Revised PORT Recommendations

by T. Scott Stroup, Joseph P. McEvoy, and Jeffrey A. Lieberman

The updated Schizophrenia Patient Outcomes Research Team (PORT) recommendations (Lehman et al. 2004) represent an excellent, well-reasoned, and appropriately cautious synthesis of the available evidence on treatments for schizophrenia. Importantly, the authors caution against "biological reductionism," by which they mean neglect of psychological and social issues that affect individuals with schizophrenia and their families. They stress the need to develop and test new modalities that may facilitate the recovery of individuals with schizophrenia. They point out the critical need for better access to mental health services and better integration of mental health, general health, and social services. They call for continued research on available treatments. We agree with all of these points.

More important for differentiating the overall effectiveness of the medicines than acute efficacy in reducing positive symptoms and the severity of extrapyramidal side effects, however, is their effect on long-term outcomes and the hope for meaningful recovery. As with acute treatment, the PORT recommendations do not specify a preference between FGAs and SGAs for maintenance treatment of patients who have responded well to an antipsychotic drug. Nevertheless, clinicians in the United States often choose the newer medicines based on the hope, also not definitively established, that they are associated with fewer negative symptoms and better cognitive functioning than the FGAs, and that these will translate into better long-term clinical and functional outcomes for patients.

The other key issue is the long-term safety of the drugs. Just as it took considerable clinical experience with FGAs to recognize the risks of tardive dyskinesia, more than a decade of experience with SGAs accumulated before the Food and Drug Administration issued in 2004 a warning about increased risk for hypoglycemia and diabetes for all the SGAs (http://www.fda.gov/medwatch/SAFETY/2004/zyprexa.htm, U.S. Food and Drug Administration 2004). Even more recently, a consensus statement from a joint panel of the American Diabetes Association (ADA), the American Psychiatric Association, the American Association of Clinical Endocrinologists, and the North American Association for the Study of Obesity issued recommendations for careful monitoring of patients taking SGAs for problems related to obesity, diabetes, and dyslipidemias (ADA et al. 2004).

Ultimately, the relative effectiveness of the drugs in promoting recovery will be a function of their effectiveness in reducing symptoms of schizophrenia, their tolerability, and their safety. We need to know whether the...
widespread use of SGAs is justified by clinical advantages or whether it is a function of unfounded hopes and aggressive marketing. The National Institute of Mental Health–sponsored Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia trial, which we lead in collaboration with researchers at more than 50 sites across the United States, may soon provide significant additional information that could confirm that there is no clear difference between FGAs and SGAs in effectiveness, or it may provide evidence that the recommendation should be revised (Stroup et al. 2003).

The CATIE schizophrenia trial is a practical clinical trial in which participants were randomly assigned to double-blind treatment with perphenazine (representing the FGAs), olanzapine, quetiapine, risperidone, or ziprasidone. The study enrolled almost 1,500 research participants meant to represent typical patients in typical treatment settings. As much as possible, treatment in the CATIE trial is meant to resemble that in usual care. Medication dosing is flexible. Additional medicines other than antipsychotics are allowed unless they are medically contraindicated. Followup is scheduled for 18 months. The primary outcome is effectiveness, as indicated by staying on the assigned medication. The study will also compare the effects of the drugs on symptoms, extrapyramidal side effects, weight, lipids, and glucose metabolism. The CATIE schizophrenia trial’s head-to-head comparison of SGAs and a representative FGA over a substantial period of time is thus expected to contribute significantly to the evidence base on these key issues.

As a practical trial, CATIE is meant to produce results that will be widely generalizable and to inform clinical and policy decision makers. Exclusion criteria were minimal; persons with co-occurring substance use disorders, psychiatric disorders, and medical conditions were included. The research sites included community mental health centers, private practices, Veterans Affairs Medical Centers, university clinics, and state hospitals. When the study results are available in early 2005, we hope that clinicians and policy makers who want evidence-based guidance will believe that our results are applicable to their patients and their clinical settings.

From Our Perspective as Clinicians

We strongly agree that clozapine should be considered for treatment of treatment-resistant positive symptoms, hostility, or persistent suicidal thoughts or behavior. In spite of clozapine’s advantages in these situations, it is underused, probably because of both physician and patient reluctance about a trial of a medicine that is truly difficult to use. The risk of agranulocytosis and consequent white blood count monitoring, elevated risk of seizures, and increased risk of myocarditis and cardiomypathy make clozapine considerably more difficult to prescribe than other antipsychotic drugs. We suggest that clinicians who do not commonly prescribe clozapine consult with or refer to a clinician who is experienced in its use. This may help overcome some of the barriers to clozapine’s use and may lead to better outcomes for individuals who are severely affected by schizophrenia.

With regard to the metabolic side effects of antipsychotic drugs, we emphasize that particular attention should be paid to certain groups at high risk of complications due to these side effects. Included in these high-risk groups are individuals with a personal or family history of diabetes mellitus, those who are obese or hypertensive, and those whose ethnicity is African-American, Native American, Pacific Islander, or Asian.

An alarming finding in 1998 that “concordance” with the original PORT recommendations was extremely poor highlighted important problems with our mental health system (Lehman and Steinwachs 1998). Only 29 percent of patients studied received antipsychotic medications within the recommended dosage ranges. Only 10 percent of patients with regular contact with family members received family psychoeducation, and only 22 percent of patients appropriate for vocational rehabilitation received it.

We informally looked at our own practices and found many instances in which treatment plans did not conform to the PORT recommendations. For example, although we aggressively prescribe clozapine for patients with treatment-resistant symptoms, many cannot tolerate or otherwise refuse dosages deemed adequate in the peer-reviewed literature. Similarly, we strongly advocate the use of long-acting antipsychotics for patients at risk of treatment nonadherence but find it difficult to keep long-stabilized patients on medications they find painful or inconvenient. We recognize the importance of family involvement, and in inpatient settings usually we are able to garner the resources necessary to engage family members. In outpatient settings, however, this is much more difficult for many reasons, including costs, access, logistics, and motivation of family members. Unfortunately, in the settings where we work, as in many other settings, the recommended evidence-based treatments are not always available.

The PORT guidelines challenge us to overcome barriers to an appropriate array of services and to do a better job for our patients.

From Our Perspective as Teachers

For many years we have used the PORT recommendations to teach psychiatry residents and other trainees about
evidence-based medicine, the quality of different types of evidence, and the range of treatments available for schizophrenia. We talk about the concordance problem and acknowledge the gaps in our own treatment settings. We discuss the reasons for the shortcomings in our settings and strategies for making improvements. We also emphasize the importance of individualized treatment plans and the importance of a good working alliance with patients, including the need to work collaboratively with patients to develop common treatment goals. We emphasize that an individualized collaboration with each patient can be informed by recommendations like those from the PORT but should not be dominated by them. On the other hand, we stress that anecdotal evidence or an idealized view of psychiatry as an "art" should not justify a disregard for the PORT recommendations.

Conclusion

The updated Schizophrenia PORT recommendations address only one of the goals of the President's New Freedom Commission on Mental Health—the one that calls for delivery of excellent mental health care and for accelerating research (President's New Freedom Commission 2003). Other important goals of the New Commission report are beyond the scope of the PORT guidelines. These other goals include a better understanding that mental health is essential to overall health; the elimination of disparities associated with race, ethnicity, and social class; and the use of information technology to improve access to care. These other goals are also critical to reducing the gap between outcomes achieved with available treatments under ideal circumstances compared to those under typical treatment settings. This so-called efficacy-effectiveness gap reflects a larger problem—the sharp contrast between the amazing technical quality of treatments in medicine and the quality of the actual health care received by persons who need access to treatments and other services. Major improvements in the U.S. health care system, particularly in access to treatment and coordination of care, are likely needed to substantially diminish this contrast.

The updated Schizophrenia PORT recommendations are highly informative and useful. The limited number of treatments for which the PORT is able to make clear recommendations provides evidence that there is still much room for technical improvement in the treatment of schizophrenia. Our hope is that the new PORT recommendations will lead to better quality of care and better chances of recovery for individuals with schizophrenia, and that continued research will allow the next set of PORT recommendations to cover a broader range of evidence-based interventions.

References


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