

The Case Against Antipsychotics

Robert Whitaker
September 2016

The Common Wisdom

The introduction of chlorpromazine into asylum medicine in 1955 “initiated a revolution in psychiatry, comparable to the introduction of penicillin in general medicine.”

--Edward Shorter, *A History of Psychiatry*

The Evidence for Antipsychotics

Short-term Use

Antipsychotics reduce target symptoms of a disorder better than placebo in six-week trials.

Long-term Use

In relapse studies, those withdrawn from the medications relapse at a higher rate than those maintained on the medications.

Clinical Perceptions

The physician sees that the medications often work upon initial use, and sees that patients often relapse when they go off the medications.

What's Missing From The Evidence Base?

A. It does not provide evidence that medications improve the long-term course of schizophrenia (or other psychotic disorders,) particularly in regard to functional outcomes.

B. The relapse studies reflect risks associated with drug-withdrawal effects, rather than just the return of the natural course of the disorder. (Most relapse studies involved abrupt withdrawal of the medication.)

C. Physicians today no longer have clinical experience with the long-term course of schizophrenia patients off medication.

Recognition that the Evidence Base For Long-term Use of Antipsychotics is Lacking

“After fifty years of neuroleptics, are we able to answer the following simple question: Are neuroleptics effective in treating schizophrenia? [There is] no compelling evidence on the matter, when ‘long-term’ is considered.”

And:

“If we wish to base psychiatry on evidence-based medicine, we run a genuine risk in taking a close look at what has long been considered fact.”

--Emmanuel Stip, *European Psychiatry* (2002)

Do Antipsychotics Do More Harm Than Good?

Investigators from Columbia University and City College of New York:

“Recently, Robert Whitaker advanced a troubling interpretation of the evidence base for long-term use of antipsychotic medication. He reviewed a number of epidemiological and clinical studies and concluded that antipsychotic medications are an iatrogenic cause of chronicity in schizophrenia, and that these medications may lead to the deterioration of patients’ health and well-being over time. His explanation rested on the notion that antipsychotic medication may induce a hypersensitivity to dopamine. We were concerned by Whitaker’s findings and wondered whether a systematic appraisal of published literature would produce the same results.”

Source: N. Sohler. Weighing the evidence for harm from long-term treatment with antipsychotic medications: A systematic review. *Am Journal of Orthopsychiatry*, Vol 86/2016, 477-485

They concluded:

We found the published data to be inadequate to test this hypothesis. By extension, these data were also inadequate to conclusively evaluate whether long-term antipsychotic medication treatment results in better outcomes on average. We conclude that careful reappraisal of existing data is useful to ensure standard of care treatment strategies are indeed evidence-based. In the case of long-term use of antipsychotic medications, new data may be needed to establish a sufficient evidence base to understand its benefit/risk balance for patients with schizophrenia.

Schizophrenia Outcomes in the Decade Before Antipsychotics, 1945-1955

- At end of three years following hospitalization, 73% of first-episode patients admitted to Warren State Hospital from 1946 to 1950 were living in the community.
- At the end of six years following hospitalization, 70% of 216 first-episode patients admitted to Delaware State Hospital from 1948 to 1950 were living in the community.
- In studies of schizophrenia patients in England, where the disorder was more narrowly defined, after five years 33% enjoyed a complete recovery, and another 20 percent a social recovery, which meant they could support themselves and live independently.

Source: J Cole, *Psychopharmacology* (1959): 142, 386-7. R. Warner, *Recovery from Schizophrenia* (1985): 74.

The Revolving Door Appears

- A British study of 100 schizophrenia patients found that those treated in 1956/57, had, if anything, a “higher rate of readmission” in the three years following discharge than those treated in 1952/53, prior to the introduction of the phenothiazines.
- A Norwegian study of hospital admission and discharge records in 1948/52 and in 1955/1959 determined that while there may have been a slight improvement in discharge rates after chlorpromazine arrived in asylum medicine, the total number of readmissions “increased 41.6%,” which the researchers described as “characteristic of the drug period.”
- In a study of 221 first-episode schizophrenia patients admitted into Scottish hospitals from 1949 to 1957, with patients followed for three years, there was no difference in the percentage that suffered a single “attack” (about 70% of all patients in both the pre-drug and post-drug eras), but among all discharged patients, there was an “increased relapse frequency” in males following the introduction of chlorpromazine.

Source: Pritchard, M. “Prognosis of schizophrenia before and after pharmacotherapy: II. Three- year follow-up.” *Br J Psychiatry* 113 (1967):1353-59. Odegard, O. “Pattern of discharge from Norwegian psychiatric hospitals before and after the introduction of the psychotropic drugs.” *Am J Psychiatry* 120 (1964):772-78. McWalter, H. “Outcomes of treatment of schizophrenia in a north-east Scottish mental hospital. *Am J Psychiatry* 118 (1961):529-533.

The First Hint of a Paradox

NIMH's First Followup Study (1967):

At the end of one year, patients who were treated with placebo upon initial hospitalization “were less likely to be rehospitalized than those who received any of the three active phenothiazines.”

Source: Schooler, C. “One year after discharge.” *Am J of Psychiatry* 123 (1967):986-95.

Other Worries

- Relapse during drug administration “is greater in severity than when no drugs are given.”
- If patients relapse after quitting antipsychotics, symptoms tend to “persist and intensify.”

Source: Gardos, G. “Maintenance antipsychotic therapy: is the cure worse than the disease?” *Am J Psychiatry* 135 (1978): 1321-4.

A Retrospective Comparison of Outcomes in Pre-Drug and Drug Era

Relapse Rates Within Five Years of Discharge

1947 cohort: 55%

1967 cohort: 69%

Functional Outcomes

1947 cohort: 76% were successfully living in the community at end of five years

1967 cohort: They were much more “socially dependent”--on welfare and needing other forms of support--than the 1947 cohort.

Source: Bockoven, J. “Comparison of two five-year follow-up studies,” *Am J Psychiatry* 132 (1975): 796-801.

Bockoven's Conclusion:

“Rather unexpectedly, these data suggest that psychotropic drugs may not be indispensable. Their extended use in aftercare may prolong the social dependency of many discharged patients.”

Rappaport's Study: Three-Year Outcomes

Medication use (in hospital/after discharge)	Number of Patients	Severity of Illness (1 = best outcome; 7 = worst outcome)	Rehospitalization
No meds/off	24	1.7	8%
Antipsychotic/off	17	2.79	47%
No meds/on	17	3.54	53%
Antipsychotic/on	22	3.51	73%

Source: Rappaport, M. "Are there schizophrenics for whom drugs may be unnecessary or contraindicated?" *Int Pharmacopsychiatry* 13 (1978):100-11.

Rappaport's Conclusion:

“Our findings suggest that antipsychotic medication is not the treatment of choice, at least for certain patients, if one is interested in long-term clinical improvement. Many unmedicated-while-in-hospital patients showed greater long-term improvement, less pathology at follow-up, fewer rehospitalizations, and better overall functioning in the community than patients who were given chlorpromazine while in the hospital.”

Loren Mosher's Soteria Project

Results:

At end of two years, the Soteria patients had “lower psychopathology scores, fewer [hospital] readmissions, and better global adjustment.”

In terms of antipsychotic use, 42% had never been exposed to the drugs, 39% had used them temporarily, and 19% had used them regularly throughout the two-year followup.

Source: Bola, J. “Treatment of acute psychosis without neuroleptics.” *J Nerv Ment Disease* 191 (2003):219-29.

Loren Mosher's Conclusion

“Contrary to popular views, minimal use of antipsychotic medications combined with specially designed psychosocial intervention for patients newly identified with schizophrenia spectrum disorder is not harmful but appears to be advantageous. We think the balance of risks and benefits associated with the common practice of medicating nearly all early episodes of psychosis should be re-examined.”

William Carpenter's In-House NIMH Study,

- Compared 27 schizophrenia patients treated with psychotherapy and no antipsychotics to 22 patients treated with both psychotherapy and antipsychotics.
- Those treated without drugs were discharged sooner (108 days on average versus 126 days.)
- 35% of the group treated without drugs in the hospital relapsed within a year after discharge, versus 45% of the medicated group.
- The unmedicated group also suffered less from depression, blunted emotions, and retarded movements.

Source: Carpenter, W. "The treatment of acute schizophrenia without drugs." *Am J Psychiatry* 134 (1977):14-20.

“Patients reported experiencing more anguish with our treatment approach, whereas they felt a greater sense of frustration and of being ‘frozen in the psychosis’ in settings emphasizing drug treatment . . . insofar as the psychotic break contains potential for helping the patient alter pathological conflicts within himself and establish a more adaptive equilibrium with his environment, our present-day practice of immediate and massive pharmacological intervention may be exacting a price in terms of producing ‘recovered’ patients with greater rigidity of character structure who are less able to cope with subsequent life stresses.”

--William Carpenter

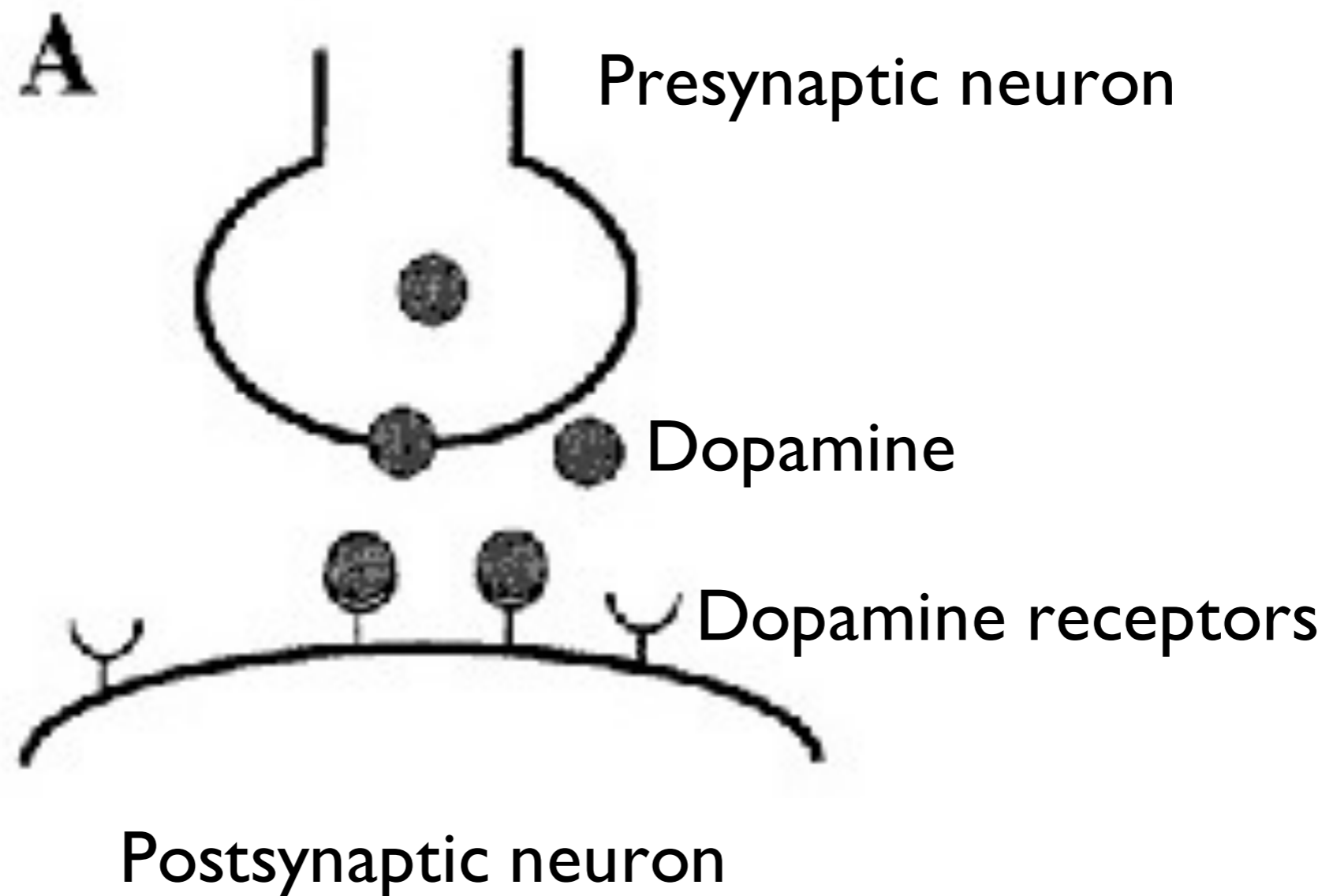
William Carpenter Raises a Question:

“There is no question that, once patients are placed on medication, they are less vulnerable to relapse if maintained on neuroleptics. But what if these patients had never been treated with drugs to begin with? . . . We raise the possibility that antipsychotic medication may make some schizophrenic patients more vulnerable to future relapse than would be the case in the normal course of the illness. Thus, as with tardive dyskinesia, we may have a situation where neuroleptics increase the risk for subsequent illness but must be maintained to prevent this risk from becoming manifest.”

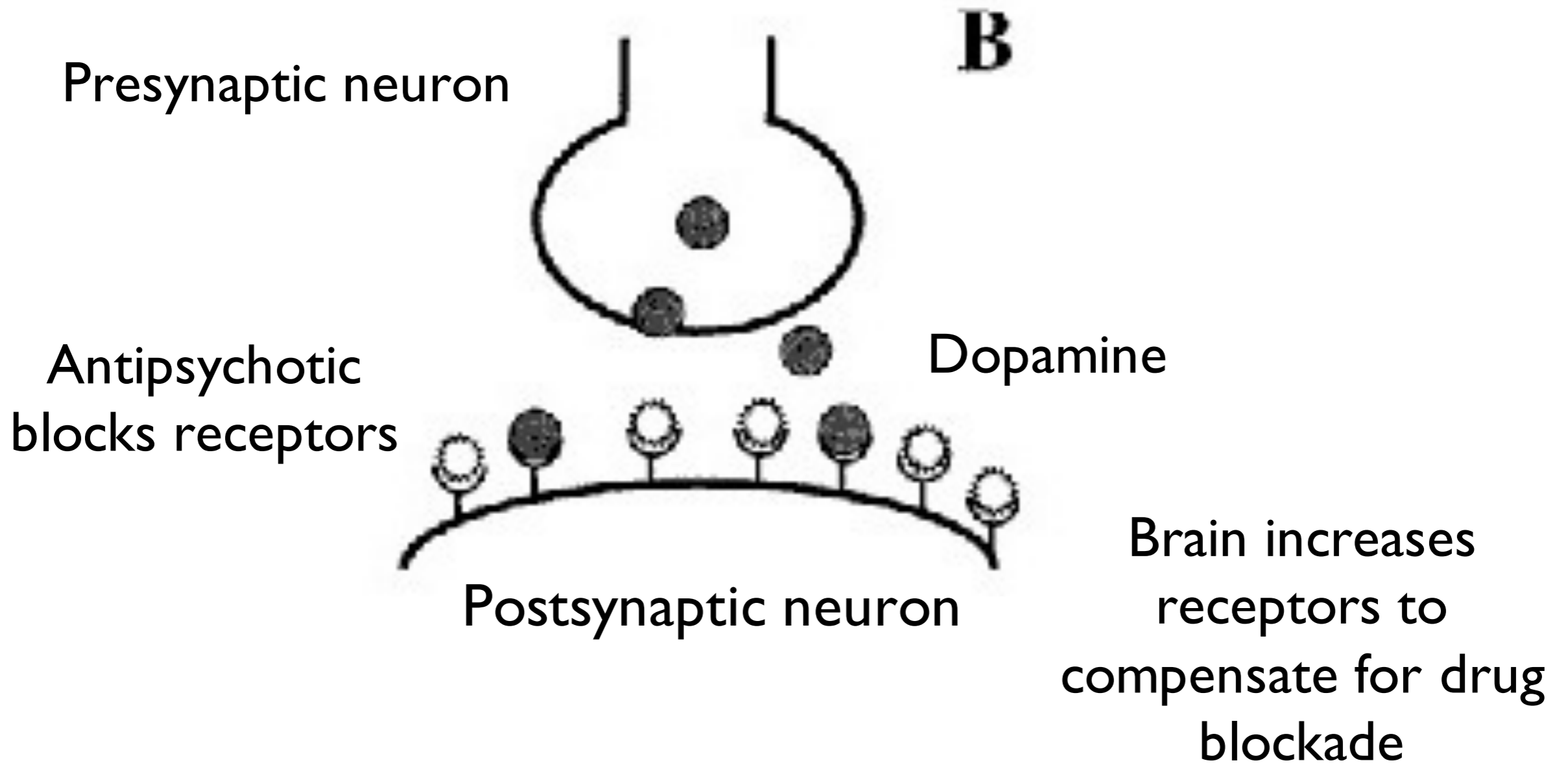
Source: Carpenter, W. “The treatment of acute schizophrenia without drugs.” *Am J Psychiatry* 134 (1977):14-20.

The Dopamine Supersensitivity Theory

Dopamine function before exposure to antipsychotics



Dopamine function after exposure to antipsychotics



The Consequences of Dopamine Supersensitivity

“Neuroleptics can produce a dopamine supersensitivity that leads to both dyskinetic and psychotic symptoms An implication is that the tendency toward psychotic relapse in a patient who has developed such a supersensitivity is determined by more than just the normal course of the illness.”

Guy Chouinard and Barry Jones, McGill University

Source: Chouinard, G. “Neuroleptic-induced supersensitivity psychosis,” *Am J Psychiatry* 135 (1978): 1409-10; and “Neuroleptic-induced supersensitivity psychosis,” *Am J Psychiatry* 137 (1980): 16-20.

Study of Drug-Induced Tardive Psychosis

In 1982, Chouinard and Jones reported that 30% of the 216 schizophrenia outpatients they studied showed sign of tardive psychosis, which meant their psychosis was becoming chronic. When this happens, they wrote, “the illness appears worse” than ever before. “New schizophrenic symptoms of greater severity will appear.”

Source: Chouinard, C. “Neuroleptic-induced supersensitivity psychosis, the ‘Hump Course,’ and tardive dyskinesia.” *J Clin Psychopharmacology* 2 (1982):143-44. Also, Chouinard, C. “Severe cases of neuroleptic-induced supersensitivity psychosis,” *Schiz Res* 5 (1991):21-33.

What Does the Evidence Since Then Show?

- UK first-episode study
- Cross-cultural study
- Animal model studies
- MRI studies
- Longitudinal studies
- Randomized tapering study
- Medication compliance study
- Quebec epidemiological study

U.K. First Episode Study, 1990

- 253 first-episode schizophrenia patients.
- In patients who had been ill less than one year, patient treated with placebo had significantly better “occupational outcome” at two years.

Conclusion: The present finding may be considered as a stronger indication [then even an earlier study] of the possible social cost of maintenance neuroleptic medication.”

Source: E.C. Johnstone. “Further investigation of the predictor of outcome following first schizophrenia episodes.” *Br J of Psychiatry* 157 (1990):182-89.

WHO Cross-Cultural Studies, 1970s/1980s

- In both studies, which measured outcomes at the end of two years and five years, the patients in the three developing countries, India, Nigeria, and Colombia, had a “considerably better course and outcome” than in the U.S. and six other developed countries.
- The WHO researchers concluded that “being in a developed country was a strong predictor of not attaining a complete remission.”
- They also found that “an exceptionally good social outcome characterized the patients” in developing countries.

Source: Jablensky, A. “Schizophrenia, manifestations, incidence and course in different cultures.” *Psychological Medicine* 20, monograph (1992):1-95.

WHO Findings, Continued

Medication usage:

16% of patients in the developing countries were regularly maintained on antipsychotics, versus 61% of the patients in rich countries.

15-year to 20-year followup:

The “outcome differential” held up for “general clinical state, symptomatology, disability, and social functioning.” In the developing countries, 53% of schizophrenia patients were “never psychotic” anymore, and 73% were employed.

Source: Jablensky, A. “Schizophrenia, manifestations, incidence and course in different cultures.” *Psychological Medicine* 20, monograph (1992):1-95. See table on page 64 for medication usage. For followup, see Hopper, K. “Revisiting the developed versus developing country distinction in course and outcome in schizophrenia.” *Schizophrenia Bulletin* 26 (2000):835-46.

Animal Models of Psychosis and Drug-Induced Dopamine Supersensitivity

In 2005, Philip Seeman at the University of Toronto reported that agents that trigger psychotic-like behavior in animals -- amphetamines, angel dust, lesions to the hippocampus, gene-knockout manipulations -- all cause an increase in D2 receptors that have a “high” affinity for dopamine. These results “imply that there may be many pathways to psychosis, including multiple gene mutations, drug abuse, or brain injury, all of which may converge via D2 HIGH to elicit psychotic symptoms,” Seeman wrote.

Source: Seeman, P. “Dopamine supersensitivity correlates with D2 HIGH states, implying many paths to psychosis. *Proceedings of the Nat Acad of Science* 102 (2005): 3513-18. Samaha, A. “Breakthrough dopamine supersensitivity during ongoing antipsychotic treatment leads to treatment failure over time.” *J Neuroscience* 27 (2007):2979-86.

Antipsychotics Increase the Density of D2 HIGH Receptors

In this same report, Seeman found that haloperidol and olanzapine both increased the density of D2 HIGH receptors, and thus cause the very biological abnormality that in animal models had been identified as a final pathway to psychosis.

Philip Seeman Tests His D2 High Theory

In rat studies, “we show that during ongoing treatment with clinically relevant doses, haloperidol and olanzapine progressively lose their efficacy . . . the loss of efficacy is linked to an increase in D2 receptor number and sensitivity. These results are the first to demonstrate that ‘breakthrough’ supersensitivity during ongoing antipsychotic treatment undermines treatment efficacy.”

Source: Samaha, A. “Breakthrough dopamine supersensitivity during ongoing antipsychotic treatment leads to treatment failure over time.” *J Neuroscience* 27 (2007):2979-86.

MRI Study in Macaque Monkeys

Finding:

- In macaque monkeys, treatment with either haloperidol or olanzapine for 17 to 27 months led to a “8-11% reduction in mean fresh brain weights” compared to controls.
- The differences (in brain weights and brain volumes) “were observed across all major brain regions, but appeared most robust in the frontal and parietal regions.”

Source: Dorph-Petersen. “The influence of chronic exposure to antipsychotic medications on brain size before and after tissue fixation.” *Neuropsychopharmacology* (2005) 30: 1649-1661.

Raquel Gur's MRI Study

Patients

- 96 schizophrenia patients
 - 21 neuroleptically naive
 - 75 previously treated

Findings

- Previous treatment associated with higher subcortical volumes (basal ganglia). Association was dose related.
- Higher subcortical volumes were mildly associated with greater severity of both negative and positive symptoms

Conclusion

“Increased subcortical volumes in treated schizophrenia patients seem to be medication-induced hypertrophy. This hypertrophy could reflect structural adaptation to receptor blockade.”

Source: R. Gur. “Subcortical Volumes in Neuroleptic Naive and Treated Patients With Schizophrenia.” *American Journal of Psychiatry* 155 (1998):1711-1717.

Nancy Andreasen's MRI Study

In 2003, Andreasen reported that schizophrenia was a “progressive neurodevelopmental disorder” characterized by “progressive reduction in frontal white matter volume.” This decline in brain volumes was seen in MRI imaging tests.

Source: Ho, B. “Progressive structural brain abnormalities and their relationship to clinical outcome.” *Arch Gen Psych* 60 (2003):585-94.

In 2003 and 2005, Andreasen reported that this brain shrinkage was associated with a worsening of negative symptoms, increased functional impairment, and, after five years, cognitive decline.

Source: Ho, B. "Progressive structural brain abnormalities and their relationship to clinical outcome." *Arch Gen Psych* 60 (2003):585-94. Andreasen, N. "Longitudinal changes in neurocognition during the first decade of schizophrenia illness." *International Congress on Schizophrenia Research* (2005):348.

In 2011, Andreasen reported that this shrinkage was drug-related. Use of the old neuroleptics, the atypical antipsychotics, and clozapine were all “associated with smaller brain tissue volumes,” with decreases in both white and grey matter. The severity of illness and substance abuse had “minimal or no effect” on brain volumes.

Ho, B. “Long-term antipsychotic treatment and brain volumes.” *Arch Gen Psychiatry* 68 (2011):128-37.

Nancy Andreasen, former editor of the *American Journal of Psychiatry*, on antipsychotics:

“What exactly do these drugs do? They block basal ganglia activity. The prefrontal cortex doesn’t get the input it needs and is being shut down by drugs. That reduces psychotic symptoms. It also causes the prefrontal cortex to slowly atrophy.”

--*New York Times*, September 16, 2008

More Evidence That Antipsychotics Shrink the Brain

In a 2012 review of 43 brain-imaging studies of first-episode psychosis, European researchers determined that a loss of gray matter volume was “significantly more severe in medicated patients.”

Source: J. Radua. “Multimodal meta-analysis of structural and functional changes in first episode psychosis and the effects of antipsychotic medications.” *Neuroscience and Biobehavioral Review*, in press as of 9/04/2012.

A German Perspective on Drug-Induced Brain Shrinkage

“The findings indicate that there is evidence for grey and white matter volume changes of the frontal brain, which cannot be explained by the severity of the disease alone but are also very likely a manifestation of long-term effects of antipsychotics . . . Considering the contribution of antipsychotics to the changes in brain structure, which seem to depend on cumulative dosage and can exert adverse effects on neurocognition, negative and positive symptoms and psychosocial functioning, the guidelines for antipsychotic long-term drug treatment should be reconsidered.”

Martin Harrow's Longitudinal Study

Baseline n = 200 psychotic patients

- Median age: 22.9 years at index hospitalization
- Previous hospitalization

46% first hospitalization

21% one previous hospitalization

33% two or more previous hospitalizations

Source: Harrow M. "Factors involved in outcome and recovery in schizophrenia patients not on antipsychotic medications." *Journal of Nervous and Mental Disease* 195 (2007):406-14.

Patient Composition at 15 Years

145 patients still in study (77%)

- 64 schizophrenia patients
- 81 patients with other psychotic disorders

37 psychotic bipolar patients

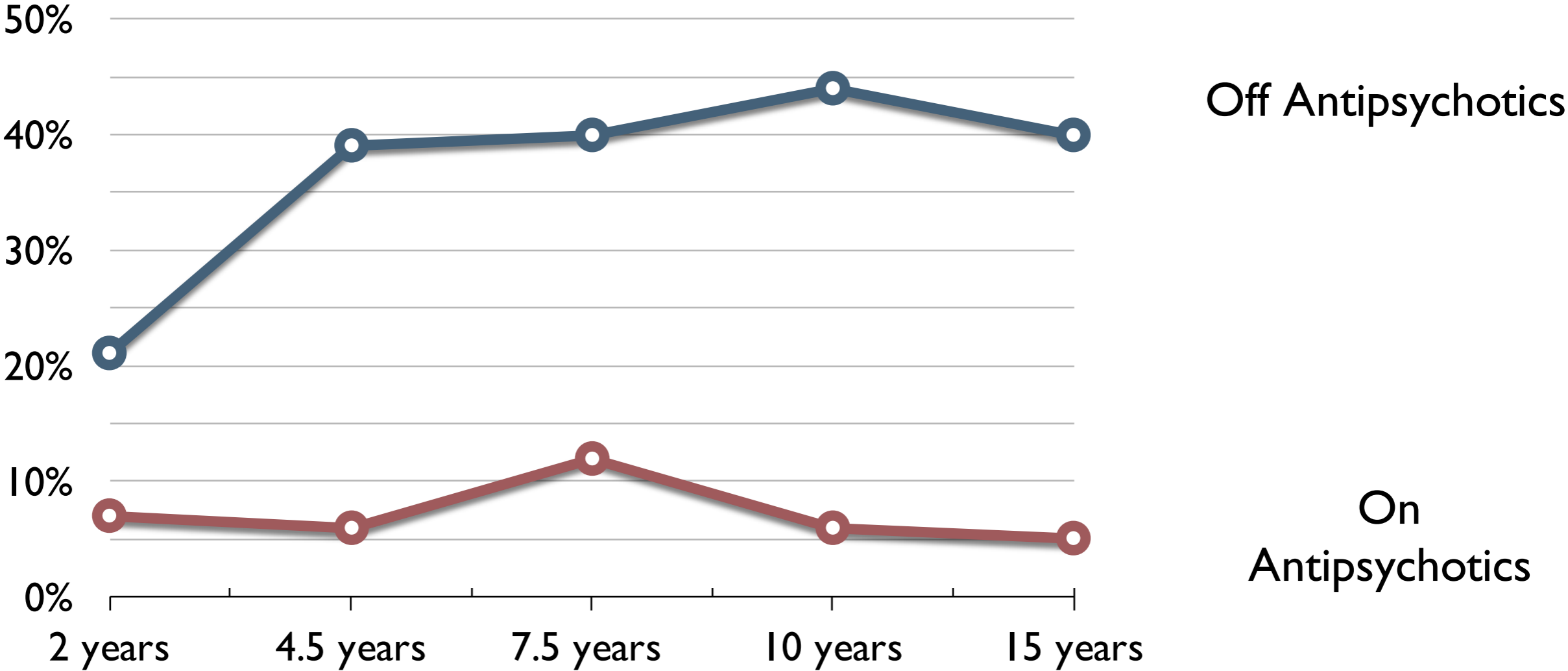
28 unipolar psychotic patients

16 other milder psychotic disorders

Source: Harrow M. "Factors involved in outcome and recovery in schizophrenia patients not on antipsychotic medications." *J of Nervous and Mental Disease* 195 (2007):406-14.

Long-term Recovery Rates for Schizophrenia Patients

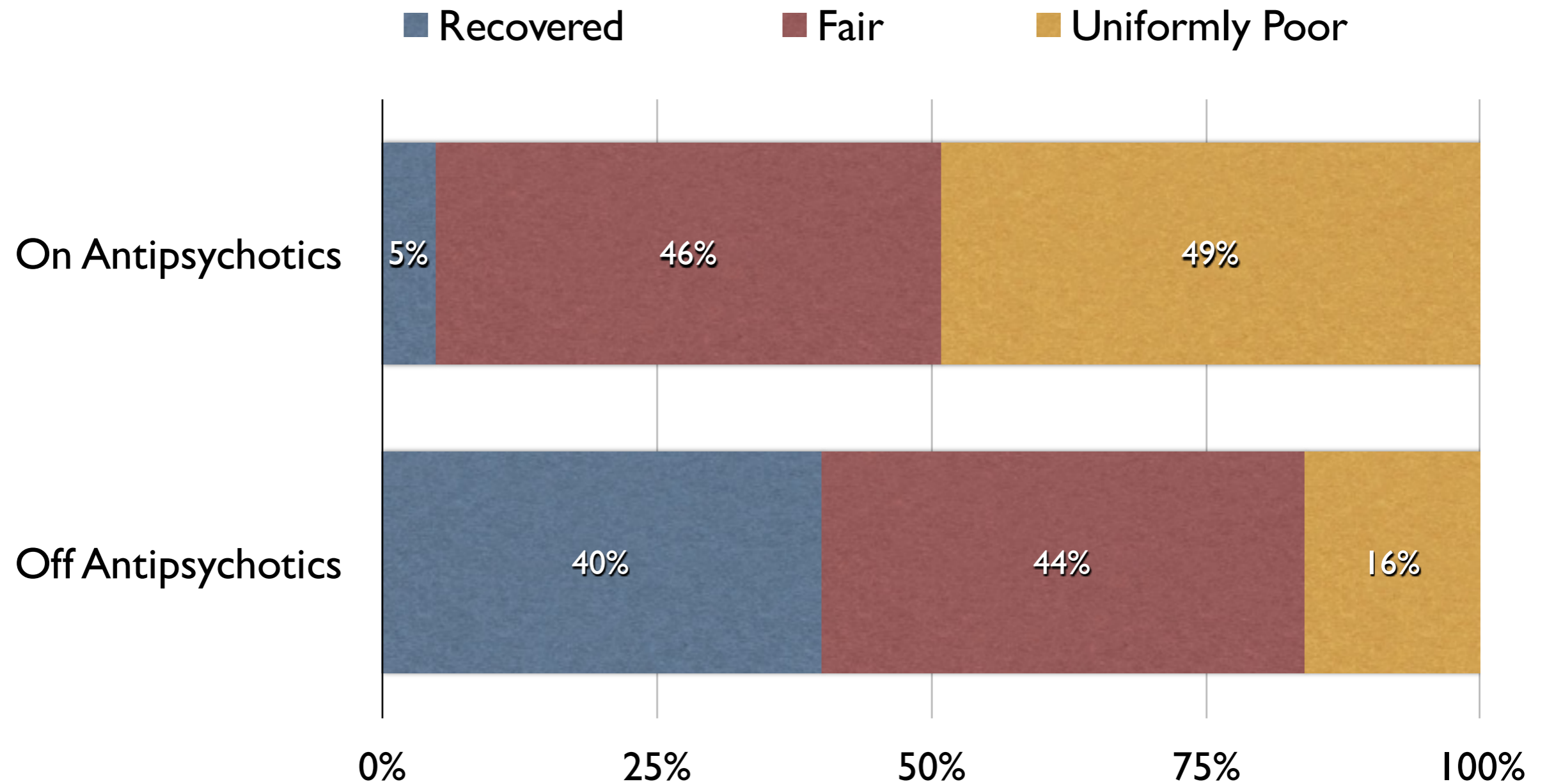
N = 64



Source: Harrow M. "Factors involved in outcome and recovery in schizophrenia patients not on antipsychotic medications." *Journal of Nervous and Mental Disease* 195 (2007):406-14.

Spectrum of Outcomes in Harrow's Study

(At 15 years)



Source: Harrow M. "Factors involved in outcome and recovery in schizophrenia patients not on antipsychotic medications." *Journal of Nervous and Mental Disease* 195 (2007):406-14.

“In addition, global outcome for the group of patients with schizophrenia who were on antipsychotics was compared with the off-medication schizophrenia patients with similar prognostic status. Starting with the 4.5-year follow-up and extending to the 15-year follow-up, the off-medication subgroup tended to show better global outcomes at each followup.”

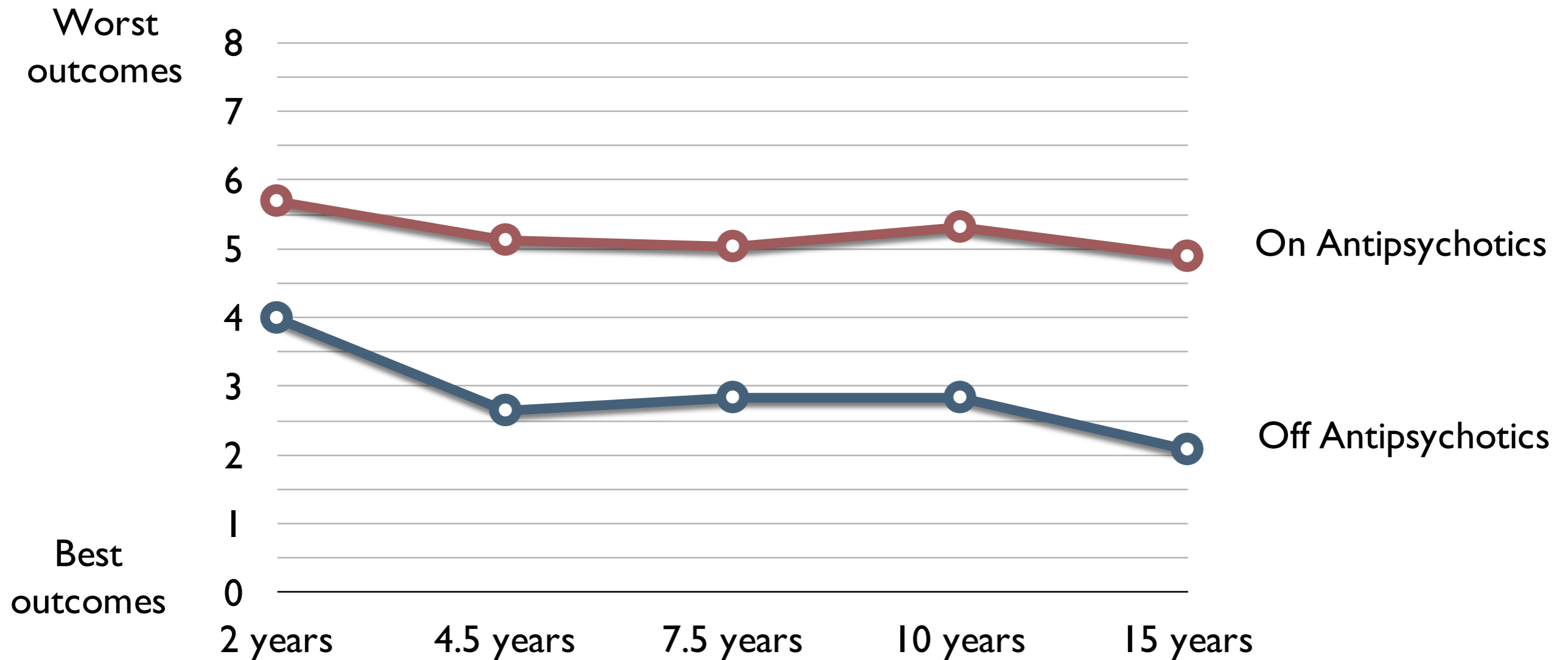
Martin Harrow, page 411.

“I conclude that patients with schizophrenia not on antipsychotic medication for a long period of time have significantly better global functioning than those on antipsychotics.”

--Martin Harrow, American Psychiatric Association annual meeting, 2008

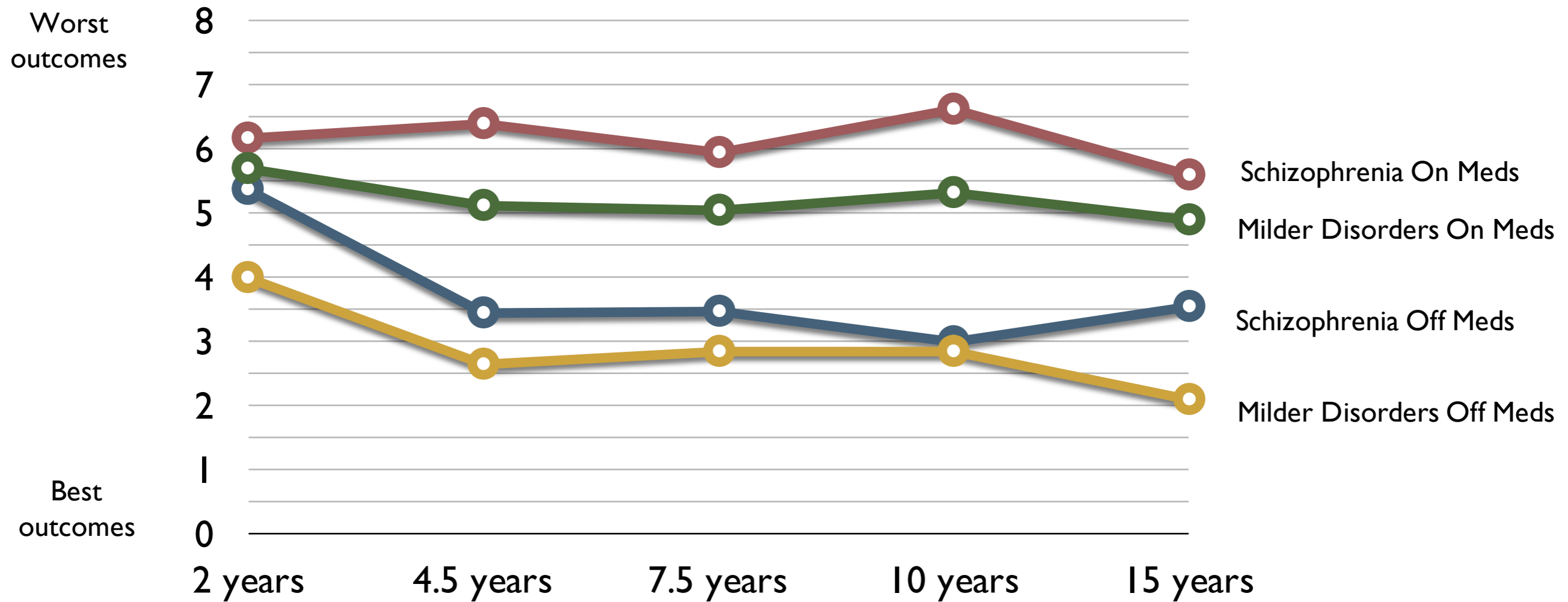
Global Adjustment of “Other Psychotic” Patients

N = 81



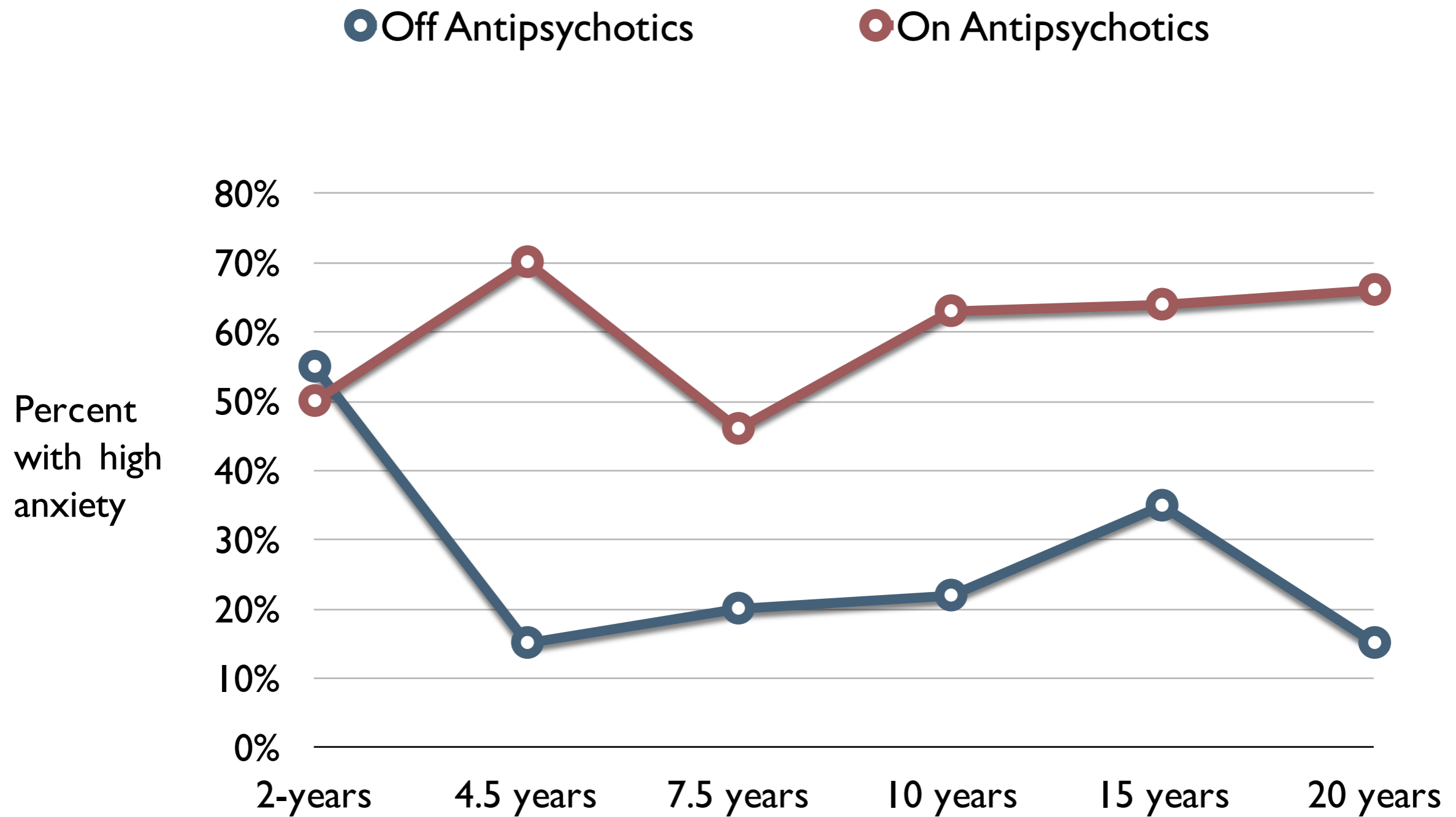
Source: Harrow M. “Factors involved in outcome and recovery in schizophrenia patients not on antipsychotic medications.” *Journal of Nervous and Mental Disease* 195 (2007):406-14.

Global Adjustment of All Psychotic Patients



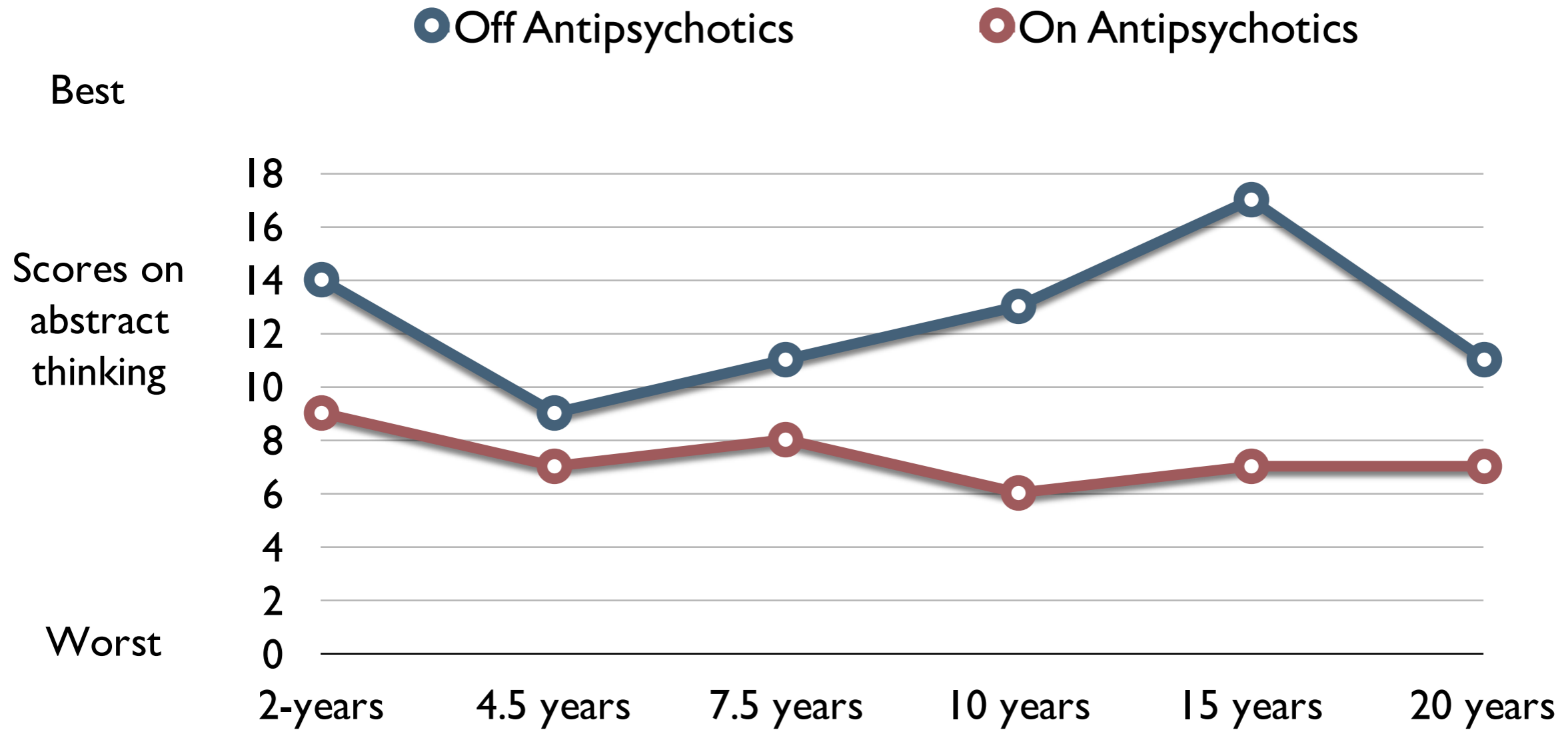
Source: Harrow M. "Factors involved in outcome and recovery in schizophrenia patients not on antipsychotic medications." *Journal of Nervous and Mental Disease* 195 (2007):406-14.

Anxiety Symptoms of Schizophrenia Patients



Source: Harrow M. "Do all schizophrenia patients need antipsychotic treatment continuously throughout their lifetime? A 20-year longitudinal study." *Psychological Medicine*, (2012):1-11.

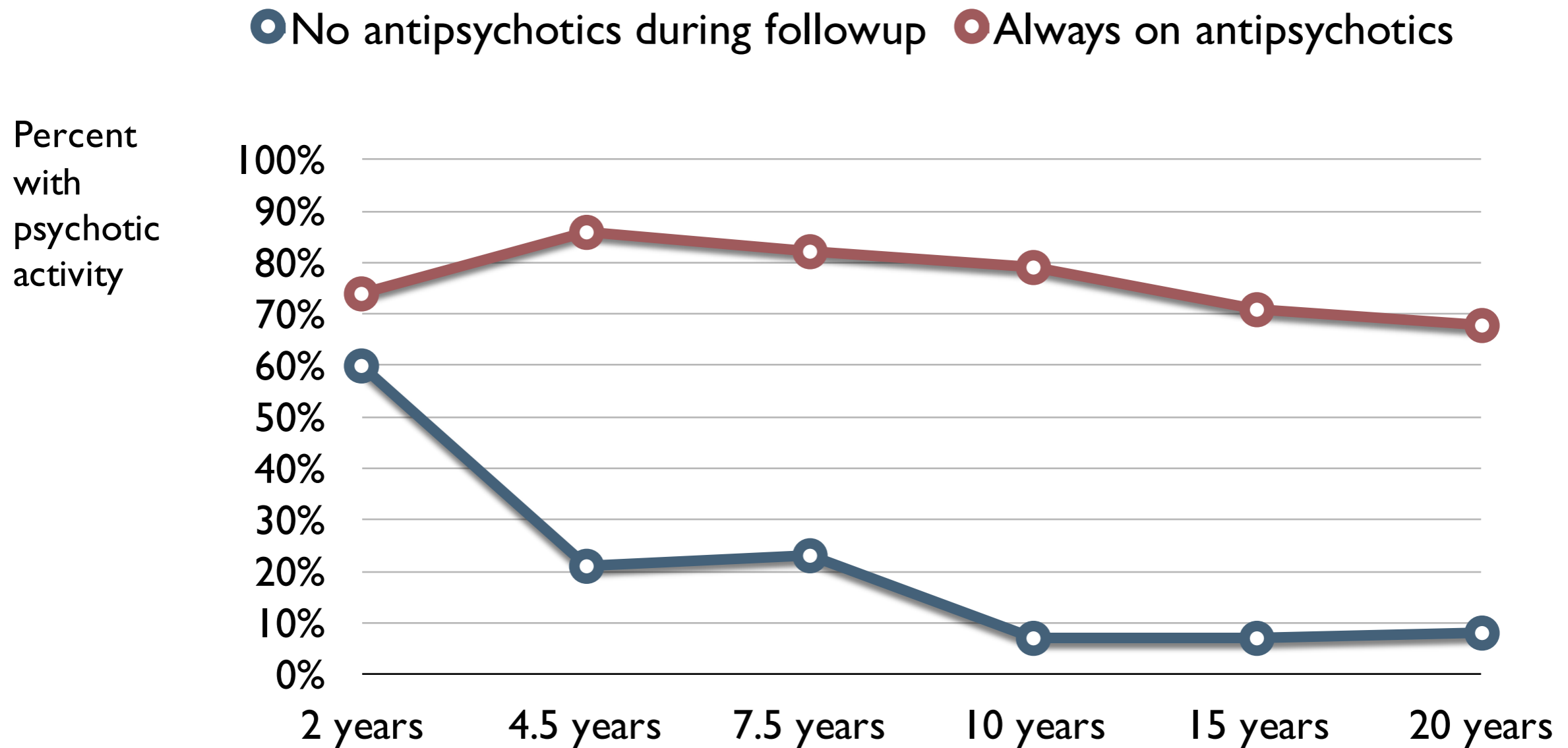
Cognitive Function of Schizophrenia Patients



Source: Harrow M. "Do all schizophrenia patients need antipsychotic treatment continuously throughout their lifetime? A 20-year longitudinal study." *Psychological Medicine*, (2012):1-11.

Psychotic Symptoms of Schizophrenia Patients

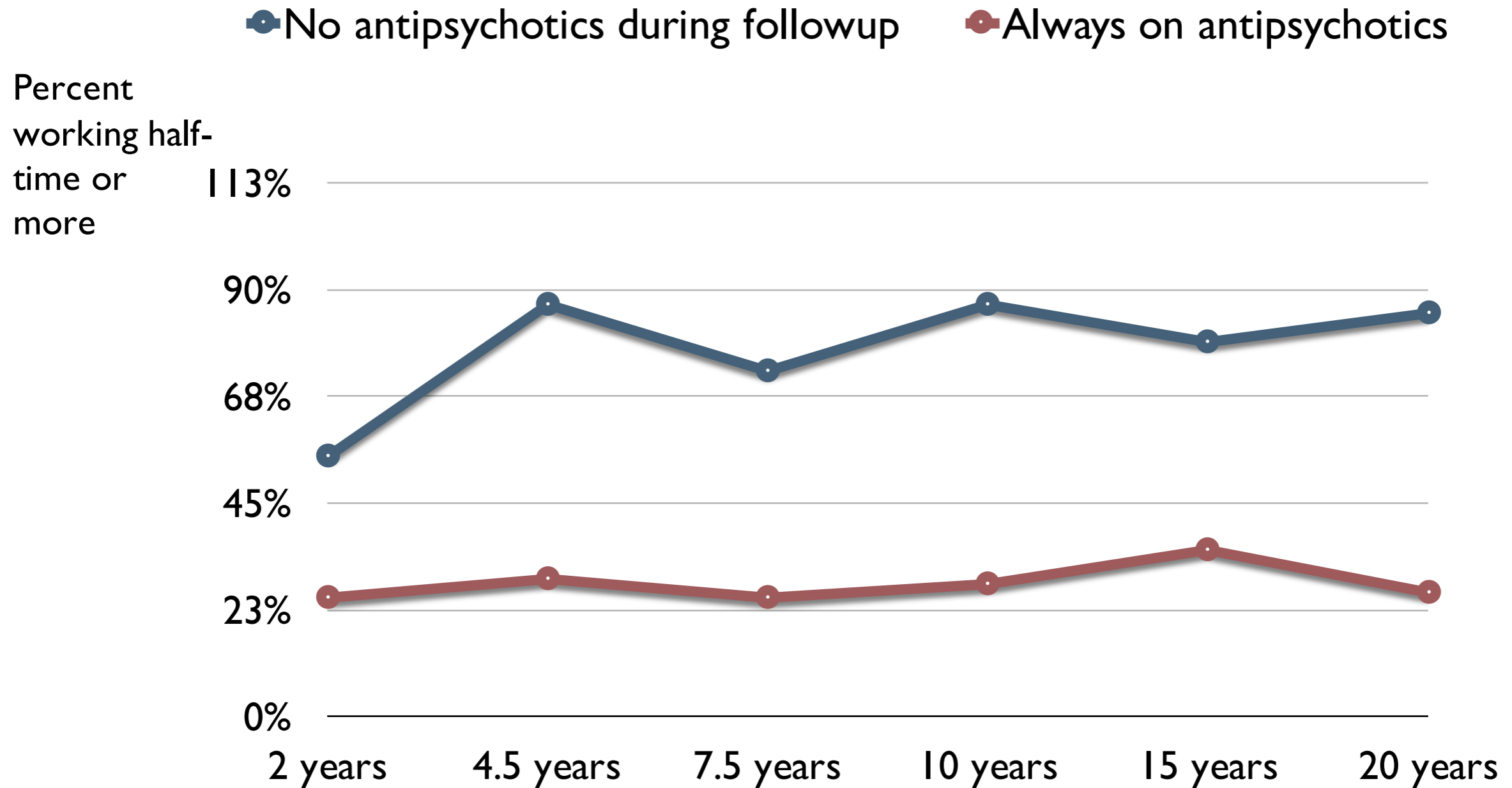
(Subset analysis of schizophrenia patients)



Source: Harrow M. "Does treatment of schizophrenia with antipsychotic medications eliminate or reduce psychosis?" *Psychological Medicine*, (2014):doi:10.1017/S0033291714000610

Work History of Schizophrenia Patients

(Subset analysis of schizophrenia patients)



Source: M. Harrow. "Pharmacological Treatment for Psychosis: Emerging Perspectives." Presentation in Syracuse, NY, October 2, 2014.

“How unique is it that the apparent efficacy of antipsychotics could diminish over time or become ineffective or harmful? There are many examples for other medications of similar long-term effects, with this often occurring as the body readjusts, biologically, to the medications.”

--Martin Harrow, 2013

Australian Study of Effects of Medication Compliance on Outcomes

- 81 first episode patients
- 41 randomized to specialized relapse prevention therapy expected to increase medication compliance
- Specialized therapy did increase medication compliance over 30 months
- However, increase in medication adherence associated with “decreases in psychosocial functioning and increases in negative symptoms.”

Conclusion:

“This is consistent with previous research showing an association between better vocational functioning at 2-year followup and placebo treatment compared with antipsychotic medication in a first-episode schizophrenia sample.”

J. Gleeson. “A randomized controlled trial of relapse prevention therapy for first-episode psychosis patients.” *Schizophrenia Bulletin* 39 (2013):436-48.

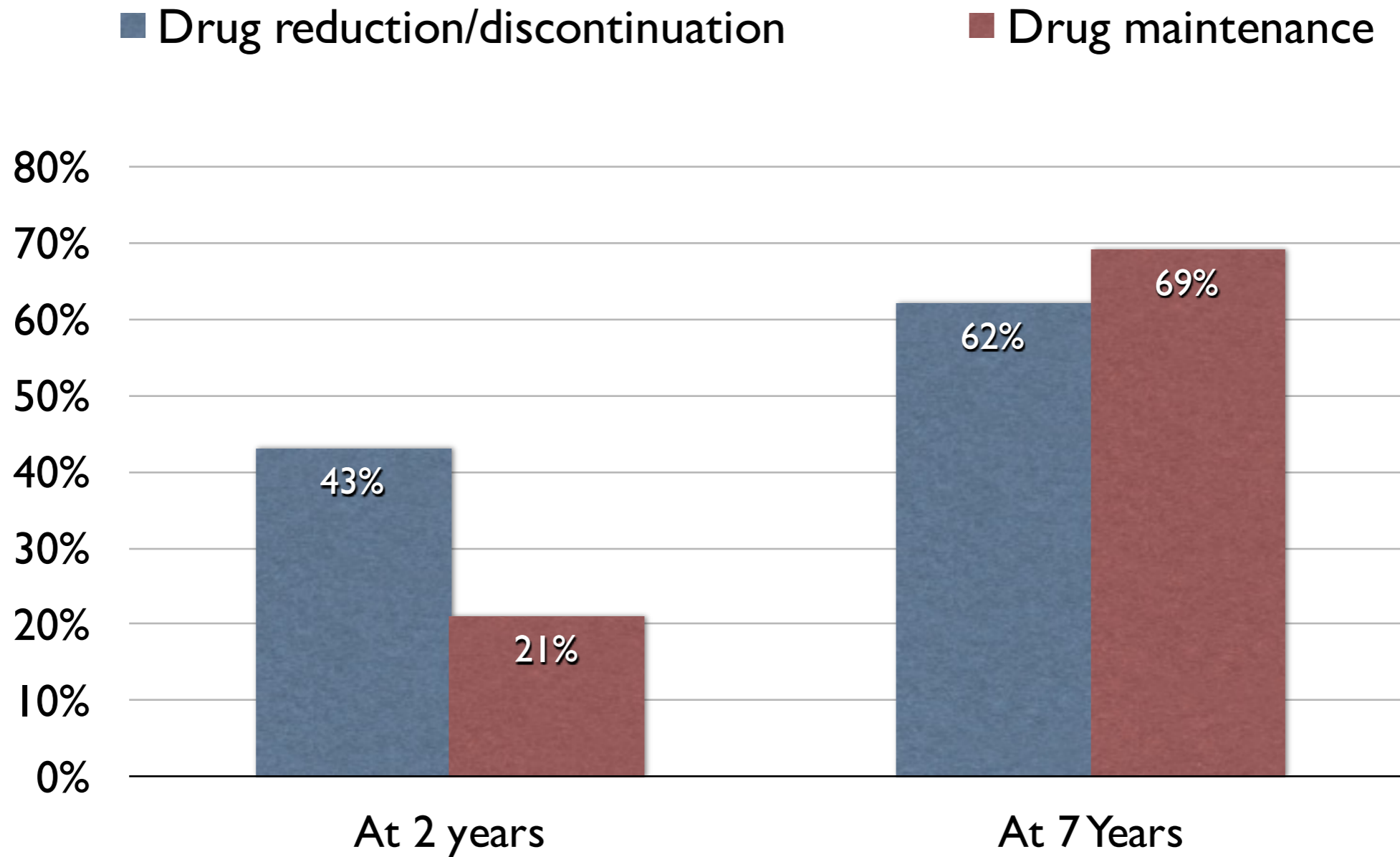
Lex Wunderink's Randomized Study of Long-term Outcomes

Study Design

- 128 stabilized first-episode psychotic patients who had been stable for six months on antipsychotics. (103 patients were still in the study at the end of seven years.)
- Randomized either to a dose reduction/discontinuation treatment (DR group), or to standard antipsychotic treatment (MT group.)

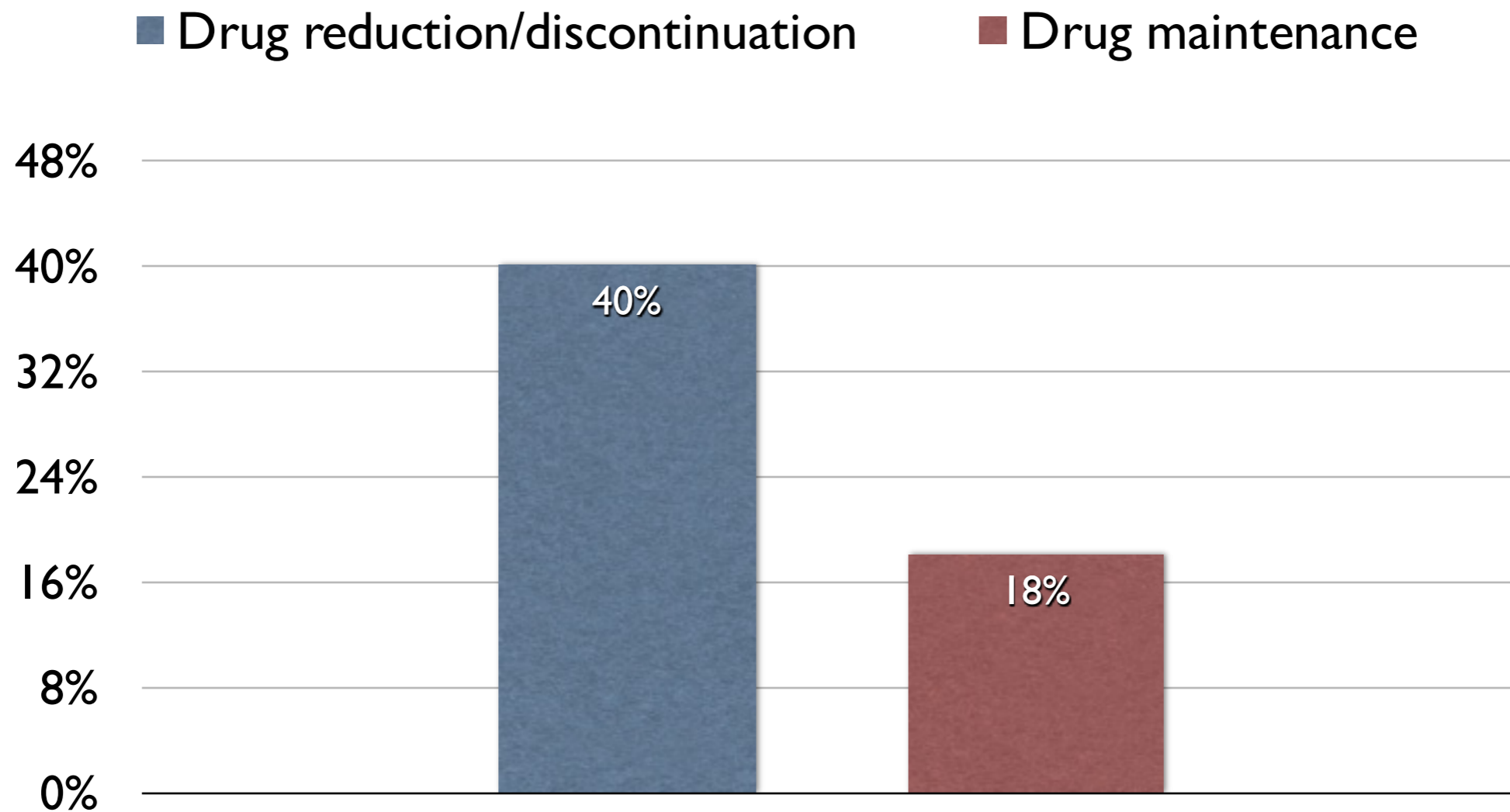
L. Wunderink. "Recovery in remitted first-episode psychosis at 7 years of follow-up of an early dose reduction/discontinuation of maintenance treatment strategy." *JAMA Psychiatry*, published online, July 3, 2013.

Relapse Rates

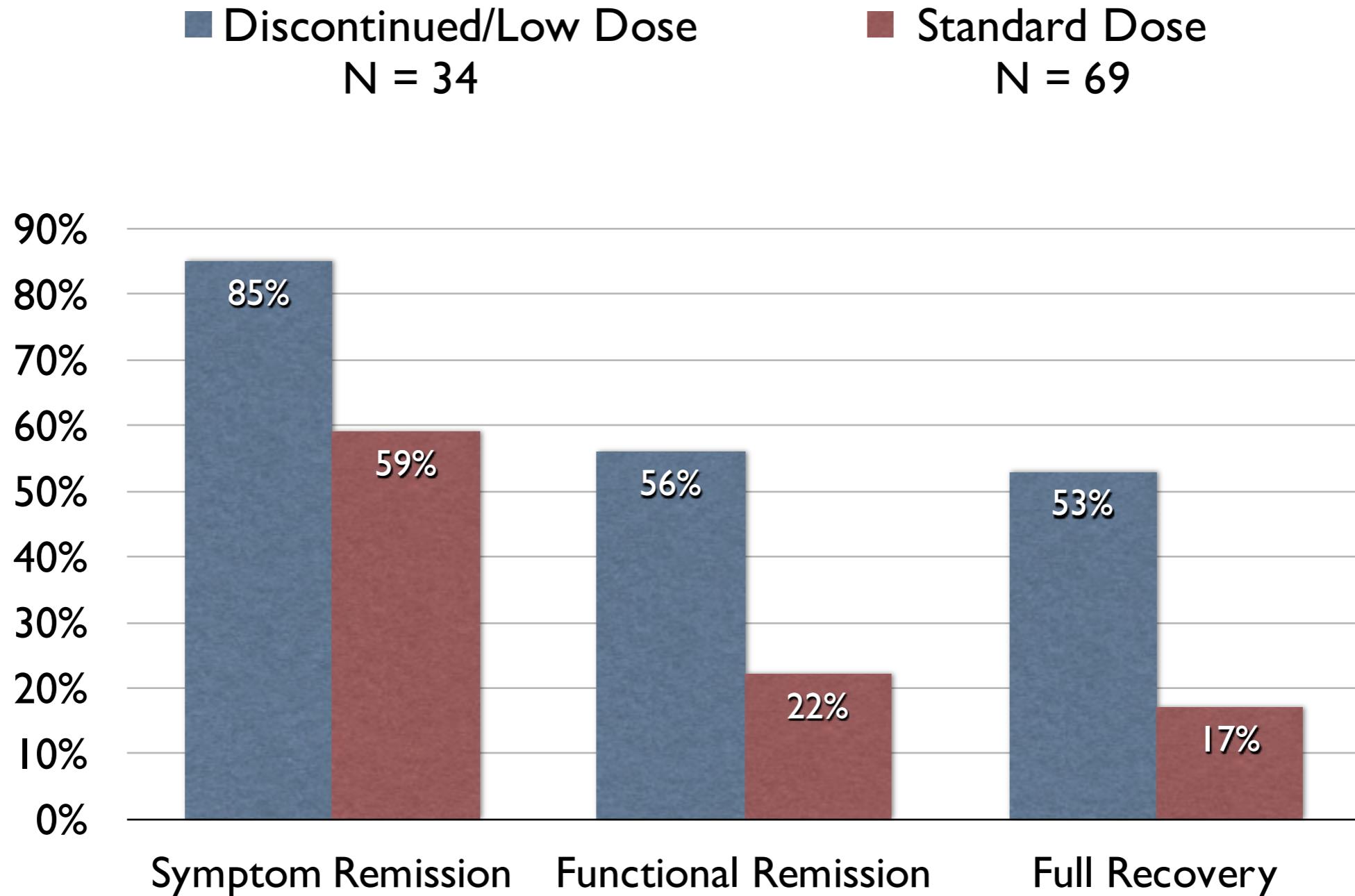


L. Wunderink. "Recovery in remitted first-episode psychosis at 7 years of follow-up of an early dose reduction/discontinuation of maintenance treatment strategy." *JAMA Psychiatry*, published online, July 3, 2013.

Long-Term Recovery Rates (at 7 Years)



Outcomes By Antipsychotic Use



Wunderink's Conclusions

I. *Antipsychotics may worsen functional outcomes:*

“Antipsychotic postsynaptic blockade of the dopamine signaling system, particularly of the mesocortical and mesolimbic tracts, not only might prevent and redress psychotic derangements but also might compromise important mental functions, such as alertness, curiosity, drive, and activity levels, and aspects of executive functional capacity to some extent.”

2. The previous methods to assess outcomes were flawed:

“The results of this study lead to the following conclusions: schizophrenia treatment strategy trials should include recovery or functional remission rates as their primary outcome and should also include long-term follow-up for more than 2 years, even up to 7 years or longer. In the present study, short-term drawbacks, such as higher relapse rates, were leveled out in the long term, and benefits that were not evident in short-term evaluation, such as functional gains, only appeared in long-term monitoring.”

Finnish Longitudinal Study

Study design: Researchers identified 70 patients in northern Finland who were born in 1966 and diagnosed as adults with schizophrenic psychoses. The 40 patients were assessed at the start of the study, when they were 34 years old (with a mean duration of illness of 10.4 years at that point), and followed for nine more years.

Results: At initial assessment, the 24 patients off medication were doing better than the 46 patients on antipsychotics: they were much more likely to be working, more likely to be in remission, and had better clinical outcomes.

During the follow-up, 46% of the non-medicated patients suffered a relapse, compared to 56% of the medicated group. Those who used antipsychotics less than 50% of the time were more likely to be functioning well, in remission, and to have a good clinical outcome than those who used medications more than half the time.

Source: Moilanen, J. "Characteristics of subjects with schizophrenia spectrum disorder with and without antipsychotic medication—a 10-year follow-up of the Northern Finland 1966 birth cohort study." *Eur Psychiatry* 28 (2012):53-58. Moilanen, J. "The use of antipsychotic medication and its association with outcomes and brain morphometry in schizophrenia – the Northern Finland birth cohort 1966 study." PhD dissertation, University of Oulu, Finland, 2016.

A Call to Rethink Antipsychotics

“It is time to reappraise the assumption that antipsychotics must always be the first line of treatment for people with psychosis. This is not a wild cry from the distant outback, but a considered opinion by influential researchers . . . [there is] an increasing body of evidence that the adverse effects of [antipsychotic] treatment are, to put it simply, not worth the candle.”

--Peter Tyrer, Editor

British Journal of Psychiatry, August 2012

Epidemiological Studies

Researchers in Quebec and Finland have reported that through analysis of prescription data for antipsychotics, patients off medication in any one month (or study period) are more likely to be rehospitalized, and have generally poorer outcomes.

“Effectiveness
of
antipsychotics
patients
community
after
first h
ospitalization
46
treatments in a
due to

Summary of Evidence Since 1980

The Case Against Antipsychotics	The Case For Antipsychotics
UK first episode study	Quebec epidemiological study
WHO cross-cultural study	
Animal model research	
MRI studies	
Harrow's longitudinal study	
Wunderink's randomized study	
Medication compliance study	

A Model for Selective Use of Antipsychotics

The practice in Western Lapland, Finland (since 1992)

- First-episode patients are not immediately put on antipsychotics. Instead, they are treated with intensive psychosocial care, and benzodiazepines on an as-needed basis, to help people sleep.
- As long as patients are getting better, antipsychotics are not used. If, after several weeks, they are not improving, then low doses of an antipsychotic are prescribed.
- After the medicated patients are stabilized, there is an effort--after six months or so--to gradually withdraw them from the medication.

Outcomes with Selective Use Of Antipsychotics

Five-Year Outcomes for First-Episode Psychotic Patients in Finnish Western Lapland Treated with Open-Dialogue Therapy

Patients (N=75)	
Schizophrenia (N=30)	
Other psychotic disorders (N=45)	
Antipsychotic use	
Never exposed to antipsychotics	67%
Occasional use during five years	33%
Ongoing use at end of five years	20%
Psychotic symptoms	
Never relapsed during five years	67%
Asymptomatic at five-year followup	79%
Functional outcomes at five years	
Working or in school	73%
Unemployed	7%
On disability	20%

Source: Seikkula, J. "Five-year experience of first-episode nonaffective psychosis in open-dialogue approach." *Psychotherapy Research* 16 (2006):214-28.

On importance of using neuroleptics in a selective fashion:

“I am confident of this idea. There are patients who may be living in a quite peculiar way, and they may have psychotic ideas, but they still can hang on to an active life. But if they are medicated, because of the sedative action of the drugs, they lose this ‘grip on life,’ and that is so important. They become passive, and they no longer take care of themselves.”

--Jaakko Seikkula