

Atypical Antipsychotics and Formulary Decisions

Based on a presentation by William M. Glazer, MD

Presentation Summary

Although drug costs are a small fraction of the total direct costs of treating schizophrenia, managed care has focused on drug acquisition costs as an area of concern. There is pressure to demonstrate by outcome measures that the increased cost of the newer atypical antipsychotics versus traditional neuroleptics is justified. Decision makers want to be convinced that newer, more expensive treatment translates to value. Evidence accumulated to date suggests that the atypical

agents are cost-effective. Studies show patients taking atypical antipsychotics have an improved quality of life, are more easily rehabilitated and reintegrated into the community, return to full- or part-time work more often, and prefer the newer agents to conventional antipsychotics. These benefits have been shown in studies of olanzapine versus haloperidol. Just as important, patients taking atypical antipsychotics show decreased medical care resource utilization, which results in cost savings.

The difference in acquisition costs between the newer atypical and traditional antipsychotics is dramatic, said William M. Glazer, MD. The monthly cost to pharmacists for haloperidol 5 mg/bid is \$1.70 compared to olanzapine 10 mg/day at \$233 or risperidone 3 mg/bid at \$241 per month [*Medical Letter*, April 11, 1997] (Figure 1). This disparity has captured the attention of institutions and state planning groups, raising concerns about whether or not the higher costs of the atypical antipsychotics translate to better value.

A 1990 survey (Figure 2) found that drug costs comprised only 2% of the total direct costs of treating schizophrenia—a “strikingly” small percentage, noted Dr. Glazer.^{1,2} By the year 2000, it is possible that drug costs may account for as much as 10% of total direct costs—still a small

percentage when considering the overall costs of the disease (Table 1).

Dr. Glazer emphasized the importance of asking these critical questions regarding drug treatment:

- What is the impact of drug costs on other *direct* costs of treating the disease including hospitalizations?
- What is the impact of drug costs on the *indirect* costs, including patient quality of life, patient satisfaction, and lack of productivity?
- Is the higher cost of the newer drugs relative to the older, generic drugs worth it?

Effect on Quality of Life and Productivity

To address drug effects on quality of life and productivity, factors in addition to efficacy should be considered, includ-

ing integration into the community, suicidality, employability, and productivity, as well as resource utilization and medical costs. Looking at how newer drugs impact these measures might provide a more comprehensive, accurate understanding of their value, Dr. Glazer explained.

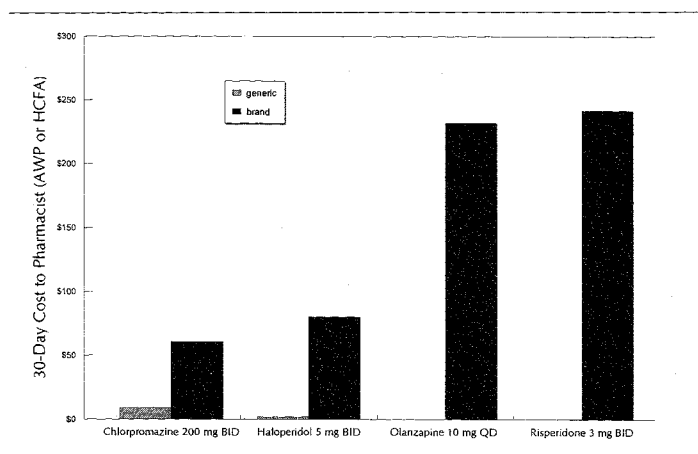
The impact of a drug can be viewed in terms of proximal effects (how a drug works on the positive and negative symptoms of schizophrenia) and distal effects (ie, functional status, quality of life, family well-being, and public safety). Feedback on the proximal and distal effects of antipsychotic agents can then be related to costs. The proximal effects of the newer agents, including clozapine, risperidone, and olanzapine, have been clearly demonstrated in clinical trials.

Clinicians are just beginning to embrace the concept of quality of life and measure it in the clinical setting, Dr. Glazer said. Quality of life is a subjective and somewhat elusive concept that has been defined by Testa and Simonson³ as the "physical, psychological, and social domains of health, seen as distinct areas that are influenced by a person's experiences, beliefs, and perceptions." Quality of life is a multidimensional domain that focuses on both the person's subjective reports and objective ratings.

In the past, clinicians were reluctant to measure quality-of-life outcomes because the concept was viewed as "soft" or undefinable (Table 2). It is difficult to devise instruments that measure quality of life and to select outcome criteria; in addition, Dr. Glazer pointed out, there is skepticism about validity of self-reports from patients with schizophrenia, as well as the lack of a conceptual model to tie in quality of life with treatment—especially for neuroleptic medications. However, there are some excellent scales with demonstrated validity, and clinicians are now in a better position to assess quality of life.

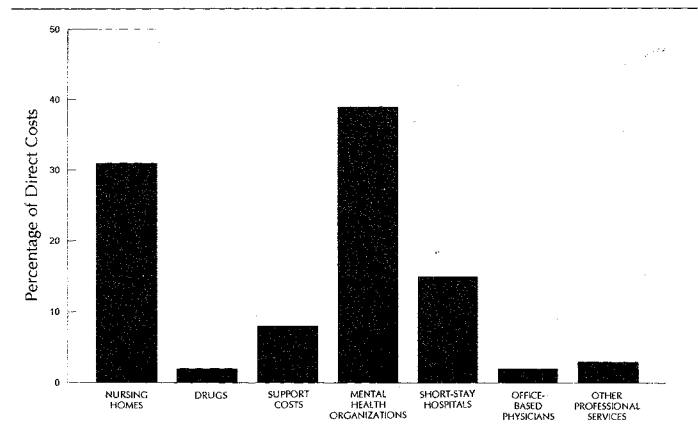
"In all probability, quality-of-life measures will become increasingly important—perhaps as important as symp-

Figure 1. Cost of Antipsychotic Drugs



Source: Medical Letter, April 11, 1997 Used with permission.

Figure 2. Direct-Cost Percentages



Source: Adapted from Rice DP, Miller LS. The economic burden of schizophrenia: Conceptual and methodological issues and cost estimates. In: Moscarelli EM, Sartornes N. *Schizophrenia*. New York: John Wiley & Sons, 1996

Table 1. Overall Direct Healthcare Costs

■ Inpatient hospitalizations
■ Outpatient hospitalizations
■ Emergency room visits
■ Outpatient visits to psychiatrists, other mental healthcare professionals, and other physicians
■ Home visits by healthcare professionals
■ Medications

Table 2. Why Quality of Life Outcomes Are Not Measured in Psychosis Treatment

- Quality of life (QOL) is viewed as too subjective, undefinable
- Instruments that measure QOL are difficult to design
- There is controversy as to what is a "good" or "optimal" outcome
- Accuracy of self-reports from patients with schizophrenia is viewed as dubious
- There has been lack of a well-accepted conceptual model linking QOL with antipsychotic medications

toms—in treatment planning," Dr. Glazer predicted.

Studies of Quality of Life

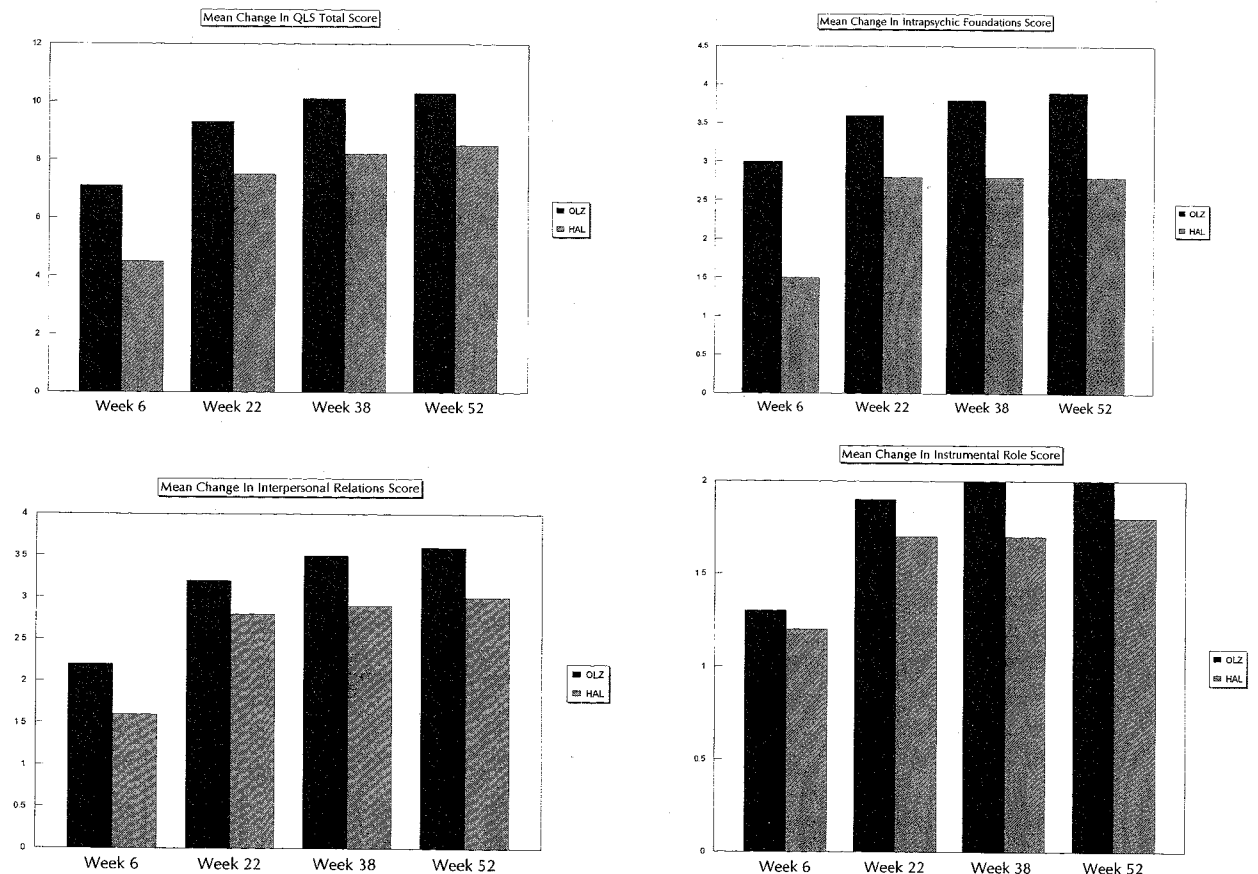
Although there is still a dearth of data on quality of life and treatment in psychosis, the list of studies is growing about quality of life as a predictor of rehospitalization in the seriously mentally ill population. In general, these

studies show improved quality of life over time with atypical antipsychotics compared to classic medications [*Psychiatric Services* 1995;46:1161-1165].^{4,5}

Several studies comparing olanzapine to haloperidol have been completed.⁶⁻⁸ In one, olanzapine was compared to haloperidol over time in responder patients (Figure 3). Outcomes instruments included the Heinrich-Carpenter Quality of Life Scale (QLS), overall treatment effectiveness, and a resource utilization questionnaire (including questions about suicide attempts, employment/schooling, and medical resource use). Costs were calculated using standard costs.

Using these measures, olanzapine was shown to be statistically superior to haloperidol in effect on quality of life.

Figure 3. Olanzapine versus Haloperidol: Long-Term Follow-Up (Weeks 6, 22, 38, and 52 LOCF)



When functional measures were used, the effect of olanzapine versus haloperidol was even more evident. A 2.3-fold difference was found in rates of suicide attempts favoring olanzapine (Figure 4). Another study showed that over time, twice as many patients taking olanzapine were able to return to part- or full-time employment compared to haloperidol-treated patients. Taken together, these data suggest that newer atypical antipsychotic agents are doing a better job at encouraging rehabilitation. This poses a challenge to policy makers to develop rehabilitation programs that would allow patients to benefit from the effects of the atypicals.

"In most of these studies, quality-of-life assessments were added on to drug studies. It would be more to the point to compare these drugs in studies that include vigorous rehabilitation efforts," suggested Dr. Glazer.

Translating Effects into Costs

If outcomes were the same for older versus newer treatments, it would be logical to choose the less expensive treatment. However, Dr. Glazer pointed out that better outcomes have been demonstrated with the atypical antipsychotics. Studies also show these better outcomes translate to cost savings. Looking at medical resource utilization, the newer drugs reduce utilization of medical resources compared to traditional antipsychotic drugs, particularly on the inpatient level. After the launch of clozapine—the first atypical antipsychotic to be introduced—a study demonstrated an \$8000 decrease in mental health costs per year per patient.⁴

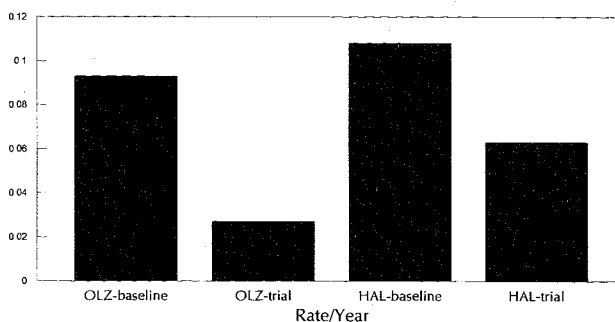
"The message from this study was that if patients remained on clozapine, it would result in cost savings," said Dr. Glazer.

An open-label study of long-term inpatients showed that patients stayed out of the hospital longer when treated with clozapine versus traditional antipsychotic medication.⁵ A prospective, randomized, head-to-head comparison of clozapine versus haloperidol in 15 hospitals in the Veterans Administration

system showed that clozapine paid for itself over 1 year by lowering total healthcare costs by \$2241 per patient.⁹

A retrospective review of 146 patients refractory to conventional antipsychotics who were then treated with risperidone showed an annual estimated cost savings of \$7925 (Canadian dollars) per patient. In this trial, the direct medical costs of risperidone treatment over 1 year, including hospitalization, were compared to costs incurred in the year prior to taking risperidone.¹⁰

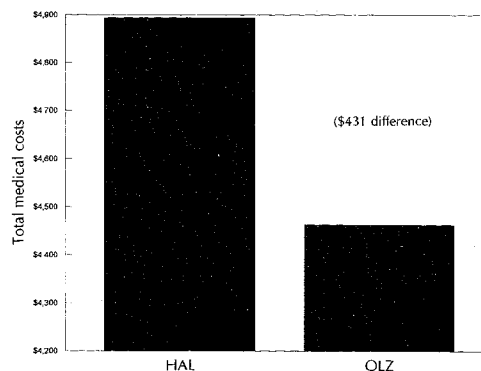
Figure 4. Suicide Attempt Rates Per Year (Adjusted)



Olanzapine rate calculated as a function of 17 suicide attempts in 627 patient months; haloperidol rate calculated as a function of 12 suicide attempts in 190.25 patient months: 2.3x difference.

Source: Olanzapine versus haloperidol and placebo studies.⁶⁻⁸

Figure 5. Mean Medical Costs Per Month by Treatment Group, Acute Phase (Weeks 1-6)



A double-blind study of 817 patients compared olanzapine 5 to 20 mg/day with haloperidol 5 to 20 mg/day. Results showed that acutely, in the first 6 weeks, haloperidol was much less expensive.¹¹ However, the extended phase of the study revealed that inpatient costs went the opposite direction. Olanzapine-treated patients had a \$615 per-patient-per-month reduction in costs for inpatient care compared to haloperidol. Outpatient medical costs were reduced by \$25 per patient per month. Olanzapine saved \$431 per patient per month in total medical costs (Figure 5).

The extended protocol of this olanzapine-versus-haloperidol study¹¹ showed that the reduction in inpatient costs over 1 year (\$403 per patient per month) more than paid for the cost of olanzapine compared to haloperidol. A reduction of \$154 per patient per month in outpatient medical costs was found in the olanzapine-treated group compared to the haloperidol group. Total medical costs over 1 year yielded a \$345 per-patient-per-month savings with olanzapine. It can be concluded from these studies that olanzapine, in a well-controlled study of responder patients, at least pays for itself.

Conclusion

Taken together, a body of evidence demonstrates that the newer atypicals improve patient quality of life, decrease resource utilization, pay for themselves, and cause less tardive dyskinesia than conventional antipsychotic agents.

"This is a strong argument that the newer drugs have tremendous value in terms of dollars and quality of life for both the patient and family," concluded Dr. Glazer.

... DISCUSSION HIGHLIGHTS ...

Atypical Agents and the Pharmacy Budget

Dr. Petty: In situations where the pharmacy budget is separate from the

budget for other items, I have heard pharmacists say that even if the drug has more benefit, they don't want to pay for it. How do you deal with that?

Dr. Glazer: This is a political issue where organizations such as the National Alliance for the Mentally Ill (NAMI) and the hoofbeats of consumerism will play a role. Consumers demand value. I predict we will see the formation of a new clinician-consumer alliance that will lobby against restricted access to newer drugs and demand data showing the impact of these drugs on total cost.

Dr. Simpson: In California, consumer groups have been successful in getting permission to use certain drugs that are then included on the formulary. It is important to make the point that the newer drugs from one class—such as the selective serotonin reuptake inhibitors (SSRIs)—and newer drugs from another—such as the atypical antipsychotics—are not alike.

Dr. Verma: Data are conflicting on the benefit of antipsychotics in nursing home patients. I remember seeing one study—I can't recall where—that showed only 18% of all patients who received conventional antipsychotics had some degree of modest improvement. The argument for newer atypicals is going to become even harder to justify in long-term settings where pharmacists and administrators are determined to use the least expensive drug possible.

Dr. Glazer: We often see this in capitated systems because capitation typically includes drug cost. In most systems, the drug cost is considered separately, so the move to the cheaper drug is natural. However, I think you will see a different attitude when drug costs are included in total capitation rates, because these data are about efficiency. If you can show what the overall cost means to the bottom line, the value of the atypicals will be clear.

Dr. Simpson: Physicians will always have to face arguments about getting new medications on the formulary—especially considering that there are so many formularies in the United States. Ironically, indigent patients on Medicare can often get a new drug more easily than more well-to-do patients who have health insurance.

The Need for Data

Dr. Kinon: The elderly are a challenging population in which to demonstrate cost effectiveness. One approach would be to use a different set of measurements: that is, determining how long an elderly person can remain at home with the family versus going into a nursing home. If one could demonstrate that the atypicals allow elderly people to remain at home with their families longer, and that these drugs control behavioral agitation or psychosis, that would translate to a significant cost savings. It may be more difficult to demonstrate benefits once a patient is in the nursing home.

Dr. Verma: Actually, it isn't. Drug costs in the nursing home account for 7% of total costs of care. The people who manage the money keep tweaking the percentage allotted for pharmaceutical agents. It would be a clear advantage if it could be demonstrated that resource utilization in the nursing home is reduced with Agent A versus Agent B. These kinds of data are needed, and it would be simple to show this in a study.

Dr. DeQuardo: Pharmacy administrators see only what is measured. They have ready access to the cost of medications, but it is more difficult to demonstrate other parameters.

Dr. Glazer: After reviewing 18 pharmacoeconomic studies of atypicals, I found a strong case can be made from these data for the value of these newer drugs.*

**Editor's Note:* This review is unpublished.

Dr. Kinon: One challenge is that these data are difficult to obtain. We have to be flexible and embrace the new health economic study design, which departs dramatically from that of the clinical trial. We have to become familiar and comfortable with the whole notion of naturalistic follow-up and try to reduce selection and crossover biases in trials. If outcomes data over the short term are favorable and if a drug has a good side-effect profile, this is a good lead into the other types of data we have been discussing.

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—George M. Simpson, MD

Stigmatization of Mental Illness

Dr. Verma: Why does it seem that mental health is the only area in medicine where the focus is on the cheapest drug possible? This doesn't seem to be the case—at least not to the same extent—in other areas of medicine; rather, the goal is to find the most effective treatment. A stethoscope is cheap, but payers recognize that it can't replace MRI, which is very expensive.

Dr. Simpson: A year ago I would have agreed with you that there is a stigma related to mental health drugs. But now our pharmacy committee carefully scrutinizes the budget for *all* types of drugs. It is strange that in psychiatry, the advent of new drugs is often greeted with questions about whether or not they are necessary.

Dr. Glazer: Psychiatry is viewed as "soft" medicine, and there are some data to support that view. I did an informal, unpublished analysis and found a 15-fold variability in psychiatric inpatient admissions per thousand of similar patient populations. In other areas of medicine, it is usually about a three-fold variation in utilization.

The Need for Guidelines

Dr. Simpson: Consensus guidelines by experts for the use of these medications would help change the view that psychiatry is "soft." For example, the guidelines could stipulate when to use traditional antipsychotics and when to use atypicals based on individual parameters and side effects of the drugs.

Dr. Glazer: I agree that practice guidelines are helpful. The consensus group guidelines for schizophrenia are a good example of this.¹²

Dr. Simpson: What is really desirable in guidelines are some clearly delineated dos and don'ts.

Dr. Verma: It would be helpful if guidelines could get the message out to the people who control drug budgets about the how important appropriate use of antipsychotics is.

Dr. Simpson: Guidelines could define an appropriate length for a trial of therapy. But if an appropriate trial of therapy for schizophrenia is defined as 6 weeks, and the average length of hospital stay for an acute exacerbation is only 10 days, it is a tough call which drug to use. Short-term predictors would also be useful.

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