Cost-Utility Analysis in Schizophrenia

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Estimation of quality of life is important to the study of the pharmacoeconomics of schizophrenia. The subject has gained popularity among policymakers, clinicians, and patients and their families, since the advent of new antipsychotic medications that are more expensive than older drugs yet have been shown to cause fewer side effects. Quantifying quality of life has been difficult, since studies often inconsistently define the concept or use rating scales that are inappropriate for the patient population. Utility analysis is a procedure that calculates subjects' preferences regarding living with various health states, given such options as trading more years of life at a lowered health state for dying sooner but having a strong health state during the last years of life. The feasibility of performing utility analysis among patients with schizophrenia was recently examined in a study carried out by the authors. This article reflects initial observations from that study of utility analysis and includes a discussion of problems still facing the study of quality of life and utility analysis.

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Estimation of quality of life is important to the study of the pharmacoeconomics of schizophrenia. The subject has gained more popularity among politicians, health maintenance organizations, policy makers, clinicians, and patients and their families in the time since the recent advent of a new generation of antipsychotic medications. The new antipsychotics have been proven to be much better tolerated, with much-improved side effect profiles. Still, they are more expensive than the old conventional antipsychotic medications. In the management of schizophrenia, a positive outcome involves more than just symptom relief, without uncomfortable medication side effects. It also involves improvement in aspects of quality of life: abilities for better self-care and use of leisure time, return to a productive role, and having fulfilling relationships with family and friends.

Raising the quality of life for persons with schizophrenia seems, at first, to lead to higher costs to the medical provider—for medications, rehabilitation programs, daily living assistance, and support groups. Clearly, the higher the level of quality of life obtained by treatment, the more likely that a person with schizophrenia will be a productive member of society and not simply a source of large medical expenditures and a recipient of social security or welfare. Therefore, the most cost-effective treatment is the one that brings about the greatest rehabilitation (the highest quality of life) even if it is more expensive in the short term. The alternative would be frequent relapses requiring repeated hospitalizations, which are the most expensive component of direct care.

Achieving the greatest improvement in quality of life serves the goals of all players in the health care system: the patient, the patient's family, the physician, the service provider, and the society at large. This article examines this goal, describes other problems that still must be addressed concerning quality-of-life research, and examines the feasibility of cost-utility analysis as a method of cost-effectiveness approach in schizophrenic populations.

QUALITY OF LIFE

Over the past few decades, quality of life has emerged as a new concept reflecting a new image of health viewed from a biopsychosocial perspective. Although the concept has been extensively outlined in several other medical conditions, it is only recently that it has received serious attention in psychiatric disorders, particularly in schizophrenia. Paradoxically, as the concept of quality of life has become so popular, it is in danger of fading away due to the lack of a coherent foundation for study. A good deal of interest has focused on measuring quality of life, with much less research devoted to understanding the concept itself, clarifying its boundaries, and elucidating the important factors that impact on it. In a recent review of measuring quality of life in schizophrenia,[1] we identified a num-

ber of problems that may have impeded research in this important area and may have contributed to the lack of interest in dealing with some basic issues.

The lack of agreement on a definition has lead to several definitions, mostly depending on the theoretical orientation of the researcher. The resulting array of measurement approaches reflects the broad boundaries of the concept but also undermines chances for comparing data across studies. There may be no agreement on a definition, or there may be several definitions that reflect the needs of different populations at different stages of the illness, yet it is imperative for researchers and authors in their publications to define the concept as they applied it in their research.

Another problem is that a plethora of rating scales is used in the studies. Many of them lack psychometric properties, are frequently unsuited to the population under study, or lack the sensitivity to discern differences, which can be small at times.

A third problem is the lack of adequate conceptual models that take into consideration the multidimensional nature of schizophrenia as well as the multiple approaches for its management. On one hand, most of the emphasis in the field of schizophrenia has been on the development of models from a rehabilitative perspective suitable for long-term management in the community. On the other hand, the recent development of new antipsychotic medications such as risperidone, olanzapine, quetiapine, and clozapine and the need to demonstrate their therapeutic superiority to offset their high cost requires the development of different conceptual models that not only can capture the impact of the illness but also the medication effects and adverse effects.

Another problem is the reluctance of researchers and clinicians to include patients' self-reports of their quality of life. Physicians have frequently viewed with suspicion the subjective assessment of treatment outcomes by their patients on the grounds that the reliability of such reports, at best, is questionable. It is true that schizophrenic patients frequently experience disturbed thinking and communication, yet an extensive literature, including ours, confirmed consistency and reliability of schizophrenic patients' reports about their level of satisfaction and inner feelings.[2–4]

Lastly, there is a lack of appreciation for the multidimensional nature of quality of life in many studies, particularly in some cost-effectiveness studies. A quality-of-life measure that produces only a single number on a scale representing global quality of life provides little help to clinicians who need specific information related to the various dimensions of functioning, to enable them to design more effective interventions. Obviously, there are several audiences for quality-of-life studies who need to be taken into account: clinicians are probably more interested in treatment strategies, health care administrators are

likely more interested in cost containment, those in charge of drug benefit plans or formulary decision making likely are interested in cost-effectiveness.

Such varying perspectives on treatment and its cost need to be taken into consideration and clarified in quality-of-life studies.

UTILITY ANALYSIS

While cost-effectiveness studies have long been used to make policy or formulary decisions for areas of medicine outside of psychiatry, they are just beginning to be used in psychiatry. These studies are greatly needed in schizophrenia, as it may be the most costly psychiatric illness to treat. Cost-effectiveness studies employ various methods of analysis, one of which is the cost-utility ratio.

The cost-utility ratio is a measure of particular treatment costs divided by the benefit the outcome produces. The paradox is that the treatment that is more expensive in the short run may provide the most economical results in the long run (better outcome and fewer relapses yielding lower expenses later). That is, if more is spent on medication and rehabilitation services at the beginning of the illness, the patient may achieve better and longer lasting work and social capabilities.

It is difficult to analyze cost of treatment for schizophrenia because there are many cost factors and several different perspectives on cost. The major expense is generally hospitalization, but comparing studies can be challenging due to differences in efficiency and procedures from one hospital to the next. Medication represents only about 5% of the total cost of treating schizophrenia,[5] which makes the use of a more expensive antipsychotic seem a rather trivial choice in the overall treatment picture. In addition, if a medication (even a more expensive one) can produce a better outcome in terms of positive and negative symptom reduction and improvements in cognitive capability, as well as fewer side effects such as extrapyramidal symptoms, then it may lead to a patient being better able to take advantage of a rehabilitation program and lessen current and future time in the hospital, which lowers cost to both the service provider and society.

Any decision making involves trading one outcome for another on the basis of individual preferences, which are determined by assigning values to the potential outcomes.[6] In order to determine medical funding priorities, decisions must be made regarding health state alternatives. Cost-utility analysis is one method that can be used to elicit preferences about health states. Subjects assign values to various health states, as to whether they are better than death and if so, how much better, and how much money the subjects would be willing to spend to use various treatments relative to the improvement(s) the treatments beget. For example, cost-utility analysis can calculate subjects' preferences about either living longer with a poor health

state or taking a treatment that may improve the state but will not lengthen life. Collective decision making, necessary for formularies, should require eliciting preferences from the appropriate constituency. If decisions are being made regarding treatment of schizophrenia, then the preferences of people with schizophrenia should be included in the process.

Two years ago, we reviewed[1] the measurement of quality of life in schizophrenia and admitted to skepticism about the feasibility of using utility analysis in a schizophrenic population, since cognitive impairments could hinder the ability of a patient with schizophrenia to complete cost-utility tests. In addition, delusions and hallucinations could be impossible for proxy test-takers to imagine. We decided to conduct a study of the feasibility of using utility analysis among a clinically stable and compliant schizophrenic population. The study was recently concluded and detailed results will appear elsewhere (A.G.A. and L.P.V., unpublished data). Here we highlight some preliminary data that illustrate the challenges and successes of utility analysis when applied to schizophrenia.

Six major questions had to be answered to determine whether the utility approach could be established as reliable and feasible in the schizophrenic population:

- Can patients with schizophrenia recall and describe the various health states experienced during the course of their illness?
- Can patients with schizophrenia judge various health states and assign value to them in a reliable and valid manner?
- Does their performance in this respect vary from that of patients with other major mental illnesses, such as depression?
- Do symptom severity and degree of insight, which often influence patients' appraisal ability, affect reliability and validity of their utility ratings?
- How extensively do patients' utility ratings concur with their clinicians' ratings?
- How extensively do the health state values obtained from traditional quality-of-life measures correlate with the utility values derived from the utility analysis techniques (i.e., what is the state of convergent validity?)

Method

The study included 120 patients with schizophrenia and a control group of 32 patients who had undergone treatment for major depression and were in the recovery phase. The control group was included to measure how the performance of the patients with schizophrenia would compare with performance of patients who had other psychiatric diagnoses. Stable schizophrenic patients were used, so that the clinical characteristics would be similar to those of patients seen in a medical clinic or in a university setting.

The clinical status of the sample was mildly to moderately symptomatic. Larger percentages of the depression group than the schizophrenia group were employed (63.3% vs. 15.9%), living independently (90.0% vs. 45.8%), and married (43.4% vs. 11.7%). A larger percentage of the schizophrenia group than the depression group were men (72.5% vs. 46.7%). The mean age at onset among the schizophrenic patients was 22.3 years, the mean duration of illness was 12.1 years, and the mean total number of hospitalizations was 4.3.

Utility measurement involves 2 steps: (1) establishing the health states experienced during the illness and (2) appraising and assigning values to them. The first research questions asked were whether the people with schizophrenia could perform both these tasks. The use of quality-of-life and utility measures in clinical populations requires that patients cooperate and have cognitive potential since utility analysis requires abstract thinking, a degree of critical self appraisal, and comparative evaluation—an ability to make trade-offs and assign numerical values to health states. It was hypothesized that the cognitive demands imposed by these tasks may be difficult for individuals with such a severe mental disorder as schizophrenia. The nature of disturbances in schizophrenia may have a detrimental impact on the subjective reference-based evaluations.

Before eliciting the health state descriptions, we established the following 5 principles. First, health state descriptions were to be obtained directly from patients and based on their personal experiences. The reason that this was insisted on is that it would be difficult for anyone without schizophrenia to approximate the experience of hallucination or delusion. Utility analysis is often used with physical disorders, in which healthy patients make preference decisions based on health state scenarios that frequently involve pain or discomfort. A proxy can imagine pain—all people have experienced physical pain at some level—but hallucinations and delusions are harder to imagine. Second, using a limited number of clearly distinguishable health states, with regard to severity and time of occurrence, for example, was considered crucial to ensure clarity and accuracy. Third, emphasis was placed on personal distress, disturbed behavior, and impaired function rather than on clinical diagnosis, hearsay impressions, or clinical/social consequences of the disorder. Fourth, descriptive verbatim accounts of personal experience were used, as opposed to multiple-choice–style questions and answers. Fifth, for the interview, a congenial setting was created, adequate time was allowed, and the use of visual aids and props was permitted, since for schizophrenic patients, some of the tasks on a utility analysis measure are quite taxing cognitively.

In appraising and assigning utility values to health states, the choice and technique of utility measurements were based on the following 4 premises. First, for the purpose of the study, all the different health states associated

Table 1. Feasibility Aspects of Utility Measurement*

Criterion	HSD	ME[a]	RS	SG[a]	TTO	WTP
Clarity of test procedure						
Schizophrenia group	9.82	9.38	9.63	4.32	9.38	9.17
Depression group	10.0	10.0	9.96	6.57	9.96	9.95
Cognitive burden						
Schizophrenia group	8.47	6.47	8.61	3.47	7.56	7.38
Depression group	10.0	8.45	9.51	5.58	8.57	8.50
Self-rated accuracy						
Schizophrenia group	8.13	5.56	8.73	6.78	8.35	8.10
Depression group	9.96	5.98	9.93	7.89	9.92	9.90
Interviewer's global ratings						
Schizophrenia group	8.44	3.26	8.78	3.56	8.43	8.12
Depression group	10.0	4.58	9.93	4.78	9.92	9.90

*Scores obtained from visual analogue ratings, ranging between 1 and 10. Abbreviations: HSD = health state descriptions; ME = magnitude estimation; RS = rating scale; SG = standard gamble; TTO = time trade-off; and WTP = willingness to pay. From A.G.A. and L.P.V., unpublished data.
[a]Data available only on the first 30 schizophrenic patients, after which ME and SG were dropped from the protocol.

Table 2. Intercorrelations Between Quality of Life and Utility Measures (for Current Health State)*

	RS	TTO	WTP	SG	SIP	QLS	GAF	Gurin's
RS	1.00	0.67[a]	0.002	0.73[a]	0.29[a]	0.17	0.06	0.71[a]
TTO		1.00	.09	0.74[a]	0.12	0.03	0.01	0.47[a]
WTP			1.00	0.09	0.26[a]	0.05	0.29[a]	0.01
SG				1.00	0.41[a]	0.64[a]	0.58[a]	0.41[a]
SIP					1.00	0.28[a]	0.34[a]	0.24[a]
QLS						1.00	0.76[a]	0.04
GAF							1.00	0.05
Gurin's								1.00

*Abbreviations: GAF = Global Assessment of Functioning; Gurin's = Gurin's quality-of-life measure; QLS = Quality of Life Scale; SIP = Sickness Impact Profile. From A.G.A. and L.P.V., unpublished data.
[a]Statistically significant (p < .05).

with schizophrenia were considered to be chronic and better than death. Second, since the nature of the disorder demands subjective assessment, patients themselves were deemed to be the most suitable judges of their own health states. Nurse-clinicians who knew the patients well were used as alternative sources for value of health states. Third, global quality-of-life measures were chosen, since little is known about the key determinants of quality of life in schizophrenia. Finally, traditional techniques of assessing quality of life (generic and disease-specific) were also employed to cross-validate the utility values obtained. The study included several quality-of-life measures: the Quality of Life Scale (QLS)[7]; a condensed version of the Sickness Impact Profile,[8] as modified by us (with permission from the scale developers) for previous clinical trials[9–11]; the Global Assessment of Functioning (GAF)[12]; and Gurin's scale,[13] which is a single question aimed at eliciting a global subjective rating of quality of life on a 5-point Likert scale. Other clinical data were collected by using instruments such as the Positive and Negative Syndrome Scale (PANSS)[14] as well as scales that assess awareness of mental disorders.

In addition to health state descriptions, 5 conventional methods of utility measure were chosen and modified to the needs of the study populations. These were the magnitude estimation, rating scale, standard gamble, time trade-off, and willingness-to-pay measures.[15] These quality-of-life measurements translate a person's subjectively appraised quality of life into more tangible criteria such as the magnitude of the risk taken or the willingness to trade some years of life or a certain amount of money in order to achieve or avoid a certain health state.[7] These measures, developed by health economists, combine quality and quantity of life to derive a figure known as quality-adjusted life-years (QALYs), or years of life with a certain health state due to a preference decision. We assessed willingness to pay in terms of percentage of income because of

concern that the willingness-to-pay questions favor people who have more money, and most patients with schizophrenia have limited incomes.

Results

In brief, the results indicate that schizophrenic patients could distinguish and describe specified health states with an equal degree of ease and accuracy and with a fair degree of reliability and validity. Severity of psychotic symptoms and lack of insight did not affect the reliability and validity of patients' appraisals, although their impact was more evident in a small proportion of patients with chronic severe forms of illness.

Table 1 shows the comparison between responses of the schizophrenia group and those of the control group. We used 4 operational criteria for determining feasibility of these methods in the schizophrenic population: clarity of the test procedure, self-rating accuracy, cognitive demands associated with each task, and raters' confidence in the data. Generally speaking, both the depressed population and the schizophrenia population had some difficulties, but the schizophrenia population had more difficulty than the depressed population. However, the depressed population was in a stage of recovery. The difficulties for the schizophrenia population were particularly with magnitude estimation and standard gamble. Many were unable to complete those tests, which were abandoned after the first 30 patients.

The results from this study were all significant (p < .05) in terms of test-retest reliability, when Pearson's product moment correlation was used to analyze the data. We were interested, also, in the convergent validity between direct measurements of quality of life and the utility measures for current health state (Table 2). The single utility approach that correlated best with direct measurement of quality of life was standard gamble. Time trade-off and rating scale correlated well. However, additional study is needed to determine the clinical significance of the correlation.

When we tested the concurrent validity of patients' and nurse-clinicians' utility ratings, we found that under

blinded conditions, there was no correlation. However, in situations where the nurse-clinicians were familiar with the patients, the ratings concurred significantly.

Discussion

On the basis of the results of our study, we conclude that utility analysis is feasible among patients with schizophrenia. However, some issues must be resolved. First, can such an approach reflect individual preferences? The calculation of QALYs, or years of life adjusted by weights, only partially incorporates patients' preferences, since the utility approach is used only to obtain the weights. Another issue is how to establish the reliability and validity of the weights assigned.

A second issue is whether the utility approach can allow for the examination of the effect of various interventions on quality of life. Utility analysis does not provide a profile of quality of life but instead establishes a numerical score to be used for comparison. This numerical score is unlikely to be useful in clinical decision making because clinicians need to assess the deficits in order to take corrective action. The utility approach is more suited to cost analysis in the course of resource allocation decisions or comparison of programs, rather than to clinical decisions.

Third, the method can be difficult to follow, and the results are often expressed in language that impedes rather than facilitates communication and understanding. Challenges to using this approach lie in getting clinicians and health economists to understand each other's languages and perspectives and in being able to translate utility analysis results into meaningful information for clinical decision making.

The utility approach is attractive and worth exploring. It appears to be feasible among at least a percentage of the schizophrenic population. Since utility analysis is unlikely to be suitable for acutely psychotic patients or those with severe cognitive impairments, study is needed to determine when to use utility analysis.

CONCLUSION

In summary, the authors strongly recommend basic studies that define the elements that comprise quality of life in terms of what abilities or freedoms must be gained for a patient with schizophrenia to attain the highest level of satisfaction possible and perhaps even become a productive member of society. Using utility analysis testing with the schizophrenic population appears to be feasible; asking the patients for a self-report about their quality of life is important in order to cater to their individual expectations and needs. However, more research is needed to clarify several important questions about utility analysis before its utility in cost-effectiveness analysis and clinical decision making is clearly established.

Drug name: haloperidol (Haldol and others).

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