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**I have obtained dramatic functional recovery after giving injectable second-generation antipsychotics continuously for 2 years or more**

# Is schizophrenia recovery a ‘myth’?

**A widespread and enduring notion about schizophrenia is that it is a hopeless brain disease associated with progressive clinical, cognitive, social, and vocational deterioration. After all, community mental health centers are replete with profoundly disabled persons who carry a schizophrenia diagnosis. Most have no friends, spouses, or significant others and have not been employed for years. So can one argue that persons with schizophrenia ever recover?**

How you define “recovery,” as discussed in this issue (*page 40*), certainly influences how you would answer that question. As a long-time schizophrenia researcher who has treated thousands of patients and conducted dozens of research projects into schizophrenia, I respond with a “definite maybe.”

## **Odds of recovery: 1 in 5?**

The severity and outcome of any illness—including schizophrenia—falls into a bell-shaped curve, from very mild to very severe. Observations can be misleading, however. Kraepelin, for example, based his deteriorative description of schizophrenia on severely ill, long-term hospitalized patients. This biased sample did not include patients who remained in the community with their families, doing well enough not to need hospitalization.

The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia study<sup>1</sup> provides a good example of schizophrenia’s heterogeneity. At enrollment, the 1,460 outpatients ranged from no symptoms to severely ill. Schizophrenia outcome is similarly distributed.

The landmark Iowa 500 study<sup>2</sup> in the 1970s was one of the most thorough examinations of long-term schizophrenia outcomes, including recovery. With funding from the National Institute of Mental Health, researchers tracked down and interviewed hundreds of persons admitted 30 to 40 years earlier to the Iowa State Psychopathic Hospital and who met rigorous Research Diagnostic Criteria for schizophrenia. They found that:

- 20% had recovered completely and resumed normal life
- 80% remained ill, with variable degrees of severity.

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## Table

## Expert consensus proposed criteria for schizophrenia remission

## PANSS item Symptom

PANSS item	Symptom
P1	Delusions
P2	Conceptual disorganization
P3	Hallucinations
G9	Unusual thought content
G5	Mannerisms and posturing
N1	Blunted affect
N4	Passive/apathetic social withdrawal
N6	Lack of spontaneity and flow of conversation

Schizophrenia remission is defined as a score of  $\leq 3$  (mild or less) on all 8 core items in the Positive and Negative Syndrome Scale (PANSS) for  $\geq 6$  months.

Source: Reference 4

The best prognosis was for paranoid schizophrenia and the worst for non-paranoid schizophrenia; hebephrenia (“disorganized”) and undifferentiated schizophrenia had similarly poor outcomes.

A major confound for recovery from schizophrenia is that patients with psychotic bipolar disorder sometimes are misdiagnosed as having schizophrenia. Patients with bipolar disorder can achieve remission for a while, only to relapse again. If misdiagnosed, they may be reported as “recovered” schizophrenia cases when they cycle out of a severe bipolar episode.

### Treatment adherence: A key to recovery

Features associated with better outcome and possible recovery in schizophrenia include female gender, sudden onset of psychosis, paranoid subtype, high IQ, minimal negative symptoms, presence of an affective component, having a supportive family, good insight, continuity of care, and—very important—optimal treatment adherence.

Discontinuing treatment in schizophrenia leads to psychotic relapses and a lower probability of recovering. Therefore, I find it puzzling that injectable, long-acting antipsychotics are used infrequently in the United States, despite the high rate of treatment discontinuation in schizophrenia. In Europe, the rate of use of injectable antipsychotics is 3 times higher.

I have obtained extremely good outcomes—including recovery in patients who were regarded as hopelessly deteriorated—with long-acting injectable second-generation antipsychotics (SGAs) and dramatic functional recovery after giving patients injectable SGA treatment continuously for 2 years or more. My experience with depot first-generation antipsychotics (FGAs) was that they helped prevent relapse but did not help patients return to functioning. A possible explanation is that SGAs have been found to induce neurotrophic factors and stimulate neurogenesis, whereas FGAs may lead to a decline in neurotrophic factors and apoptotic loss of brain tissue.<sup>3</sup>

### A useful remission measure

To measure clinically meaningful improvement (remission), I recommend criteria developed by schizophrenia experts (Table).<sup>4</sup> These research criteria define remission based on core items in the Positive and Negative Syndrome Scale (PANSS). If symptoms remain in remission  $>6$  months, social and vocational rehabilitation is more likely to restore a patient’s functional capacity. That functional improvement—not just symptomatic remission—would constitute true recovery.

Recovery is possible but appears to occur in a minority of patients.<sup>2</sup> Many patients can achieve remission, which enables them to gradually regain various degrees of functioning. Just as a stroke patient may need rehabilitation to learn to talk and walk again, individuals with schizophrenia can reclaim their lives with a balanced regimen of effective antipsychotic medication, coupled with personalized social, cognitive, and vocational rehabilitation.



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