

# Perspective and the Measurement of Costs and Benefits for Cost-Effectiveness Analysis in Schizophrenia

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A valid and compelling cost-effectiveness analysis of psychopharmacologic treatment of schizophrenia requires the application of analytically rigorous methods. All cost-effectiveness analyses must consider the issue of perspective as well as the appropriate measurement of benefits and costs. Many of these issues are particularly difficult to address in the case of schizophrenia. Since costs may be borne by a wide range of parties, the choice of perspective is of critical importance. The fact that treatments for schizophrenia can extend life and the complexities raised by taking a broad perspective on the benefits and costs of treating schizophrenia can create challenges in the measurement of both benefits and costs. The measurement of benefits through quality-adjusted life years is also crucial in demonstrating the cost-effectiveness of treatments for schizophrenia, but is challenging because of the difficulty of measuring quality of life in schizophrenic patients. Attention to these important methodological issues is essential if cost-effectiveness analyses are to be useful in shepherding scarce resources to worthwhile treatments for patients with schizophrenia.

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Constructing a meaningful cost-effectiveness analysis of psychopharmacologic medications, especially ones used to treat schizophrenia, requires attention to crucial methodological issues including perspective, the measurement of costs, and the measurement of benefits. Considering a social perspective is important since the costs of schizophrenia are shared by many different parties. This distribution of the costs of schizophrenia across many parties requires a broad perspective on costs, including those borne by patients, their families, and society, both now and in the future. However, considering a more narrow perspective can also sometimes be informative. Finally, to be useful, a cost-effectiveness analysis must also adequately reflect the benefits of treatment in a metric that allows comparison with the benefits of other medical interventions. The most commonly used form of cost-effectiveness analysis uses quality-adjusted life-years as a unitary measure of outcome. The choice of this metric has important implications for the measurement of costs, particularly costs incurred over time. Without appropriate attention to these important methodological issues, a cost-effectiveness analysis may produce misleading results and is less likely

to provide a valid or compelling justification for the allocation of scarce resource to mental health care.

The issue of perspective is a key starting point for any cost-effectiveness analysis. In measuring health care costs, one could choose to look only at the costs to some private entity, such as a health maintenance organization (HMO) or an individual consumer. These approaches will generally neglect important components of costs, however, since costs are generally not completely borne by either the HMO or the consumer alone. For example, an HMO might refuse to cover the cost of some treatment for an illness, in which case the costs are borne by the consumer or by a hospital that is not reimbursed for the care it has provided. Similarly, consumers with insurance generally bear only a small fraction of the costs of their care. The same concerns apply to a public perspective such as that of Medicare or Medicaid, since they do not fully cover the costs of all medical conditions. Likewise, state mental health systems do not cover all the costs associated with mentally ill patients, whether these are costs related to criminality or, more importantly, costs to the families of patients.

A social perspective that considers all costs and benefits, no matter to whom they accrue, aims to address these concerns. The Panel on Cost-Effectiveness in Health and Medicine<sup>1</sup> has recommended that a social perspective on costs be the standard in cost-effectiveness analysis. This approach makes sense when the goal is to promote the greater good of society and when distributional concerns or the incentives faced by specific parties, such as a managed care organization, are not a concern. In the latter instances, however, taking a more narrow perspective, such as that of

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**Table 1. Annual Costs of Treatment\***

Type of Intervention	Hospital-Based, \$	Community-Based, \$
Inpatient	3138	94
Outpatient	0	4704
Other costs	4158	3295
Total costs	7296	8093

\*Data from reference 1.

the managed care organization, may reveal whether that entity would be motivated to support an intervention.

The importance of a social perspective in cost-effectiveness analysis becomes particularly evident in the context of mental illness (Table 1). In 1980, Weisbrod et al.<sup>2</sup> studied the costs of community treatment of mental illness in Wisconsin by comparing hospital-based treatment to community-based treatment. Not surprisingly, they found that patients in community-based treatment had lower inpatient treatment costs. Those gains were offset, however, by additional costs accrued in outpatient treatment. When total costs of treatment were compared, those for the community-based group were slightly higher. Other studies have since replicated these findings, which suggest the difficulty of decreasing health care costs solely by moving mentally ill patients out of inpatient programs. This is not to say that moving patients into a community setting may or may not be desirable for other reasons, however.

Weisbrod et al. also considered changes in costs other than health care costs in moving mentally ill patients to community-based programs. In assessing the overall cost of the program, they looked at net cost (narrowly defined health care costs) and net benefit (broader benefits to the community, chiefly earnings). As indicated above, the net cost of community-based treatment was greater than that for inpatient care, but the earnings of people in outpatient care increased by approximately \$1200 per patient per year. Considering this increased income made the community-based care of schizophrenic patients less expensive than inpatient care by approximately \$400 per patient per year, although the total difference was not statistically significant. The essence of the problem in demonstrating statistical significance is that one is spending a large and highly variable amount of money to save a large and highly variable amount of money with only modest net savings. In this instance, an average of about \$6000 was spent, out of which community-based care decreased total costs by only about \$400. Thus, the challenge in this sort of analysis is that in many instances the statistical significance of these savings will be very difficult to demonstrate without using very large sample sizes. This analysis is further complicated by the need to consider both medical and nonmedical costs, both direct and indirect costs—including lost earnings, costs to the family, and other social costs—and both present costs and future costs that may be incurred over years.

In 1994, Davies and Drummond<sup>3</sup> studied the costs of care for people with schizophrenia in England. They

**Table 2. Annual Costs of Schizophrenia to Family\***

Nature of Cost	Cost, \$
Support	2467
Treatment	670
Time	7980
Other	402
Total	11,519

\*Data from reference 4.

considered both the direct treatment costs—about £397 million annually—and indirect costs, chiefly lost earnings—about £1700 million annually. These findings illustrate that treatment costs account for only a very small percentage of total costs of the disease. Davies and Drummond also estimated lifetime costs of schizophrenia, estimating the average lifetime cost at £157,000 per person per lifetime.

In 1990, Franks<sup>4</sup> considered the cost of schizophrenia to the family (Table 2). He looked at the variety of costs incurred by families of schizophrenic patients, including the costs of actually supporting the patient—from room and board to providing clothing—and some treatment costs borne by the family as opposed to the health care system. Critically, time costs—the substantial amount of time spent by family, including time lost from work as well as time at home—comprised the largest figure in this accounting.

The question of future costs has interesting and important implications for thinking about schizophrenia. The general question is, if a patient's life is saved today through a medical intervention, and that patient requires care in the future, should those future costs be considered as a cost of the life-saving intervention? What about a related illness? For example, if a patient has angioplasty today, should the cost of a future bypass be assessed as a cost of angioplasty? What about an unrelated illnesses? If a patient is immunized against influenza today and needs dialysis 20 years later, should the cost of dialysis be attributed to the influenza vaccination? Should these future costs be included when the patient otherwise would have died of influenza without incurring high costs? Should nonmedical costs and benefits be considered in a cost-effectiveness analysis? In the context of schizophrenia, should the future earnings of a patient prevented from committing suicide today be credited against the cost of that intervention? Should the cost of future consumption be attributed to that intervention?

Recent research has demonstrated that cost-effectiveness analysis should include all these future costs, both medical and nonmedical.<sup>5</sup> Failure to do so biases one to favor interventions that extend life over interventions that improve the quality of life, particularly in the elderly and for people who will be earning more than they consume in health care and other costs, which is often the case for patients with schizophrenia.

Figure 1. Accounting for Future Costs of Illness\*

$$\frac{\Delta \text{ cost}}{\Delta \text{ QALY}} = \frac{\Delta \text{ present cost}}{\Delta \text{ QALY}} + \frac{\Delta \text{ future cost}}{\Delta \text{ QALY}}$$

$$\frac{\Delta \text{ cost}}{\Delta \text{ QALY}} = \frac{\Delta \text{ present cost}}{\Delta \text{ QALY}} + \frac{C \times \Delta \text{ LE}}{\Delta \text{ QALY}}$$

$$\frac{\Delta \text{ cost}}{\Delta \text{ QALY}} = \frac{\Delta \text{ present cost}}{\Delta \text{ QALY}} + C \times \frac{\Delta \text{ LE}}{\Delta \text{ QALY}}$$

\*Abbreviations:  $\Delta \text{LE}$  = life years saved,  $\Delta \text{QALY}$  = quality-adjusted life-years saved.

One way to assess these costs is to calculate the cost per quality-adjusted life-year as the sum of the present cost per quality-adjusted life-year plus a future cost per quality-adjusted life-year (Figure 1). That future cost can be approximated as a constant amount— $C$ —per life-year saved multiplied by the number of life-years saved ( $\Delta \text{LE}$ ). Ultimately, the cost per quality-adjusted life-year is the sum of present costs per quality-adjusted life-year plus  $C$  multiplied by the ratio of change in life expectancy to change in quality-adjusted life expectancy. As a result, in a cost-effectiveness analysis of an intervention that extends the length of a patient's life greatly relative to its effects on quality-adjusted life expectancy, this ratio can be very large, which can dramatically change the cost-effectiveness of an intervention.

In this analysis,  $C$  reflects net resource use, which includes consumption and medical expenditures net of earnings by age for an average person.  $C$  is generally negative through most of patients' lives, because young people work and produce more than they consume. However, as people retire and accumulate more health care costs,  $C$  tends to become positive. If a 25-year-old person's life is saved through a medical intervention, the result is a savings in economic resources. Saving an older person's life can result in a loss of economic resources. Such an analysis reveals the danger of focusing only on the fiscal aspects of costs and benefits.

Meltzer<sup>5</sup> contrasts the effects of including future costs on the cost-effectiveness of treating severe hypertension, adjuvant chemotherapy for colon cancer, and hemodialysis for end-stage renal disease, all in men aged 60 years. If one does not count future costs, the first two interventions, at \$60,000 per quality-adjusted life-year for the treatment of hypertension and \$67,000 per quality-adjusted life-year for chemotherapy, appear quite cost-effective, but the third, at \$117,000 for hemodialysis, does not. If future costs are added to the analysis, however, there are dramatic changes. The cost of the treatment of severe hypertension increases only modestly to \$67,000 per quality-adjusted life-year and

the cost of hemodialysis for end-stage renal disease increases only to \$129,000 per quality-adjusted life-year. In contrast, the cost of adjuvant chemotherapy increases to \$211,000 per quality-adjusted life-year, because the intervention has a substantial effect on length of life compared with its effect on quality of life, making the ratio of the change in life expectancy to change in quality-adjusted life expectancy quite high and causing a large change in the cost-effectiveness ratio.

This analysis illustrates that when future net resource use is positive, including future costs in a cost-effectiveness analysis will improve the relative cost-effectiveness of interventions that improve quality-of-life compared with those that increase length of life. In contrast, when future net resource use is negative, as it generally is among young adults, including future costs can make life-extending interventions more cost-effective. One might conclude that including future costs would also make improved treatment for schizophrenia look much more cost-effective, since schizophrenia most commonly affects young people who would otherwise be just entering their prime earnings years. However, if one considers a schizophrenic patient who is not working during these years, future costs will be positive and the opposite might be the case. This suggests that if one wants to show cost savings or even cost-effectiveness with improved treatment, demonstrating an effect on earnings might be extremely important.

Especially with the inclusion of future costs, cost-effectiveness ratios may be very sensitive to the ratio of increases in life expectancy to increases in quality-adjusted life expectancy. Thus, cost-effectiveness ratios will be dependent on the denominator, which points to the critical nature of the challenges in measuring quality of life and the need for caution when doing so. Because quality of life in schizophrenia is exceptionally difficult to measure, it presents a particular problem for cost-effectiveness studies in the area. It may be because of these difficulties in measuring quality of life in schizophrenia that very few cost-effectiveness studies have been attempted for treatments for schizophrenia.

In a cost-effectiveness study of clozapine that included a cost-utility analysis, Revicki et al.<sup>6</sup> examined the use of clozapine in treatment-resistant patients in a historical, nonexperimental cohort. They suggested that the use of clozapine resulted in cost savings from \$12,000 to \$15,000 per patient and improvements in Brief Psychiatric Rating Scale (BPRS) scores. Because costs appeared to fall, Revicki and colleagues did not need to calculate a cost-effectiveness ratio. Unfortunately, there are other problems with the study. For example, they did not consider dropouts and did not discount future benefits. The resulting likelihood of underestimating the net cost leads one to question the cost savings suggested by the study.

Davies and Drummond<sup>7</sup> took results from the Revicki study and extrapolated them to England. With clozapine,

one saved £91 per patient per year and gained 5.87 years of life during which a patient scored less than 35 on the BPRS. Davies and Drummond assigned 1 quality-adjusted life-year to patients whose BPRS scores were less than 35 and no quality-adjusted life-years to those whose BPRS scores exceeded 35. It is unlikely that this specification of quality of life provides a very rich description of the actual quality of life for patients with schizophrenia. However, because Davies and Drummond also found that the use of clozapine saved money and improved outcomes, they also did not need to calculate a cost-effectiveness ratio. Had costs risen, their results would have been dependent on the ability to quantify improvements in quality of life. Recalling the sensitivity of this kind of study to the ratio of cost to quality-adjusted life-year reminds one of the need for skepticism in relying on analyses like this one that use such a crude measure of quality of life.

A related issue about the validity of outcome data concerns the use of observational data versus that from randomized clinical trials. The Davies and Drummond study was based on observational data. There are obviously important questions about the validity of this observational study as opposed to a randomized comparison. Davies and Drummond estimated lifetime costs by extrapolating based on 2 years of follow-up data, and one might have justifiable questions about the accuracy of such an extrapolation. There are no completely satisfying solutions to this problem. Clearly, randomized controlled studies are an improvement, but they introduce their own problems: consent will be difficult, particularly over the long term, and long-term follow-up will not only be costly but will also lead to delays. Eventually, many of these treatments may be shown through carefully designed randomized clinical trials to improve outcomes in a cost-effective way, but it would certainly be valuable to have evidence of the cost-effectiveness of treatment more immediately.

Modeling is one possible way to address this problem. Davies and Drummond create a decision tree to model the long-term outcomes of treatment based on short-term treatment data. To do this, they take the distribution of pa-

tients between inpatients and outpatients at the end of the 2-year study and assume that this distribution will be constant in subsequent years. However, while some patients may remain in the setting that they are in at the end of 2 years, many are likely to transition between settings, and their model cannot capture such movements. Markov modeling is another possible approach, but is difficult to do well with existing data. For example, there is not adequate data to deal with heterogeneity, which means that, over time, one may be studying a group of extremely well or extremely treatment-resistant patients who may make fewer transitions and likely have differing benefits of treatment.

Psychiatric outcomes researchers must deal with serious methodological problems such as these if they are to make progress towards producing convincing cost-effectiveness analyses that are capable of influencing resource allocation decisions. Although the solutions to these problems are seldom either clear or perfect, investing effort in improving the sophistication of the measurement of benefits and costs and in careful attention to the appropriate choice of perspective would be highly valuable in channeling resources to worthwhile new treatments for people with schizophrenia.

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