

The Impact of Schizophrenic Patient Functionality on Service Utilization and Cost

Based on a presentation by Sandra L. Tunis, PhD

Presentation Summary

With the advent of atypical agents in the treatment of schizophrenia, physicians and policy makers must consider the costs that may accompany greater clinical efficacy. Analyses reveal that olanzapine shows a greater clinical cost effectiveness, as well as a greater functional cost effectiveness, than haloperidol, and that functional outcomes, in particular, show promise as important measures of effectiveness.

Functional outcomes can help differentiate medications and can be used to help demonstrate the

cost effectiveness of atypical agents. Mental health and physical health functioning, as well as work status, are all measures of functioning that have been used to evaluate treatment strategies. When comparing olanzapine with haloperidol, cost savings are seen throughout the treatment period (1 year), with physical functioning most highly affected over time. Functional outcomes can therefore serve 2 purposes: to enhance compliance by improving health-related quality of life and to assist in making both treatment and formulary decisions.

In looking at the true value of new-generation antipsychotic medications, it is important to look not only at clinical cost effectiveness but also functional cost effectiveness," said Sandra L. Tunis, PhD, Research Scientist, Health Outcomes Evaluation Group, Lilly Research Laboratories, Eli Lilly & Company, Indianapolis, Indiana. She added that the overall goal of the research is to assess whether the superior safety and efficacy profile of newer medications translate into improved quality of life for the individual with schizophrenia. The impact of patient functionality on cost is a timely topic in the age of consumer awareness and cost containment.

Quality of life and its aliases—community adjustment and reintegration—are sometimes difficult to quantify, according to Dr. Tunis. Yet for the schizophrenic patient, they are important factors in determining the best treatment option. As Dr. Tunis emphasized, quality-of-life criteria are describing, in essence, a return to a more normal level of functioning. And if medications produce this return to more optimal functional levels, then a simultaneous reduction in the need for health services and costs is expected.

Dr. Tunis presented results from 2 data analyses from a randomized, double-blind, clinical trial. The clini-

cal trial had 2 phases: the acute 6-week phase and the responder-extension phase to 1 year. Analyses were performed to examine the incremental cost effectiveness of olanzapine versus haloperidol on both clinical and functional outcomes.^{1,2} (Incremental cost effectiveness is defined here as the difference in the mean annual treatment cost between olanzapine and haloperidol divided by the mean difference in effectiveness measures.) The results suggest significant cost savings and improved outcomes for both criteria. They validate the importance of including both types of measurements in comparing outcomes associated with pharmacotherapies.

Table 1. Intent-to-Treat Analysis: Outcomes

<p>Effectiveness: Total number of BPRS-based symptom-free days, defined as a BPRS total score of ≤ 18, normalized scoring system, over the 52-week interval</p> <p>Cost: Total direct healthcare expenditures incurred by patients in US dollars (1995 values) over the 52-week interval of therapy</p>

Table 2. Medical Resource Utilization

<p>Estimates of direct healthcare expenditures included:</p> <ul style="list-style-type: none">■ Hospitalizations■ Day hospital sessions■ Emergency room visits■ Outpatient visits to psychiatrists■ Outpatient visits to other mental health providers■ Outpatient visits to other physicians■ Home visits by health professionals■ Study and concomitant medications

Clinical Cost Effectiveness

The clinical trial compared olanzapine to haloperidol in patients with diagnosed schizophrenia, schizophrenic disorder, and schizophreniform disorder.³ Dr. Tunis and colleagues performed an intent-to-treat analysis on US patients to answer the following question: Do patients (responders and nonresponders) who initiate on olanzapine (versus haloperidol) achieve superior clinical, functional, and economic outcomes over 1 year?

Using the number of Brief Psychiatric Rating Scale (BPRS)-defined symptom-free days to measure effectiveness and the total direct healthcare expenditures incurred by patients as costs, the incremental cost-effectiveness ratio was calculated (Tables 1 and 2). Medication acquisition costs were incorporated within the total cost calculations.² The results showed savings of \$563 per symptom-free day based on incremental cost effectiveness.

Bootstrapping analysis, in which the calculations are repeated 25,000 times, reveals a 96.4% probability of replicating the data, validating the stability of the calculations. These results are especially striking when the acquisition costs of olanzapine are considered. Olanzapine costs more in up-front acquisition expenditures yet still produces significant cost savings when considering improved effectiveness.

Are Functional Outcomes a Reliable Indicator?

Functional outcomes, while providing a wealth of valuable information, do not offer the same level of precision as clinical outcomes. Yet, Dr. Tunis' early work on functional outcomes using the Medical Outcomes Study 36-item short form health survey (SF-36), a quality-of-life indicator, reveals a compelling picture that the instrument is valid and reliable in a schizophrenic population with no significant floor or ceiling effects.⁴⁻⁸ The

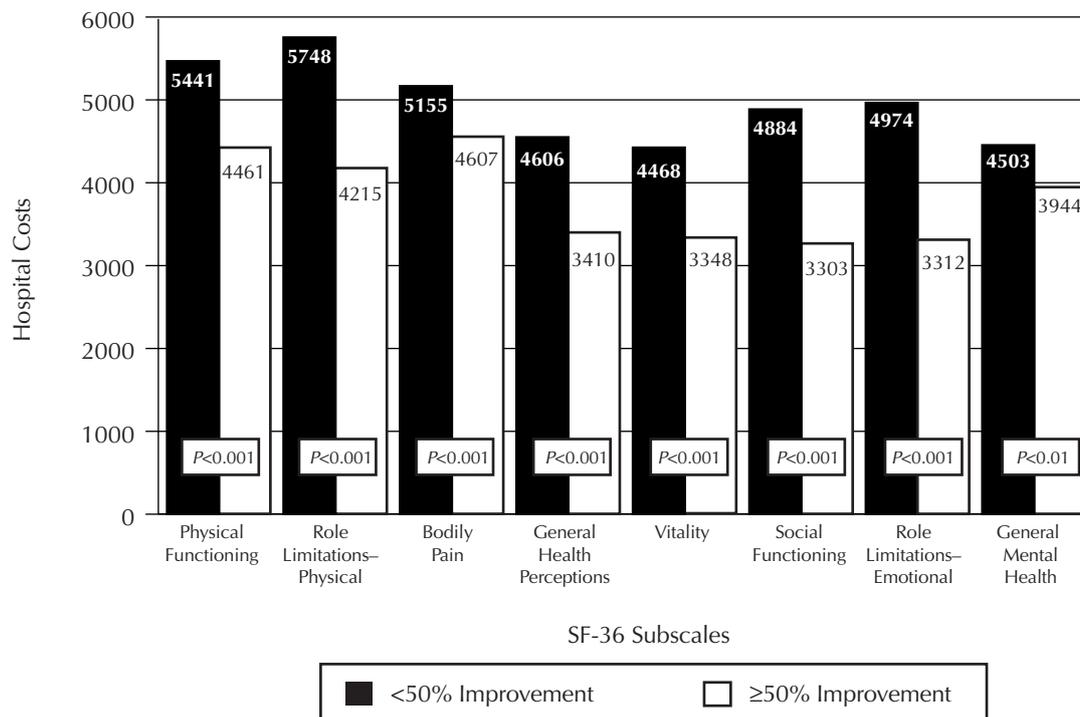
data also offer interesting insights into the individual burden of illness, changes in health status while patients are medicated, and the importance of specific physical and mental health variables in evaluating functional outcomes. For example, baseline comparisons of SF-36 values between the general US population and those of the study participants showed significant levels of impairment in several health and functioning domains, including general health perception, vitality, social functioning, physical and emotional role limitations, and general mental health.^{8,9}

After 6 weeks, olanzapine had a significantly greater effect for 5 of the 8 SF-36 subscales, illustrating that the self-report of social functioning and health status can differentiate treatments (in this case, medications).

Functional Cost Analyses With SF-36

Results of an exploratory analysis of the relationship between health-related functioning and well-being to hospital costs at 6 weeks are shown in Figure 1. For each of the 8 SF-36 domains, patients who achieved at least 50% of their possible improve-

Figure 1. Tests of Differences in Hospital Costs in Dollars at 6 Weeks for Patients Who Improved by 50% in Health Status Versus Patients Who Did Not Report Major Improvements



Source: Tunis SL, Johnstone BM, Gibson PJ, Loosbrock DL, Dulisse BK. Changes in perceived health and functioning as a cost-effectiveness measure for olanzapine versus haloperidol treatment of schizophrenia. *J Clin Psychiatry* In press. Physicians Postgraduate Press. Reprinted by permission.

ment over baseline in the first 6 weeks of treatment had significantly lower hospitalization costs. Also, at 52 weeks, patients who reported at least 50% improvement in perceived physical functioning, general health, and vitality had significantly lower hospitalization costs.

Cost Effectiveness With Functional Outcomes

Having established functional outcomes as reliable indicators of cost, Dr. Tunis performed cost-effectiveness analyses using 2 factors of the SF-36 data: physical health and well-being and mental health and functioning. The results indicate substantial savings (\$9386.87) with olanzapine treatment after 1 year, as well as improvements in both physical health and mental health criteria.

Bootstrap analyses showed these savings calculations to be highly stable for the physical domain (89%) and somewhat less stable for the mental health domain (Figures 2 and 3).

According to Dr. Tunis, this reflects that the mental health domain is a distal outcome (ie, an outcome upon which extrinsic factors other than the treatment of interest exert influence).¹⁰ Over 52 weeks, Dr. Tunis added, that there were a number of potentially powerful intervening variables, resulting in significant impact on the outcome data.

Dr. Tunis suggested that given the complexity and multiple determinants of functional outcomes, demonstrating even modest effects represents an important advance.¹¹

Supporting Studies

Employment status has shown to be another valuable indicator of functional outcome. Analyses from the same clinical trial of olanzapine versus haloperidol show that observers can differentiate between these medications by looking at employment status. Although the percentage of olanzapine-treated patients who reported working full- or part-time was similar to haloperidol-treated patients during the first 6 weeks of treatment (11.2% versus 9.4%, respectively), the proportions diverged significantly in favor of olanzapine during the next 46 weeks (19.4% versus 8.4%, $P < 0.001$) among those responding to treatment.^{11,12}

Dr. Tunis briefly discussed other heuristic studies that support the relationship between employment intervention and the effects of different medications. Those studies showed that negative symptoms represent a major barrier to employment for people with schizophrenia.¹³ Atypical agents may allow these individuals to take increased advantage of rehabilitation efforts.^{14,15}

Dr. Tunis further supported this paradigm by presenting data from an outside investigator. A cross-sectional observational pilot study at a rehabilitation center in Chicago was performed to evaluate the interaction between medication (atypical versus

Figure 2. Percent of Bootstrap Replication Results in Each Cost-Effectiveness Quadrant: Physical Health

		Hospital Costs	
		HAL less costly	OLZ less costly
Effectiveness Physical Health Factors (BP, PF, RP)	OLZ more effective	< 1 %	89 %
	HAL more effective	< 1 %	11 %

Results at 52 weeks.

OLZ = olanzapine; HAL = haloperidol; BP = bodily pain; PF = physical functioning; RP = role limitations due to physical health problems.

Source: Tunis SL, Johnstone BM, Gibson PJ, Loosbrock DL, Dulisse BK. Changes in perceived health and functioning as a cost-effectiveness measure for olanzapine versus haloperidol treatment of schizophrenia. *J Clin Psychiatry* In press. Physicians Postgraduate Press. Reprinted by permission.

conventional antipsychotic agents) and supportive employment interventions.¹⁴ The Positive and Negative Syndrome Scale (PANSS) data were examined using 5-factor analytic subscales (positive, negative, and cognitive symptoms; hostility; and emotional discomfort).¹⁶ Those taking atypical agents showed significantly fewer cognitive symptoms and significantly less hostility than those taking the older drugs. Hostility was, in turn, significantly correlated with level of employment as measured by an 8-point continuum. Furthermore, fewer cognitive symptoms were significantly related to placement in an integrated work setting.¹⁷

What is clear is that there is a difference in cognitive symptoms between atypical agents and conventional treatments and, according to Dr. Tunis, “this points to neuropsychological symptoms as potentially instrumental in work-placement outcomes.” In fact, others have suggested a paradigm shift in the definition of treatment success for schizophrenia, in which success is measured by improved cognitive function, rather than by clinical symptom improvement alone.¹⁸

Conclusion

In these analyses, olanzapine displayed both cost- and functioning-effectiveness advantages over haloperidol over the 52-week treatment interval. This was particularly true when effectiveness was defined by perceived physical health and functioning. Olanzapine treatment reduced average annual hospital costs in this analytical sample by \$9387.87 compared to haloperidol treatment.

These findings for physical health and functioning seem to indicate that olanzapine may hold great promise for improving the long-term physical aspects of functioning, which may have important implications for health service utilization. This study adds to the body of accumulating evidence that subjective patient experi-

ences of outcomes are not only valuable from an individual patient perspective, but can be linked to tangible endpoints of medical resource utilization and cost.¹⁹⁻²²

Furthermore, several secondary or pilot analyses suggest the superiority of atypical agents for strengthening work outcomes, possibly through neuropsychological effects. Together, these data suggest that functional measurements hold promise for quantifying important aspects of a medication’s cost effectiveness.

As Dr. Tunis stressed, future intervention studies should include patient functioning as effectiveness domains. Data on patient functioning and resource utilization must continue to be linked in order to capture the full economic and humanistic value of the new generation of atypical antipsychotic medications.

Acknowledgement

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Figure 3. Percent of Bootstrap Replication Results in Each Cost-Effectiveness Quadrant: Mental Health

		Hospital Costs	
		HAL less costly	OLZ less costly
Effectiveness Mental Health Factors (MH, SF, RE)	OLZ more effective	< 1 %	62 %
	HAL more effective	< 1 %	38 %

Results at 52 weeks.

OLZ = olanzapine; HAL = haloperidol; MH = mental health; SF = social functioning; RE = role limitations due to emotional problems.

Source: Tunis SL, Johnstone BM, Gibson PJ, Loosbrock DL, Dulisse BK. Changes in perceived health and functioning as a cost-effectiveness measure for olanzapine versus haloperidol treatment of schizophrenia. *J Clin Psychiatry* In press. Physicians Postgraduate Press. Reprinted by permission.

Laboratories, Eli Lilly and Company, Indianapolis, IN and School of Public and Environmental Affairs, Indiana University, Blomington, IN; P. Joseph Gibson, PhD and Danielle L. Loosbrock, MHA, Health Outcomes Evaluation, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN; and Brian K. Dulisse, PhD, Statistical and Mathematical Sciences, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN assisted in the compilation of data for this study.

... DISCUSSION HIGHLIGHTS ...

Dr. Lehman: A recent paper showed that symptoms measured by PANSS/BPRS and clinician-rated quality of life by Heinrichs-Carpenter measure or Level of Function Scale were sensitive to between-treatment effects, and that the self-report measures were not.²³ You have also found a stronger effect for clinician ratings than for patient self-report. It raises the dilemma of whether patient self-report measures are not as reliable, or if patients have a different perspective on what is considered outcome. How do you manage this dilemma when evaluating the utility of your cost measures?

Dr. Tunis: The patient self-report is not perfect, but it is better than most have believed. My own opinion is that it's a combination of the things you mentioned. Human behavior is not as predictable as clinical symptoms. We can't try to show with 95% confidence that someone can function in a more optimal way due only to long-term medication effects. Medication allows patients to become more engaged in their treatment. So we have to take a more global perspective.

Dr. Noordsy: When we talk about recovery, we need to measure that from all directions. You're talking

about a multiply-determined overall outcome. And I don't think there's a problem with having some independence between improvements in symptom ratings—improvement in clinician-rated quality of life—and that of patients. They may, in fact, improve at different rates and relate to different things.

Dr. Aquila: They may improve at different times as well. As you separate out the proximal from the distal outcomes, I think you'll see the quality-of-life scales go up in accordance with BPRS and PANSS. The distal outcomes take more time. I think the measures are valid, and over time it starts to come out.

Dr. Lehman: Hans Strupp, a psychotherapy researcher at Vanderbilt, coauthored an article discussing the different perspectives on outcomes: for the patient, the therapist, and the family.²² It's important to know the different perspectives as it may help to explain why a patient wants to stop therapy, but the therapist and the family want to continue. Measuring those differences can help to improve compliance. It's not so important to determine which one is valid.

Dr. Tunis: I'm very happy we are discussing these issues, as the relationship of cost effectiveness to quality-of-life measures was not considered a few years ago. My own view is that it is important to look at both clinical and functional outcomes in cost-effectiveness studies and to apply this information in making treatment decisions.

Dr. Noordsy: Your findings on improvement in quality of life and reductions in healthcare costs are important for the field. They allow us to say, "This is important to measure."

Dr. Tunis: The bottom line is: it is important to show that patient rat-

ings are not only valid and reliable, but also have implications for service utilization and cost. They are worth our attention.

Dr. Noordsy: It validates the beliefs of those of us in the field who want to make holistic interventions by addressing housing and work, etc. These issues have a big impact on people's quality of life.

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