At Issue: Medication-Free Intervals and Schizophrenia Research—Editors’ Introduction

Early in 1995, in response to growing concerns by patient advocacy groups and clinical researchers, the National Institute of Mental Health (NIMH) sponsored a workshop on Ethical Issues in Schizophrenia Research. One of the challenges in clinical mental health research is that the most severely ill patients suffering from disorders like schizophrenia, those most desperately in need of research advances, may not always be able to give informed consent (when acutely ill) for participation in such research. The workshop was NIMH’s first formal attempt to deal with this difficult issue, and it led to an NIMH Program Announcement on Informed Consent in Clinical Mental Health Research (MH-95-080), as well as a National Institute of Health-Wide Request for Applications to study Informed Consent in Research Involving Human Participants (OD-97-001). In addition to informed consent, the NIMH workshop identified a companion ethical issue in schizophrenia research, namely the risk of participating in clinical research protocols involving a period of time off medication.

The impact of drug-free periods on the clinical course of schizophrenia has become one of the field’s more controversial subjects. Clearly, remaining psychotic and untreated for many years can have an adverse effect on an individual. Early intervention and integrated followup seem the best treatment approach, whether based on the desire to minimize subjective suffering, functional impairment, or potential “progression” of the disorder. Given side effects and concerns over risk/benefit issues, especially for recent-onset schizophrenia, clinicians are encouraged to seek the lowest effective dose of antipsychotic medications. We know that a few patients do not need to continue on medication, but we do not know how to predict which patients will do well. At the same time, however, we cannot now recommend a lifetime on antipsychotic medications after a single psychotic episode.

Most people with schizophrenia who have been started on antipsychotic medications will discontinue them without supervision within a year or two, and others will experience relapses despite continuing on medications. Because of side effects and other factors, compliance remains a major problem in the treatment of schizophrenia. The issue of placebo controls has been raised as an ethical concern and debated in several contexts, including clinical trials. Experts have emphasized the importance of placebo control groups to ensure that a treatment is really efficacious, and the trial comparison valid. We see no reason to conclude that brief periods off medications in well-supervised settings have a persistent adverse effect.

In response to the issues raised during the NIMH workshop on Ethical Issues in Schizophrenia Research, the Editorial Board of the Schizophrenia Bulletin recommended the following At Issue dialog, involving two of the world’s leading schizophrenia researchers, as a way to present the evidence and discuss potential implications. We believe this can be useful in minimizing misconceptions and misinterpretations, and may serve to spur further research on this important topic.

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