sound. Useful as an outcome measure.
Quality of Life Interview (Lehman and others 1982)	Structured rating scale; contains 143 items; requires 45 min; explores physical economic, social, psychological, and other functioning	Tested across a variety of samples: psychometrically sound; never been used as an outcome measure.
Quality of Life Scale (Heinrichs and others 1984)	Semistructured interviewer-administered rating scale; contains 21 items; requires 45 min; measures intrapsychic foundations, interpersonal relations, and instrumental role in physical, economic social, and psychological spheres	Designed to assess deficit syndrome in patients with schizophrenia. Reliable; validity unknown. Used in a clinical trial involving clozapine.
Wisconsin Quality of Life Index (Becker and others 1993)	Self-administered scale; contains 9 domains and 103 items exploring symptom severity, social functioning, daily living skills, ability to do meaningful work, and overall sense of well-being	Undergoing field trials; psychometric data not yet available. Potentially useful for screening or evaluation. Length might prove to be a limitation.

[a]Modified from Lehman and Burns (1996) and Awad and others (1997).

across different medical treatments or health interventions, and across demographic and cultural groups. Disease-specific quality of life scales, by contrast, are designed to assess specific patient populations, diagnostic groups, or individual differences. Some of the disease-specific scales available for assessing quality of life in schizophrenia have been critically examined in recent reviews (Awad and others 1997; Lehman and Burns 1996). Examples of global quality of life measures include the Global Scale of Adaptive Functioning (Endicott and others 1976) and Gurin's Quality of Life Questionnaire (Gurin and others 1960).

Indirect approaches to quality of life measurement employ econometric methods or preference-based methods of evaluation and involve a translation of an individual's subjectively appraised quality of life into more tangible criteria, for example, the magnitude of the risk taken or the willingness to trade some years of life or a specified amount of money in order to achieve or avoid a certain health state. Techniques of quality of life measurement developed on the basis of these principles are known as value and utility scales (Revicki and Murray 1994). The terms value and utility refer to the desirability of or preference that individuals exhibit for a certain state of health. Value and utility measures have traditionally been developed by health economists and have helped to combine the criteria of quantity and the quality of life together to derive a concept known as quality-adjusted

Table 3

Choosing a quality of life measure for outcome evaluation in schizophrenia[a]

Pitfalls	Remedial strategies
Conceptual issues	
Problems involving definition, scope, and models of quality of life	Define the salient features of the clinical population under study in terms of their age, duration, level of disability, and other relevant characteristics; identify patients' needs and expectations (domains) and develop a situation-specific explanatory model of quality of life, which should guide the selection of appropriate scale
Measurement issues	
Problems with choosing a scale that can provide clinically sensible and scientifically acceptable data	Select scale items that are able to capture the key components of quality of life of the specified clinical population (content validity), to identify the differences in the quality of life of patients with differing severities of illness (discriminability), and also to detect changes over time with or without an intervention (responsivity)
Clinical/assessment issues	
Problems with data gathering and data quality—restlessness, poor attention span, thought disorganization, impaired self-appraisal due to psychotic symptoms, and poor insight	Screen rigourously to exclude clinically unstable and severely ill subjects; reduce respondent burden through paying attention to the length of the scale, clarity of language, visually appealing format, use of simplified scaling techniques (eg, dichotomous responses such as yes/no), and simultaneous documentation of symptom severity, medication status, side effects, and insight to cross-validate data quality; a pilot study could clarify the issues related to test administration
Feasibility issues	
Problems related to financial and human resources, expertise, and organizing multicenter studies	Availability of resources should dictate the measurement strategy from the beginning. The approach to measuement and the choice of a scale is determined by the availability and expertise of research staff, funds, and time. Multicenter studies demand additional training to achieve sufficient interrater reliability

[a]Modified from Patrick and Erickson (1993).

life years. Standard gamble, time trade-off, magnitude estimation, and willingness to pay are some of the actual measures of evaluation (Froberg and Kane 1989a, 1989b). Unlike the clinical–psychometric approaches, econometric or preference-based techniques have not yet been adequately developed or employed to measure the quality of life in psychiatric disorders (Revicki and Luce 1995).

Key aspects of antipsychotic drug therapy in schizophrenia

Employing general principles of quality of life measurement in the context of antipsychotic drug therapy of schizophrenia warrants a clear understanding of the issues involved. Two aspects are particularly significant—illness-related and treatment-related issues. From a quality of life perspective, schizophrenia shares some of the clinical characteristics of other chronic illnesses, such as arthritis and diabetes, while other aspects are unique to this disorder. Shared characteristics include chronicity and lack of completely effective treatment, while the subjective nature of illness and the associated social stigma are the specific features. The occurrence of personally distressing inner psychotic experiences, the lack of a completely effective treatment approach, unpleasant side effects of antipsychotic drugs, a chronic, unremitting clinical course, a stigmatizing social environment, and the combined net effect of these factors on the hopes and expectations of the individual lead to a compromised quality of life in schizophrenia. A global, all inclusive, and subjective outcome measure such as quality of life is ideal to capture the cumulative effects of the disease, deficits, disability, disadvantage, drug therapy, and the resulting distress. Measuring quality of life in schizophrenia also presents some unique problems and dilemmas, however, as described below.

Pitfalls of measuring quality of life in schizophrenia

Despite the enthusiasm and momentum they have generated, contemporary techniques for measuring quality of life are far from satisfactory. There has been a conspicuous difficulty in translating the amorphous concept of quality of life into a personally meaningful, scientifically measurable, and clinically applicable criterion (Awad 1995). The sources of difficulties rest with the conceptual, psychometric, clinical, and feasibility aspects of quality of life measurement.

Conceptual problems include the lack of a widely accepted definition of quality of life, a failure to identify the key components of the phenomenon, and the lack of adequate integrative models that could explain the interaction between various determinants of quality of life in a specific clinical situation. Psychometric problems refer to the shortcomings of various scales in terms of their integrity and properties. Few of the currently available scales are tested in large numbers of patients across a variety of clinical settings and geographical locations. Psychometric criteria such as reliability and validity have been reported for some scales, although little information is available about their differentiation abilities and their sensitivity to change. For example, few of the scales have been used in prospective follow-up studies or controlled clinical trials.

The 3rd source of difficulties lies at the clinical level, which has been so far largely underrecognized or ignored. Since many of the quality of life scales are completed on the basis of patients' self-reports, the reliability of these reports is crucial for making a valid estimation of quality of life. In fact, quality of life measurement has been shifting away from the traditional generic, objective, clinician-rated modes of evaluation toward a client-centered, context-specific, subjective, self-rated method of assessment (Gill and Feinstein 1994). The growing number of self-administered quality of life scales and the development of preference-based quality of life assessment methods are suggestive of the increasing emphasis being placed on patients' subjective feelings and personal preferences (Torrance and Feeny 1989). At the same time, however, there has been a widespread notion among clinicians and researchers that patients with schizophrenia are unreliable historians, an opinion based on observations of impaired judgement, distorted reality perception, poor insight, and various neurocognitive deficits (Amador and others 1993). Other sources of difficulties include practical problems related to test administration, such as the patient's motivation and span of attention and the investigator's ability to discriminate sensitively between responses.

Besides these illness-specific problems, other feasibility issues involving the availability of personnel, expertise, time, and funds are frequent obstacles to performing meaningful quality of life measurements. Multicenter studies or clinical trials often face these difficulties, which may be compounded by problems of interrater reliability and cross-cultural differences. The following section presents some approaches to overcome these obstacles and adopt a meaningful measurement strategy.

A practical approach to quality of life measurement in schizophrenia

Translating the concept of quality of life into a scientifically acceptable and clinically applicable outcome measure involves 5 key steps: 1) defining the purpose of the study, 2) characterizing the clinical population, 3) identifying their needs, 4) delineating the resources, and 5) choosing a battery of appropriate rating scales.

The purpose of quality of life measurement may involve screening or outcome evaluation, and clarifying the needs of a study has implications for choosing a measure. Studies involving health economic evaluations also insist on specifying the perspective from which the work is conducted (for example, the patient, the institution, government, or society). Quality of life, in this instance, is equated with objectively measurable criteria such as psychosocial performance or standard of living estimates. These simplistic but easily generalizable concepts may facilitate decision making in large-scale organizational matters, but they are of limited value in the context of clinical research or drug trials. The stipulation that it must be defined by objectively measurable criteria is inherently contradictory to the idea of quality of life being an exclusively client-centered, subjective attribute. A form of health economic evaluation known as cost-utility analysis is primarily based on quality of life or utility measurement and is presumed to be performed from the patients' perspective.

Establishing the clinical profile of the study population in terms of age, sex, diagnosis, stage of illness, and treatment status is crucial to identifying their specific needs and developing a situation-specific quality of life model. Such a model would represent a comprehensive formulation of the interaction between key factors potentially contributing to the quality of life in a particular setting. In the field of schizophrenia, Lehman's model of quality of life was originally developed from a rehabilitation perspective and addressed the issues involved in community care (Lehman 1983). A new model of quality of life of patients receiving antipsychotic drug treatment, which was formulated more recently, has attempted to integrate the illness, drug therapy, and psychosocial factors of schizophrenia. According to this model, the dynamic interactions among the subjective effects of illness, the outcome of its treatment, and the ensuing psychosocial adjustment determine the ultimate personal impact of schizophrenia and the quality of life of an

individual (Awad 1995). Purpose-driven models such as this one are crucial in identifying the determinants of quality of life, understanding their interaction, and facilitating the process of measurement.

Defining the clinical study population may also help to assess the credibility of patients' self-reports. Recently, it was demonstrated that clinically stable patients with schizophrenia can evaluate and report their quality of life with a high degree of reliability, and their self-reported quality of life ratings were fairly accurate when compared with clinicians' objective evaluations (Voruganti 1996). In that study, 63 symptomatically stable patients with schizophrenia were evaluated at weekly intervals with both a self-administered scale (Sickness Impact Profile) and a clinician-administered scale (Social Performance Schedule). The results indicated that patients' self-reports were highly consistent over a 4-week period ($r = 0.80$ to 0.87, $P < 0.0001$), and their quality of life ratings correlated significantly with the clinicians's estimates ($r = 0.52$ to 0.54, $P < 0.002$). While these results are quite convincing, they are not immediately generalizable to a clinically heterogeneous or severely ill schizophrenia population. It is likely that subjects with unstable mental status and acute psychotic symptoms will be unable to provide reliable and valid estimates of their quality of life. The relationship between patients' degree of insight and their ability to appraise quality of life also remains to be examined.

Reviewing the scope of a study and the resources available is the next step in choosing a quality of life measure. Availability of funding, research personnel, sample size, and the time period of the study should be carefully considered in the beginning, since these aspects will have a bearing on the choice of appropriate rating scales. Multicenter clinical trials should pay special attention to aspects such as interrater reliability and potential cross-cultural differences. Based on the defined purpose, the formulated model, and the availability of adequate resources, a battery of rating scales capable of capturing the key components of quality of life of the specified population are selected. The actual process of choosing the battery may involve reviewing a larger number of available scales and considering their conceptual basis, length, content, psychometric properties, statistical maneuverability, and user-friendly structure. It has been shown that for schizophrenic populations, the length and layout of the scale, the simplicity of its language, its use of dichotomous responses, and its personally meaningful item content seemed to sustain patients' concentration and motivation (Voruganti and others 1995). Ideally, the battery should include a self-administered scale, a clinician-administered scale, and a method to quantify clinical symptom severity, insight, and side effects of antipsychotic medication.

Two general limitations are worth noting. First, making trade-offs while devising a quality of life measurement strategy is often inevitable. Reconciling with limitations imposed by the study design, methodology, clinical population, and resources is a frequent and vexatious experience for researchers in the field. While the trade-offs are often inevitable, their effect on the overall purpose of the study should be kept in perspective. The shortcomings of a design influence the quality of data obtained and impose restrictions on where and how it might be used. Second, quality of life is an evolving field of study, and the proposed approach is intended to outline the issues that need to be considered in a field marked by considerable confusion and controversy. This comprehensive strategy, however, allows clinical validation and further refinement of quality of life models in schizophrenia. Considering its elusive nature, all attempts at studying quality of life in clinical populations should have a built-in mechanism to test the original assumptions and theoretical frameworks, which remain far from perfect at this juncture.

Implications for further research

Future research in this area should explore the sources of difficulties identified earlier. Conceptual studies should concentrate on identifying the goals of the study and developing situation-specific models of quality of life suitable for various subpopulations of schizophrenia (for example, acute versus chronic, 1st-episode versus recurrently ill, and early-onset versus late-onset cases). Research into psychometric issues should involve studying new approaches to measurement, for example, applicability of econometric measures of quality of life (utility), as well as expanding the role of quality of life measures, for example establishing their sensitivity to change. The value of self-administered scales can be further enhanced by improving the accuracy of patients' responses through developing visual aids, using novel rating methods, and exploiting the range of options offered by computers (Llewellyn-Thomas 1984). At the clinical level, determining the effect of insight, neurocognitive deficits, and psychotic symptoms on the validity of patients' self-evaluations is crucial to refining the use of self-administered rating scales (Voruganti 1996; Atkinson and others 1997).

CONCLUSION

Quality of life measurement is often based on 2 simplistic and erroneous assumptions. First, there has been a tendency to measure isolated and circumscribed components of a clinical condition and present them as a quality of life profile. Second, researchers have placed too much emphasis on choosing a rating scale without appreciating the actual needs of the clinical population under study. The stakes involved

in quality of life measurement are too high and the implications of the measurement process too far-reaching for researchers to fail to appreciate these complexities. Instead, quality of life should be initially identified as a patient's global subjective judgement, and a sound measurement strategy should be employed once the clinical population is identified and its specific needs determined. Considering the vast range of rating scales already available, developing new scales seems redundant unless current measures can be demonstrated to be inappropriate. The emphasis should be on knowing what to measure under given circumstances, not on how to measure it.

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