The Case Against Psychiatric Drugs:

History, Science, and the Long-term Effects of Psychiatric Medications

The Common Wisdom

The introduction of Thorazine into asylum medicine in 1955 "initiated a revolution in psychiatry, comparable to the introduction of penicillin in general medicine."

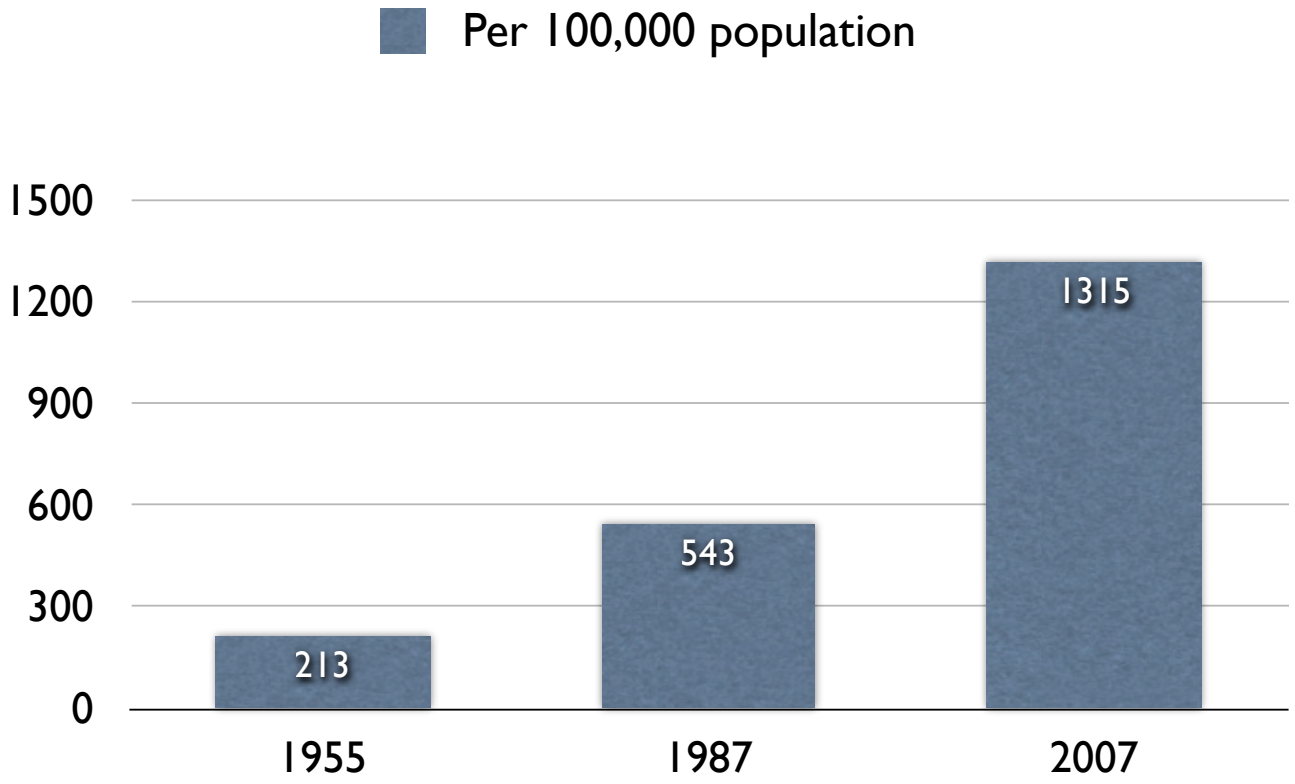
--Edward Shorter, *A History of Psychiatry*

Question Number One

Is this paradigm of care working for societies?

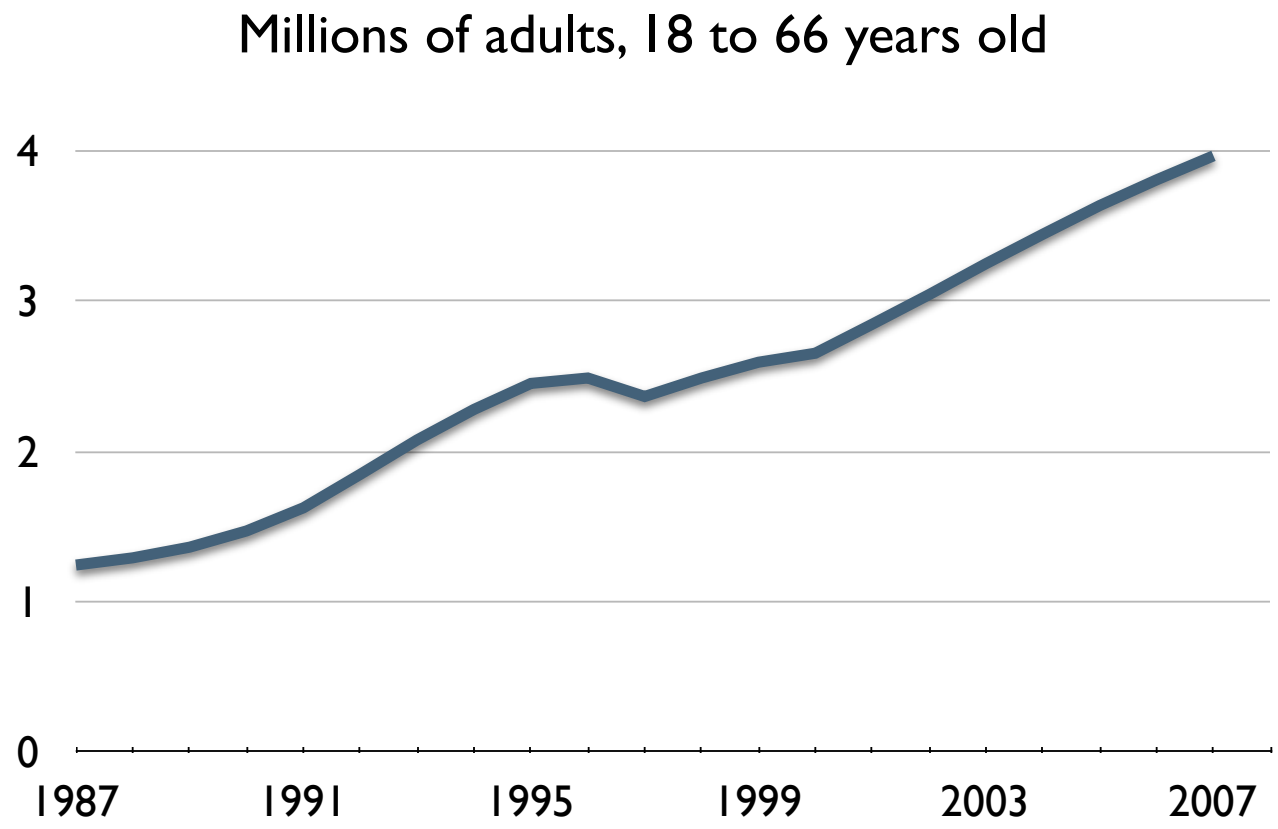
The Disabled Mentally Ill in the United States, 1955-2007

(under government care)



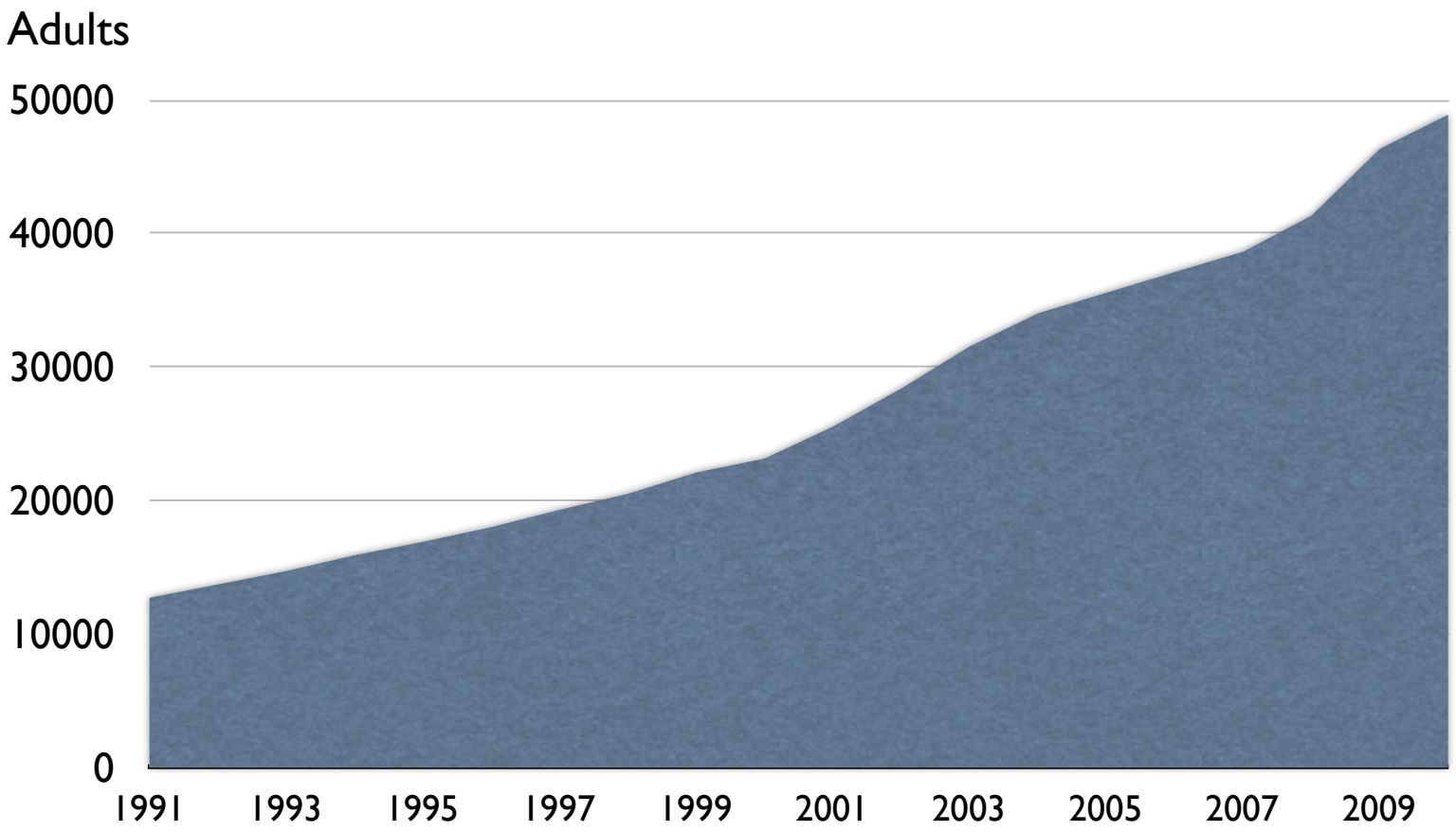
Source: Silverman, C. *The Epidemiology of Depression* (1968): 139. U.S. Social Security Administration Reports, 1987-2007.

U.S. Disability in the Prozac Era



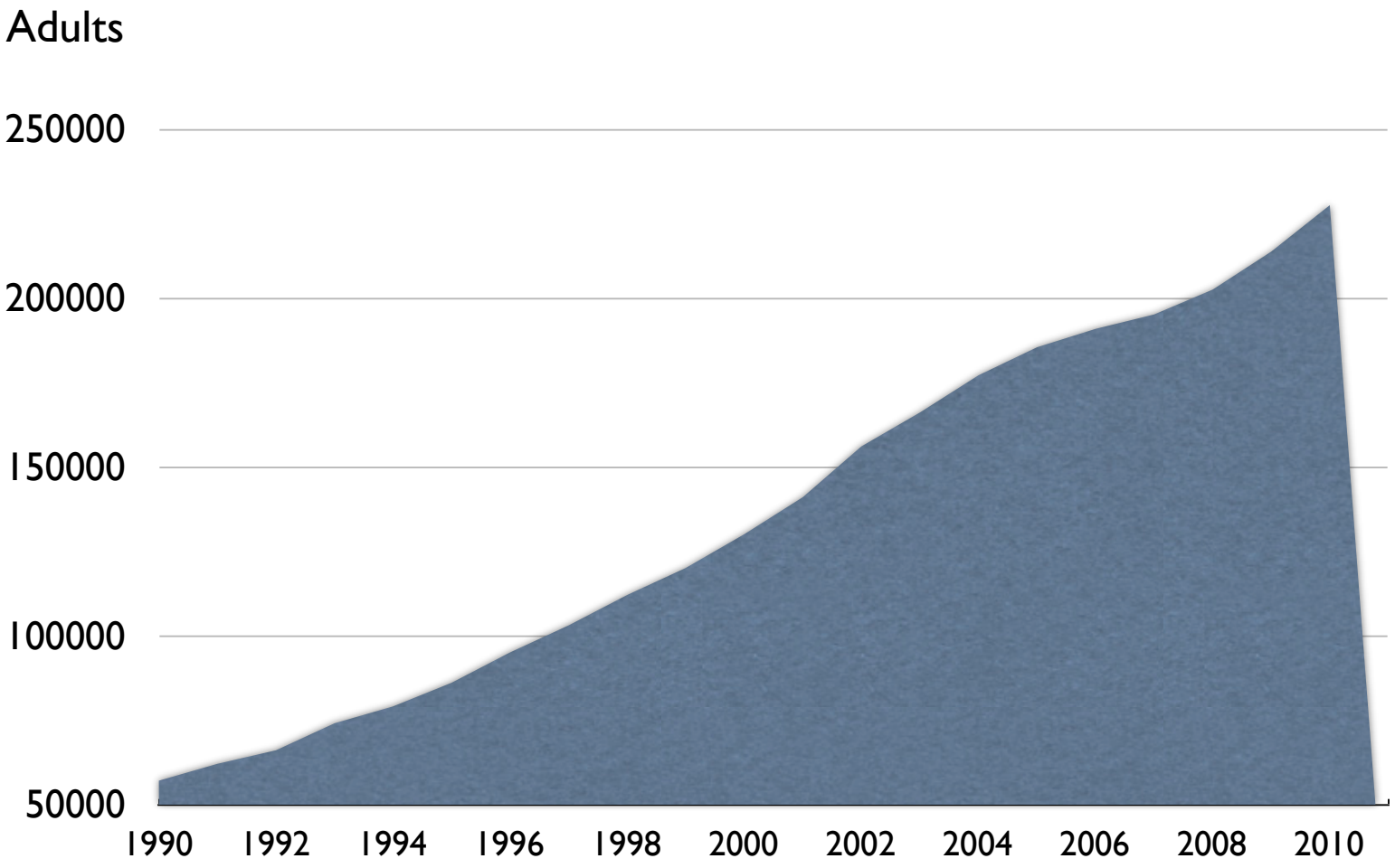
Source: U.S. Social Security Administration Reports, 1987-2007

Disability Due to Psychiatric Disorders in New Zealand, 1991-2010

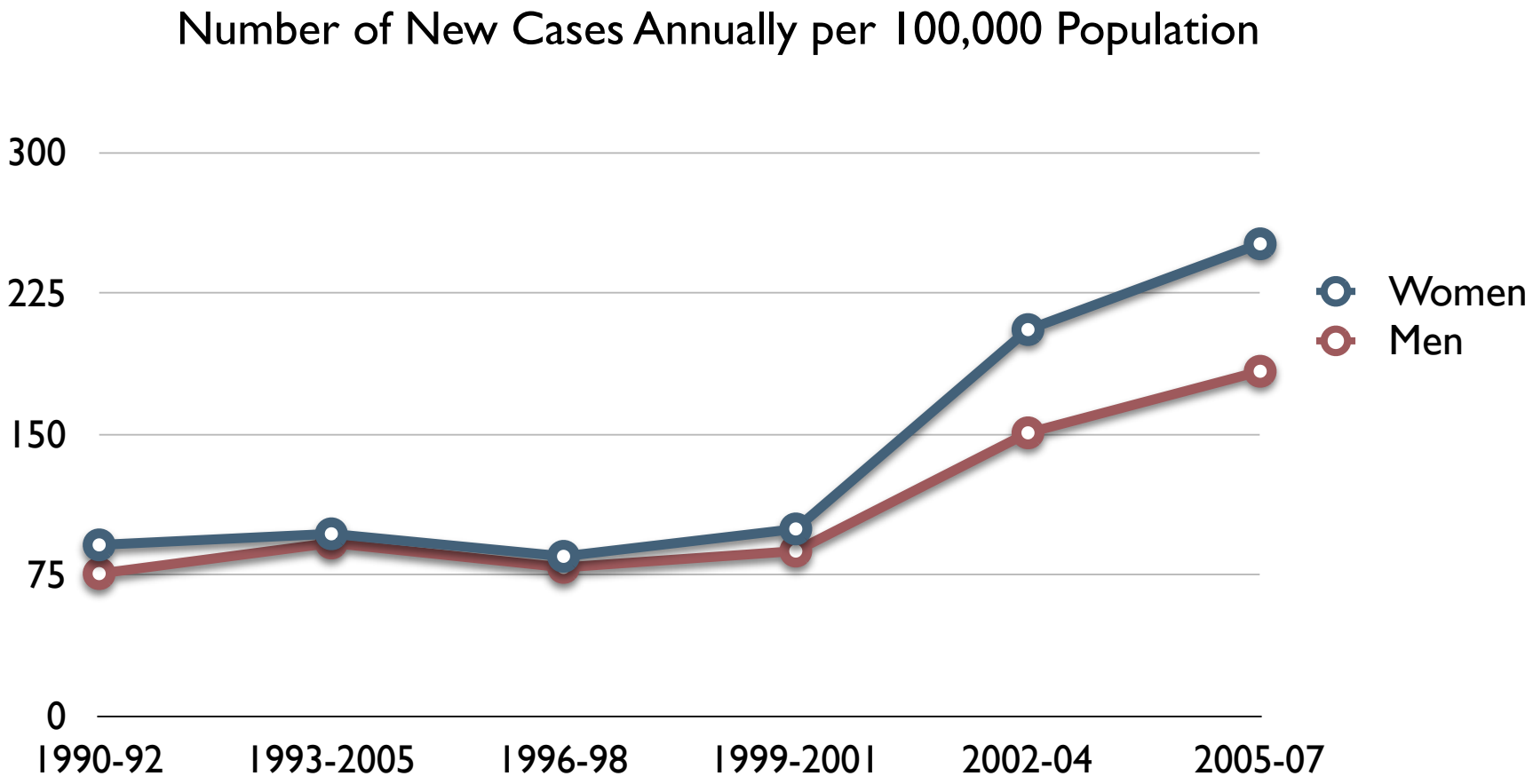


Source: *Statistics New Zealand,* Annual reports, 1999-2010

Disability Due to Psychiatric Disorders in Australia, 1990-2010



Disability Due to Mental and Behavioural Disorders in Iceland, 1990-2007



Source: Thoriacius, S. "Increased incidence of disability due to mental and behavioural disorders in Iceland, 1990-2007." *J Ment Health* (2010) 19: 176-83.

Question Number Two

Is The Chemical Imbalance Story True?

The Chemical Imbalance Theory of Mental Disorders

- Arose from understanding of how drugs act on brain (1960s-1970s)

- Investigations of dopamine theory of schizophrenia and serotonin theory of depression started in 1970s

Findings re the Chemical Imbalance Theory of Mental Disorders

A. Serotonin Theory of Depression

"Elevations or decrements in the functioning of serotonergic systems per se are not likely to be associated with depression." --NIMH, 1984.

"There is no clear and convincing evidence that monoamine deficiency accounts for depression; that is, there is no real monamine deficit."--Stephen Stahl, *Essential Psychopharmacology,* 2000

"After more than a decade of PET studies, monamine depletion studies, and genetic association analyses examining polymorphisms in monaminergic genes, there is little evidence to implicate true deficits in serotonergic, noradrenergic, or dopaminergic neurotransmission in the pathophysiology of depression. This is not surprising, as there is no a priori reason that the mechanism of action of a treatment is the opposite of disease pathophysiology." Eric Nestler, "Linking Molecules to Mood," 2010.

B. Dopamine Theory of Schizophrenia

"There is no compelling evidence that a lesion in the dopamine system is a primary cause of schizophrenia." *Molecular Psychiatry*, 2002

C. Chemical Imbalance Theory of Mental Disorders (in general)

"We have hunted for big simple neurochemical explanations for psychiatric disorders and have not found them." Kenneth Kendler, *Psychological Medicine*, 2005.

A Paradigm for Understanding Psychotropic Drugs

Stephen Hyman, former director of the NIMH, 1996:

• Psychiatric medications "create perturbations in neurotransmitter functions."

• In response, the brain goes through a series of compensatory adaptations in order "to maintain their equilibrium in the face of alterations in the environment or changes in the internal milieu."

• The "chronic administration" of the drugs then cause "substantial and long-lasting alterations in neural function."

• After a few weeks, the person's brain is now functioning in a manner that is "qualitatively as well as quantitatively different from the normal state."

Source: Hyman, S. "Initiation and adaptation: A paradigm for understanding psychotropic drug action." *Am J Psychiatry* 153 (1996):151-61.

Question Number Three

How Do Psychiatric Medications Shape Long-Term Outcomes?

The Evidence for Psychiatric Drugs

Short-term Use

The medications 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. See antipsychotics in particular.

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 major mental 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. This heightened risk of relapse is due to the fact that the brain has been changed by exposure to the drug.

C. The medical profession no longer has an understanding of the "natural course" of major mental disorders, such as depression, bipolar disorder, and psychotic disorders, and thus its clinical perceptions about the efficacy of the drugs isn't informed by that long-term perspective.

Assessing Long-Term Schizophrenia Outcomes

"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)

The Hippocratic Oath

In order for a treatment to do no harm, it must improve on natural recovery rates.

Schizophrenia Outcomes, 1945-1955

• At end of three years following hospitalization, 73 percent 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 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.

Clinicians' Perceptions

• Patients were returning with great frequency, which was dubbed the "revolving door syndrome."

• 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?" *American Journal of Psychiatry* 135 (1978: 1321-4.

Bockoven's 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	1.70	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, 1977

Results

• Those treated without drugs were discharged sooner than drug-treated patients in a comparison group.

• At the end of one year, only 35 percent of the non-medicated group 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.

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."

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

The Dopamine Supersensitivity Theory

"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 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.

Philip Seeman's D2 HIGH Theory

In 2005, Seeman 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." Neuropsychopharmaology (2005) 30: 1649-1661.

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

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 had a "considerably better course and outcome."

•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.

Dueling Histories: Which Is Predictive of Outcomes in Long-Term Observational Studies?

If the conventional wisdom is correct, then medicated schizophrenia patients should have markedly better outcomes.

If the science reviewed here is predictive, then medicated patients, in the aggregate, should suffer more persistent psychotic symptoms and have worse global outcomes.

Martin Harrow's Long-Term Study of Psychotic Patients

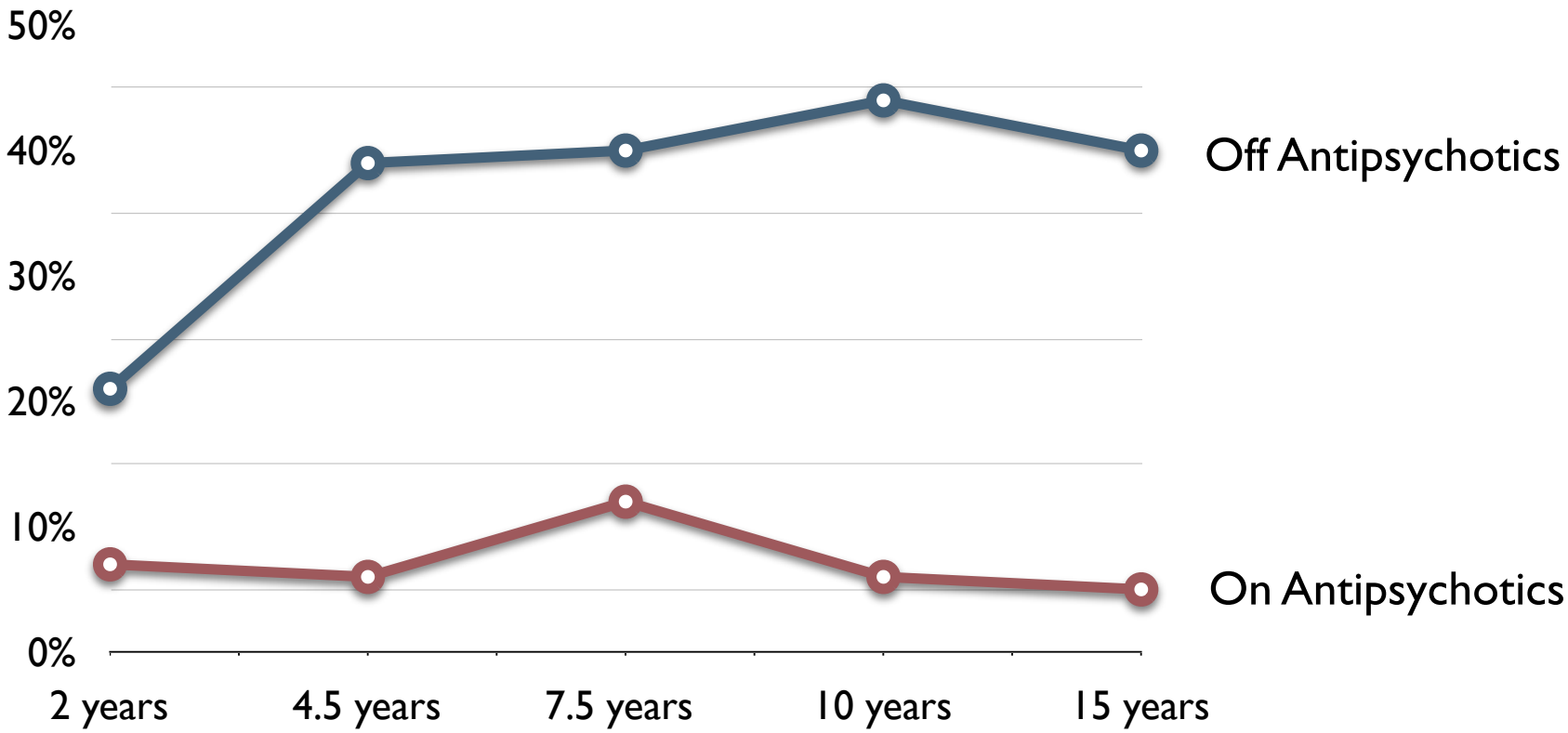
Patient Enrollment

- 64 schizophrenia patients
- 81 patients with other psychotic disorders
  - 37 psychotic bipolar patients
  - 28 unipolar psychotic patients
  - 16 other milder psychotic disorders

- Median age of 22.9 years at index hospitalization
- Previous hospitalization
  - 46% first hospitalization
  - 21% one previous hospitalization
  - 33% two or more previous hospitalizations

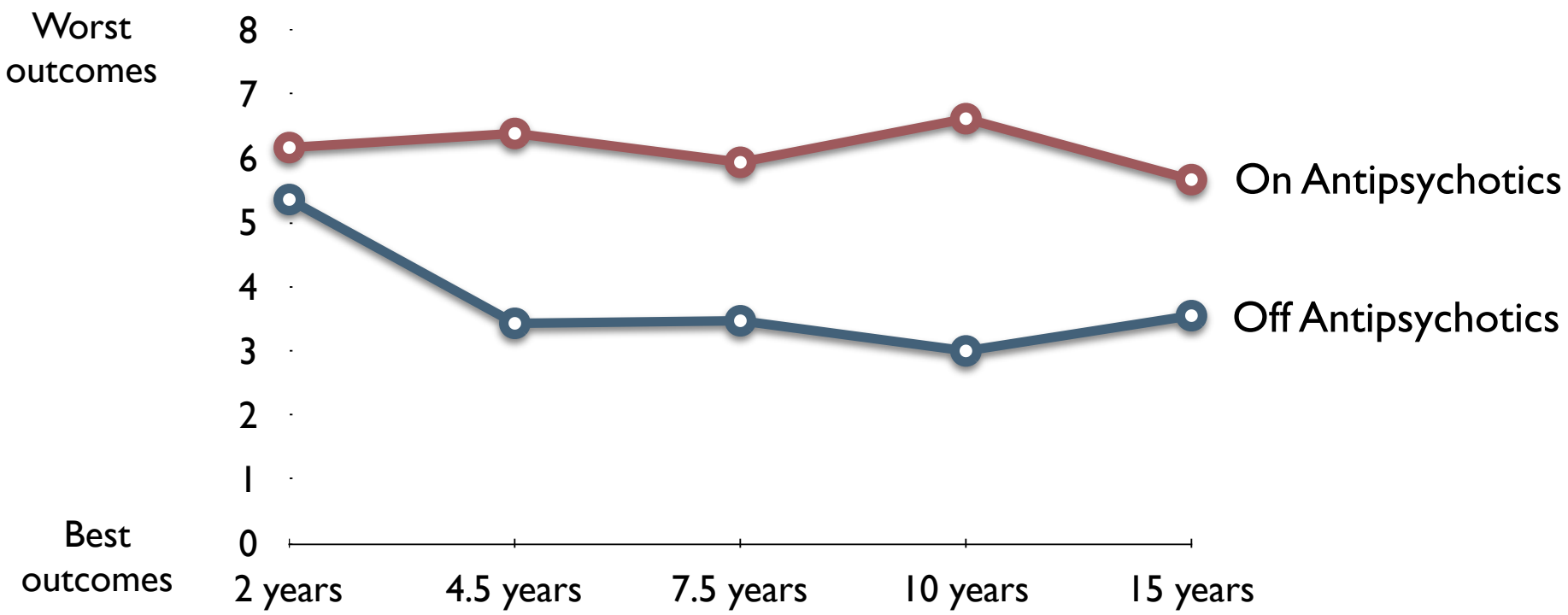
Source: Harrow M. "Factors involved in outcome and recovery in schizophrenia patients not on antipsychotic medications." *Journal of Nervous and Mental Disease* 195 (2007):406-14.

Long-term Recovery Rates for Schizophrenia Patients



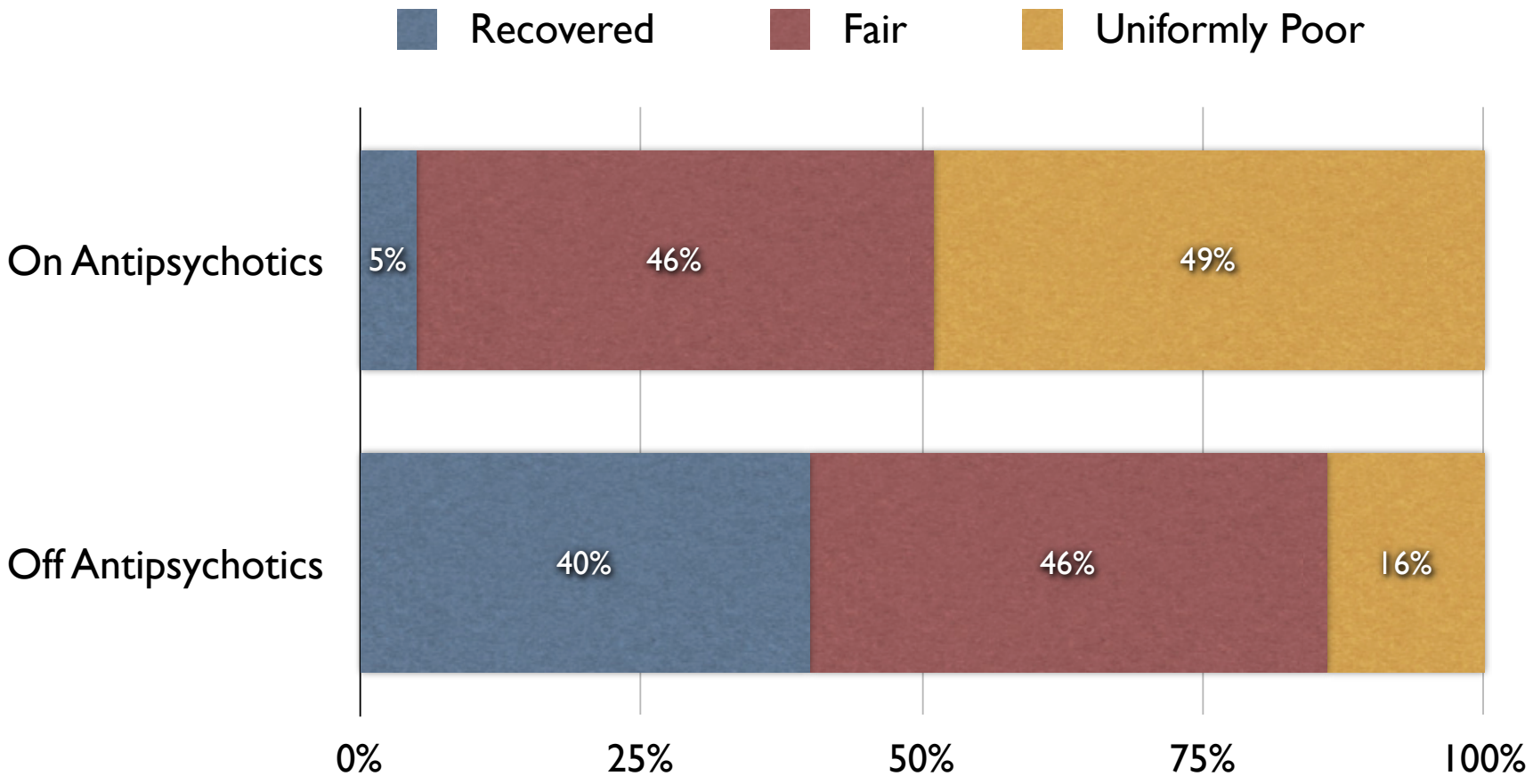
Source: Harrow M. "Factors involved in outcome and recovery in schizophrenia patients not on antipsychotic medications." *Journal of Nervous and Mental Disease* 195 (2007):406-14.

Global Adjustment of Schizophrenia Patients



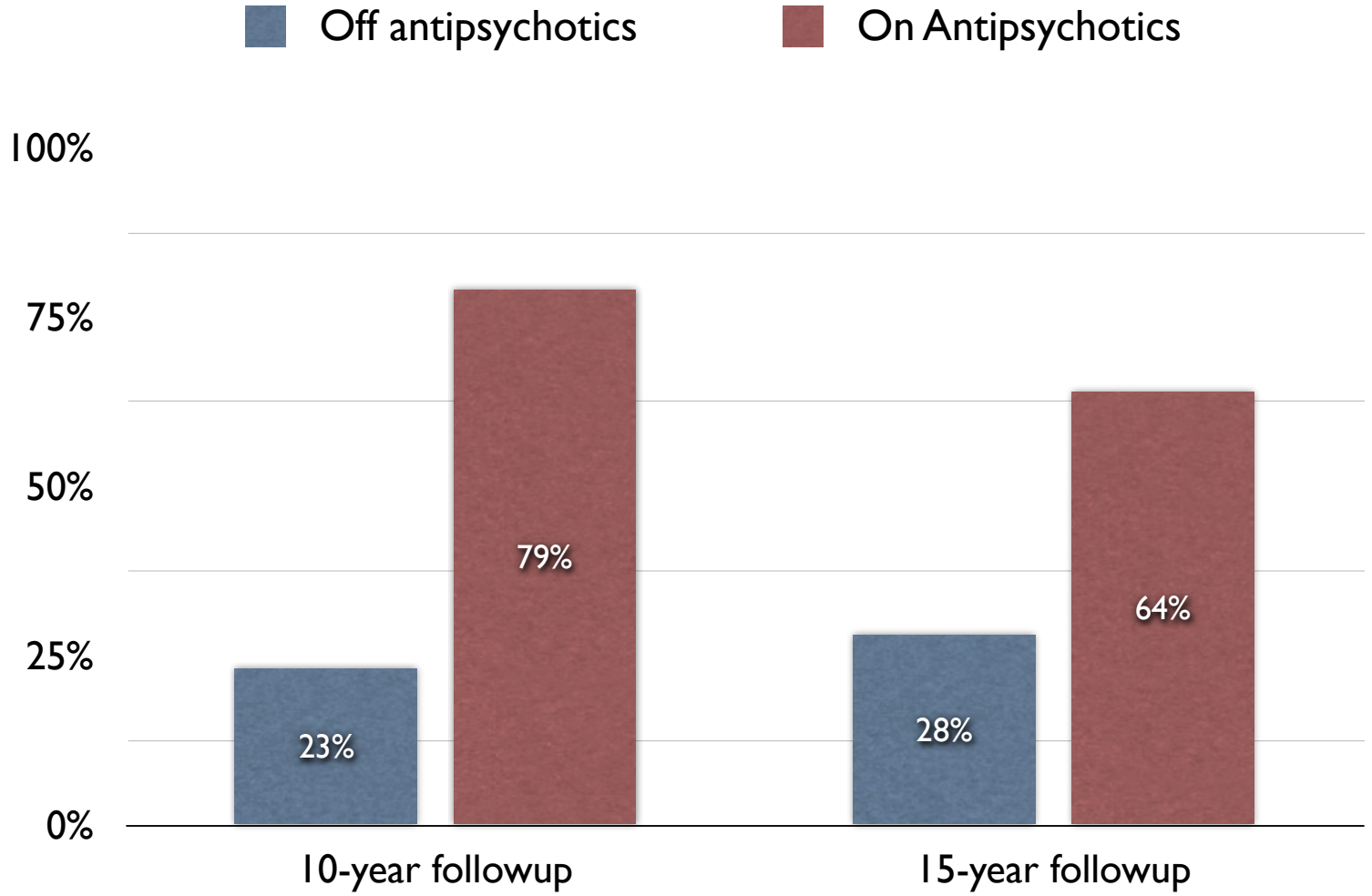
Source: Harrow M. "Factors involved in outcome and recovery in schizophrenia patients not on antipsychotic medications." *Journal of Nervous and Mental Disease* 195 (2007):406-14.

Spectrum of Outcomes in Harrow's Study



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.

Psychotic Symptoms in Schizophrenia Patients Over the Long Term



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.

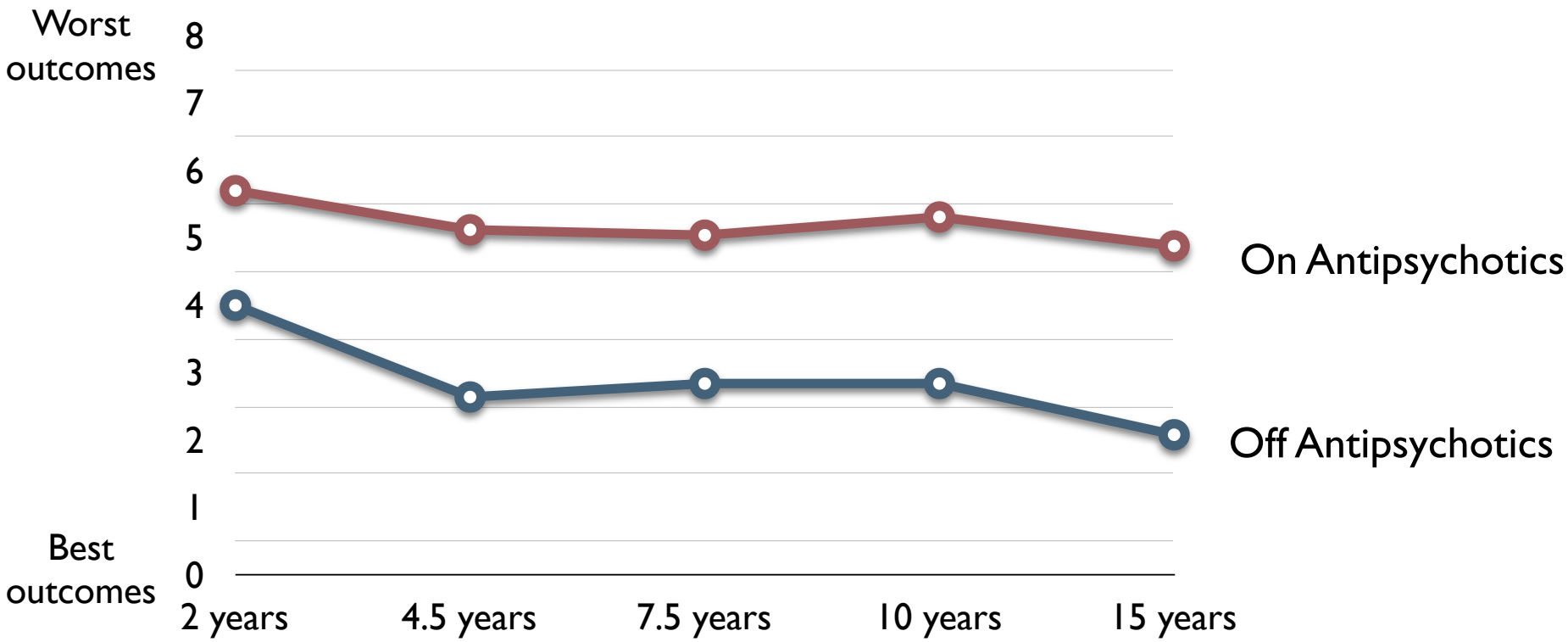
"In addition, global outcome for the group of patients with schizophrenia who were on antipsychotics was compared with the off-medication schizophrenia patients with similar prognostic status. Starting with the 4.5-year follow-up and extending to the 15-year follow-up, the off-medication subgroup tended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

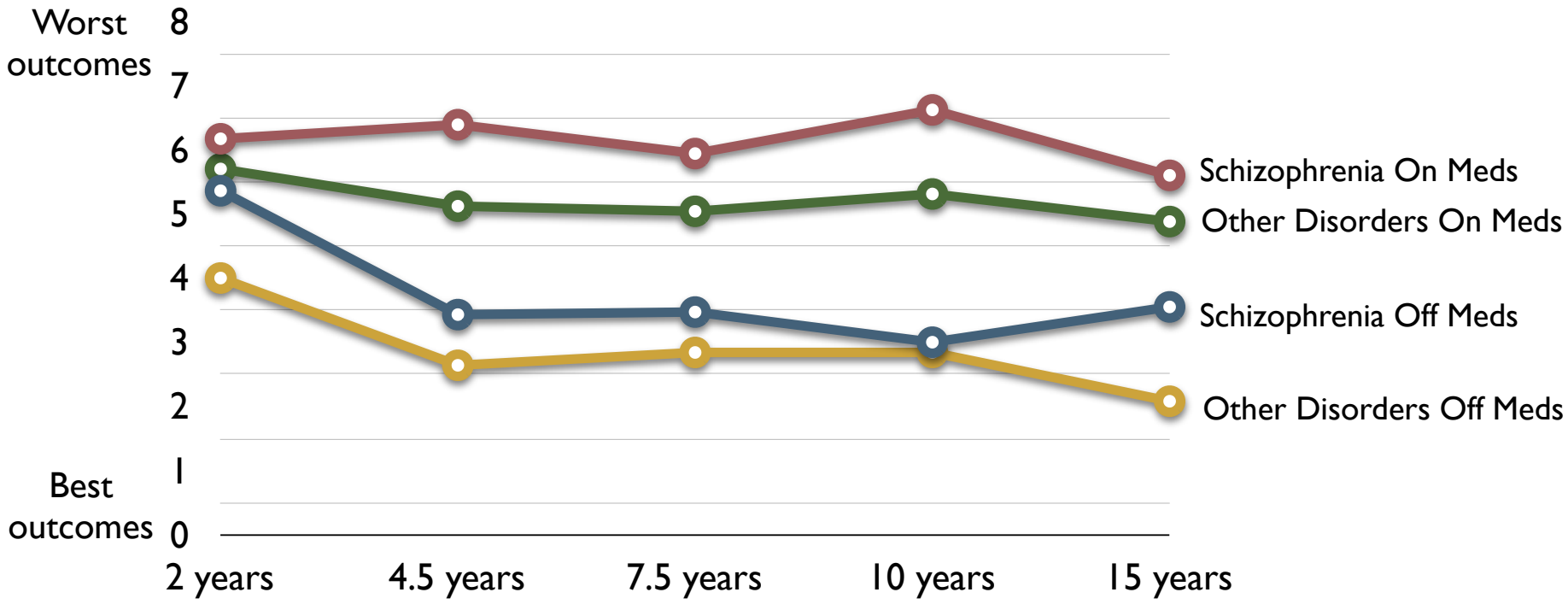
--Martin Harrow, American Psychiatric Association annual meeting, 2008

Global Adjustment of "Other Psychotic" Patients



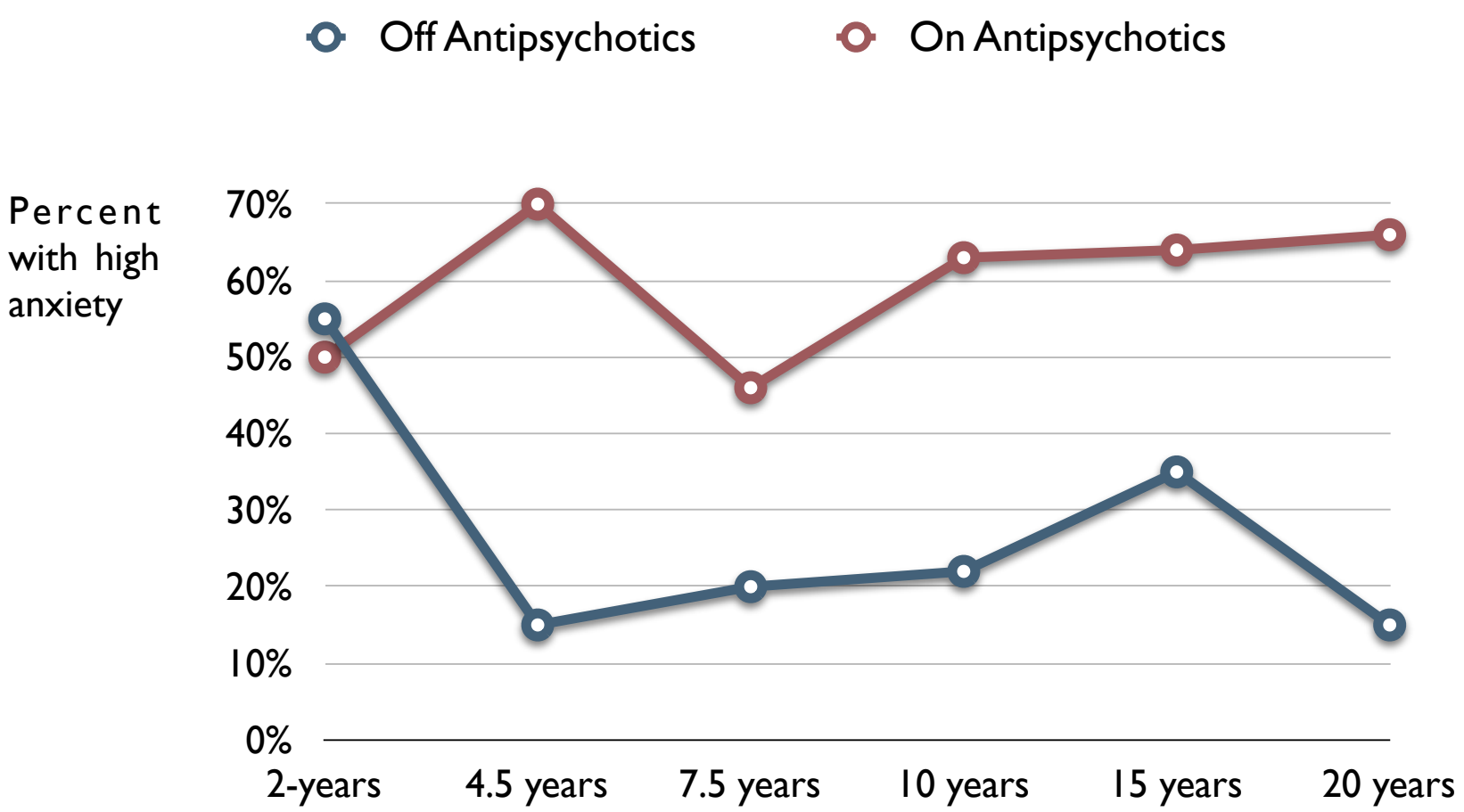
Source: Harrow M. "Factors involved in outcome and recovery in schizophrenia patients not on antipsychotic medications." *Journal of Nervous and Mental Disease* 195 (2007):406-14.

Global Adjustment of All Psychotic Patients



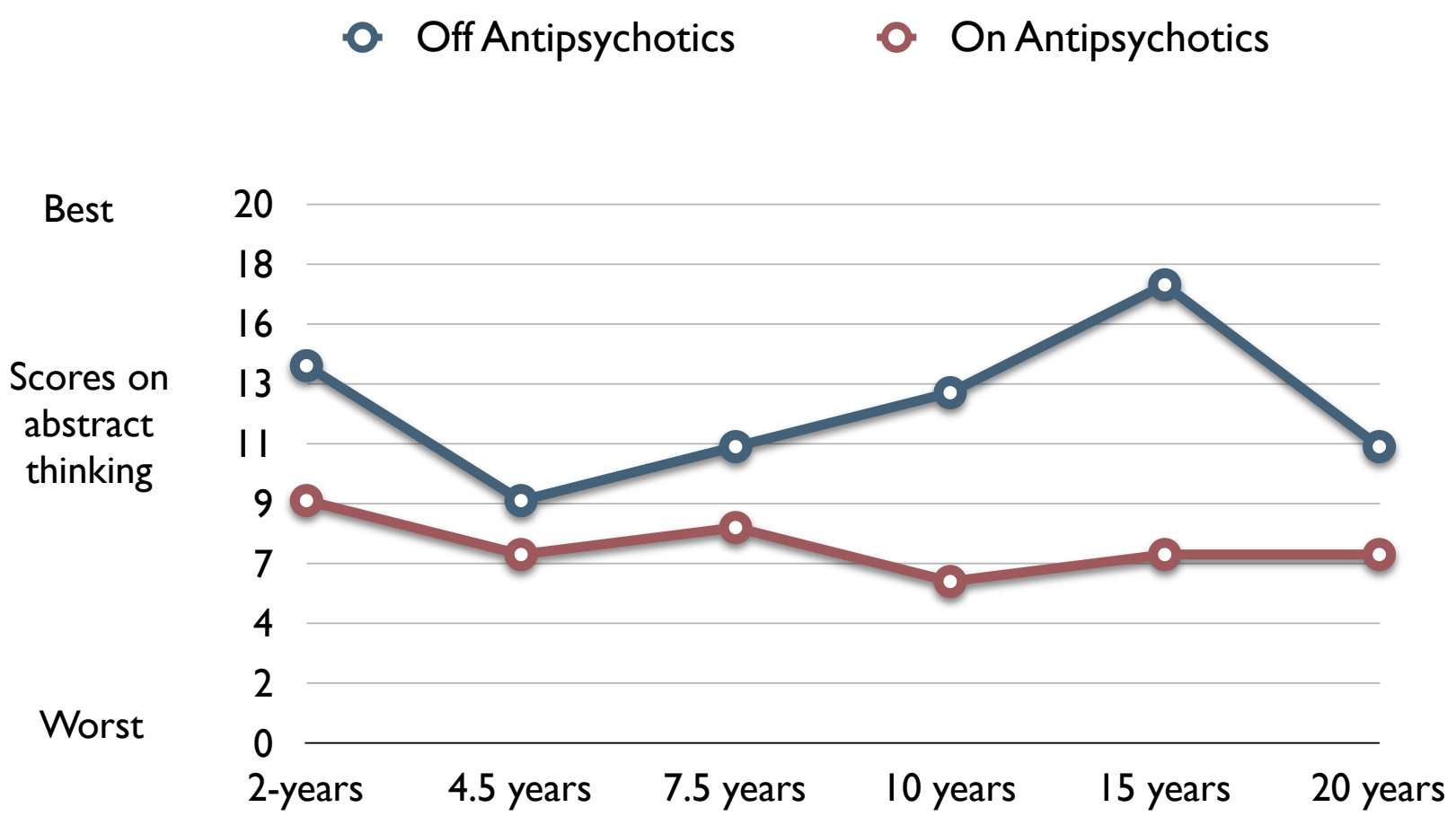
Source: Harrow M. "Factors involved in outcome and recovery in schizophrenia patients not on antipsychotic medications." *Journal of Nervous and Mental Disease* 195 (2007):406-14.

Anxiety Symptoms of Schizophrenia Patients



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

Cognitive Function of Schizophrenia Patients



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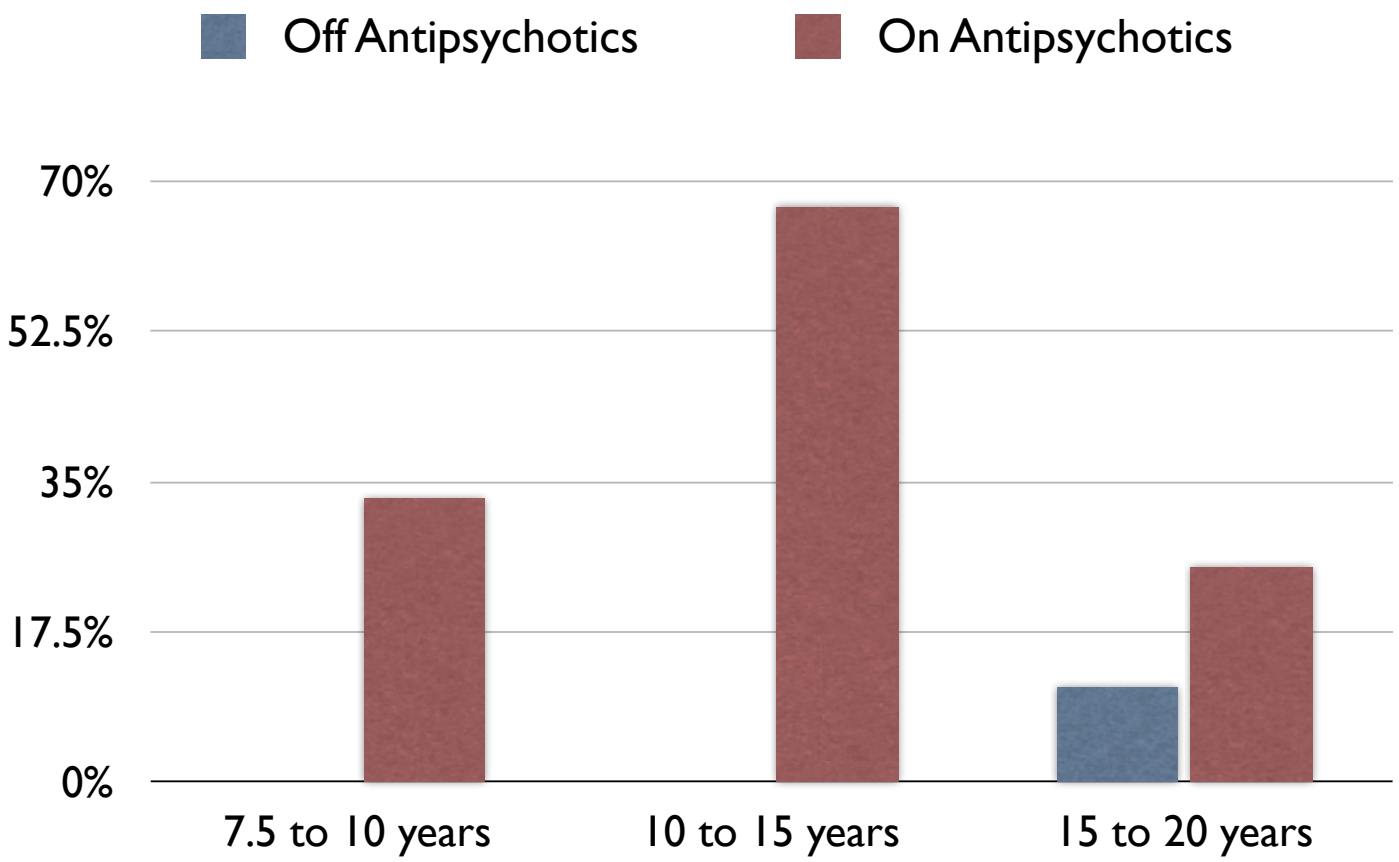
Relapse Rates Once Patients Are Stable



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

Recovery Rates

Medication compliant patients throughout 20 years: 17% had one period of recovery.

Those off antipsychotics by year two who then remained off throughout next 18 years: 87% had two or more sustained periods of recovery.

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

"Is very long-term treatment with antipsychotic medications undesirable?"

--Martin Harrow, 2012

The Long-term Effects of Antidepressants on Depression

Outcomes in Pre-Drug Era

- Recovery from index episode was expected.

- In four of five long-term studies, more than 50% hospitalized for an index episode were never rehospitalized.

- The average time between recurrent episodes was three years or more.

"Depression is, on the whole, one of the psychiatric conditions with the best prognosis for eventual recovery with or without treatment. Most depressions are self-limited."

--Jonathan Cole, NIMH, 1964

Worry About Chronicity Appears

- H.P. Hoheisel, German physician, 1966: Exposure to antidepressants appeared to be "shortening the intervals" between depressive episodes.

- Nikola Schipkowensky, Bulgarian psychiatrist, 1970: The antidepressants were inducing "a change to a more chronic course."

Chronicity Worry is Tested

J.D. Van Scheyen, Dutch psychiatry, 1973: After conducting a study of 94 depressed patients, he concluded that "it was evident, particularly in the female patients, that more systematic long-term antidepressant medication, with or without ECT [electronconvulsive therapy], exerts a paradoxical effect on the recurrent nature of the vital depression. In other words, this therapeutic approach was associated with an increase in recurrent rate and a decrease in cycle duration . . . Should [this increase] be regarded as an untoward long-term side effect of treatment with tricyclic antidepressants?"

Modern Outcomes

- High relapse rate upon drug withdrawal.

- High relapse rate with long-term drug use.

- Modern epidemiological studies find that major depression runs a chronic course.

Acknowledgment of Change in Course of Depression in Modern Era

American Psychiatric Association's *Textbook of Psychiatry*, 1999: It used to be believed that "most patients would eventually recover from a major depressive episode. However, more extensive studies have disproved this assumption." It was now known that "depression is a highly recurrent and pernicious disorder."

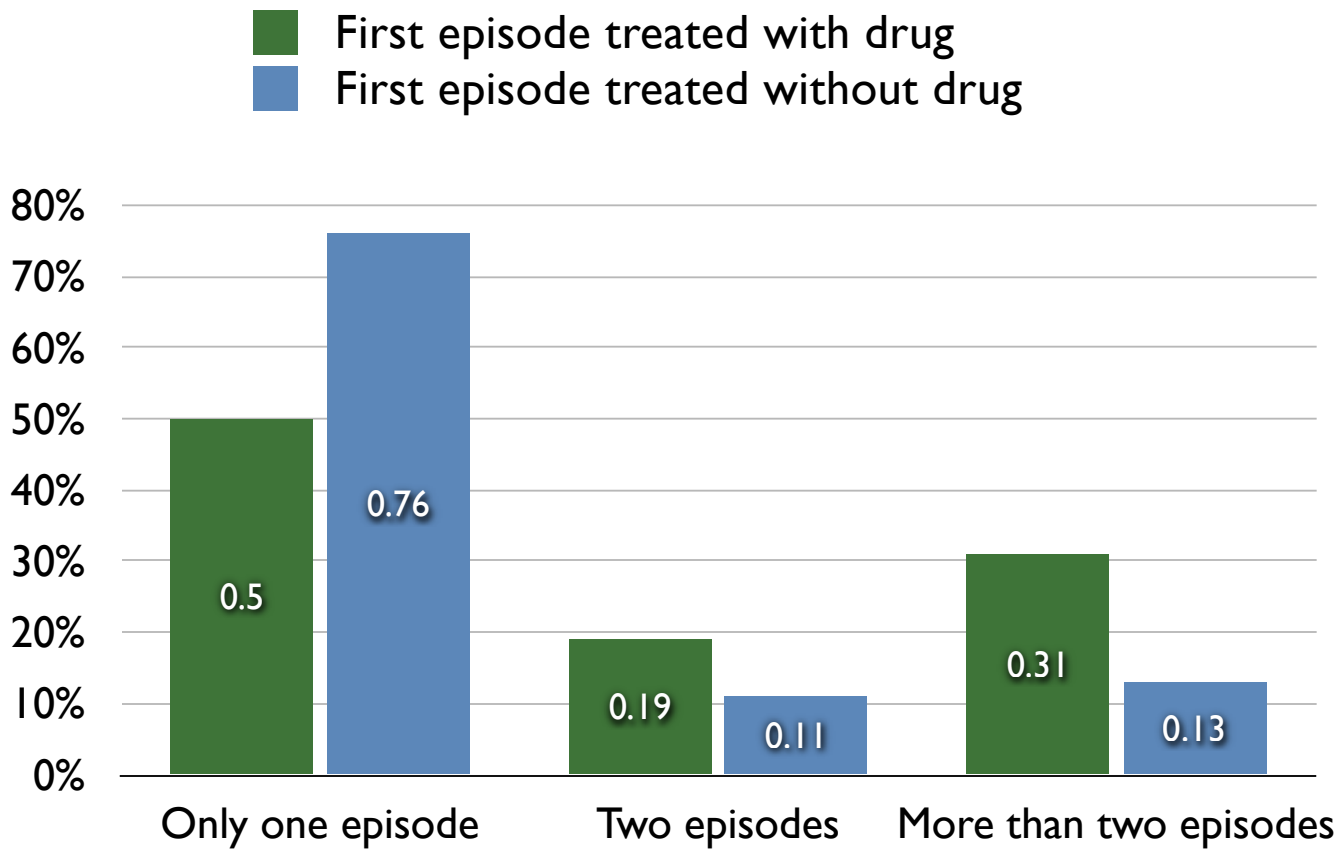
Are Antidepressants Depressogenic Over the Long-Term?

"Antidepressant drugs in depression might be beneficial in the short term, but worsen the progression of the disease in the long term, by increasing the biochemical vulnerability to depression . . . Use of antidepressant drugs may propel the illness to a more malignant and treatment unresponsive course."

--Giovanni Fava, *Psychotherapy and Psychosomatics*, 1995

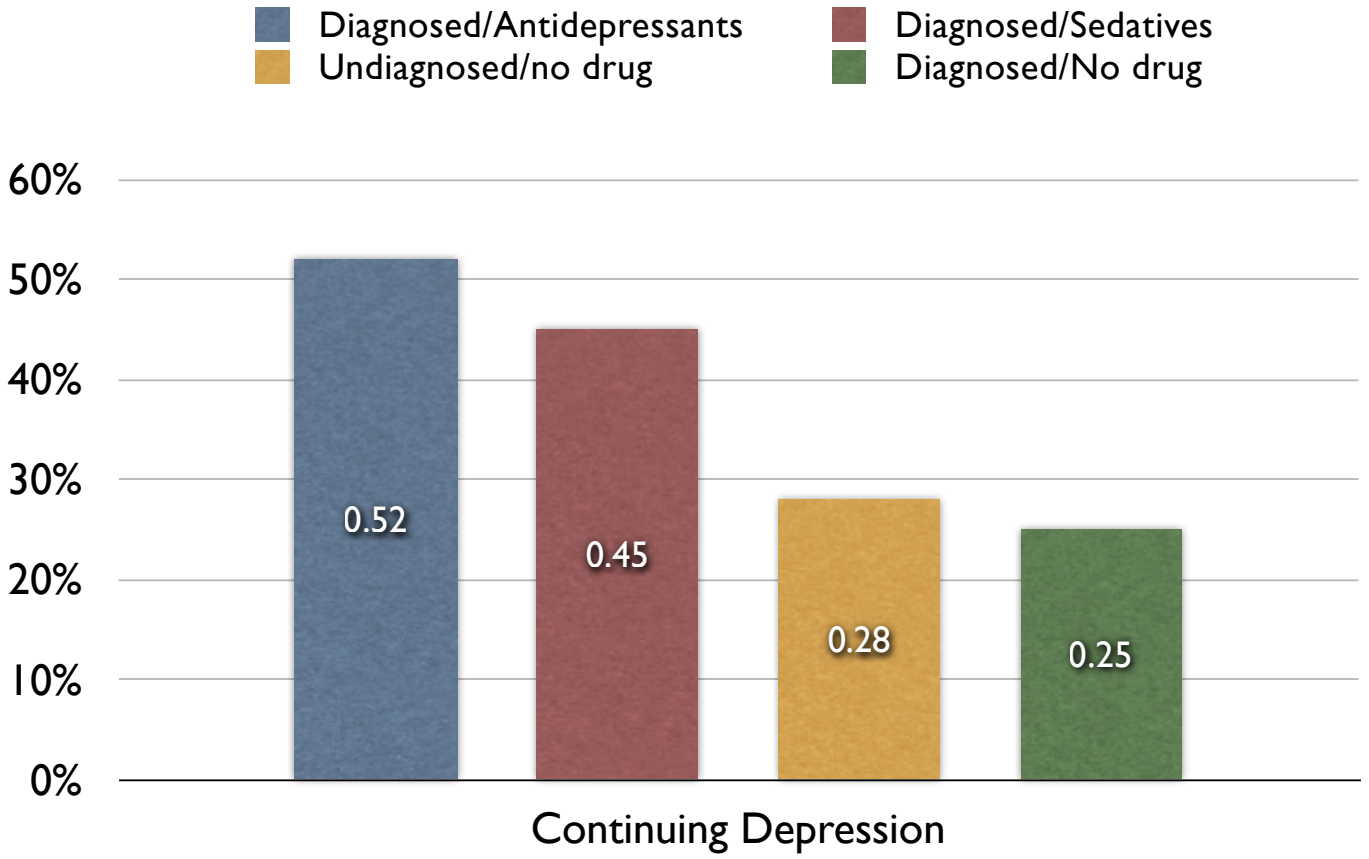
Depression in the Netherlands

(Over the course of ten years)



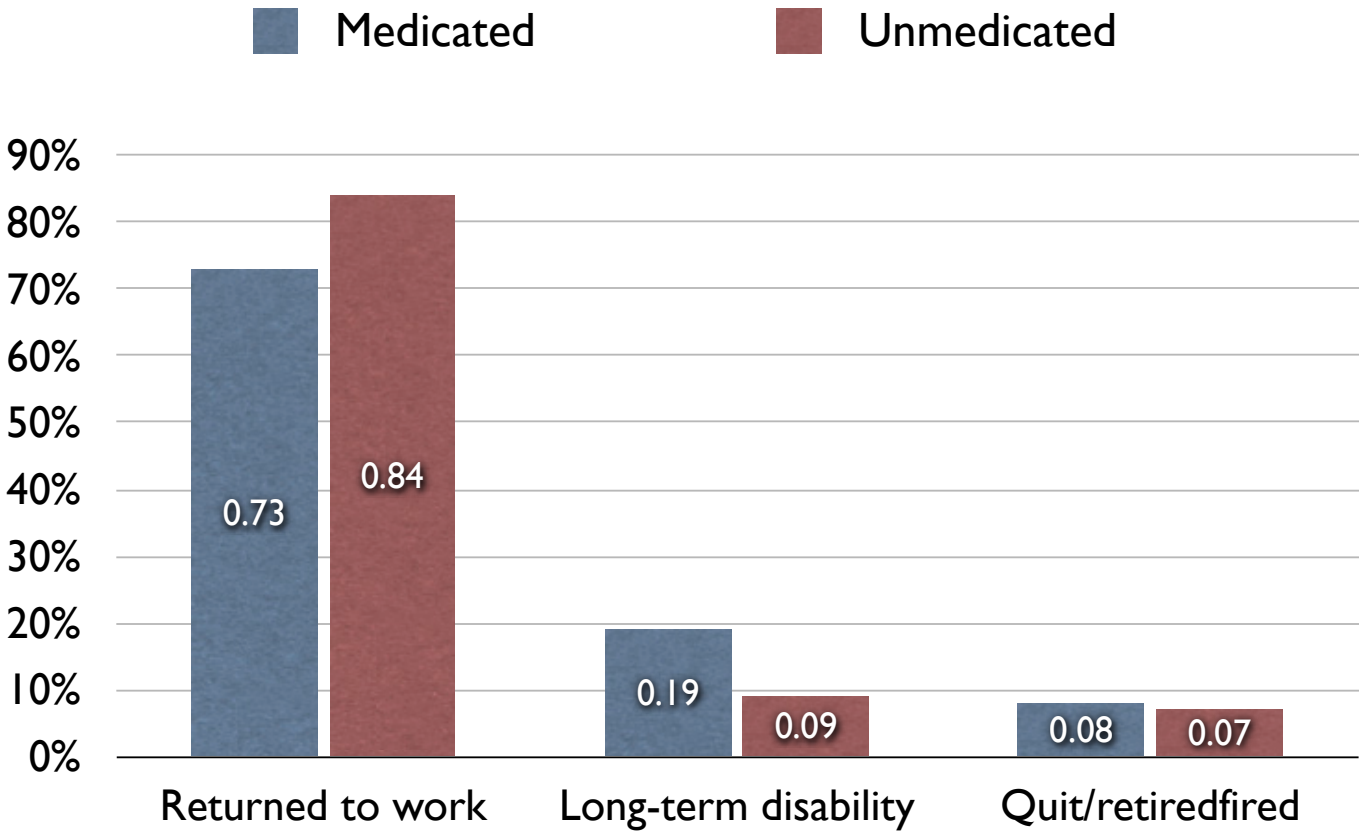
Source: E. Weel-Baumgarten, "Treatment of depression related to recurrence," *J Clin Psychiatry & Therapeutics* 25 (2000):61-66.

One-Year Outcomes in WHO Screening Study for Depression



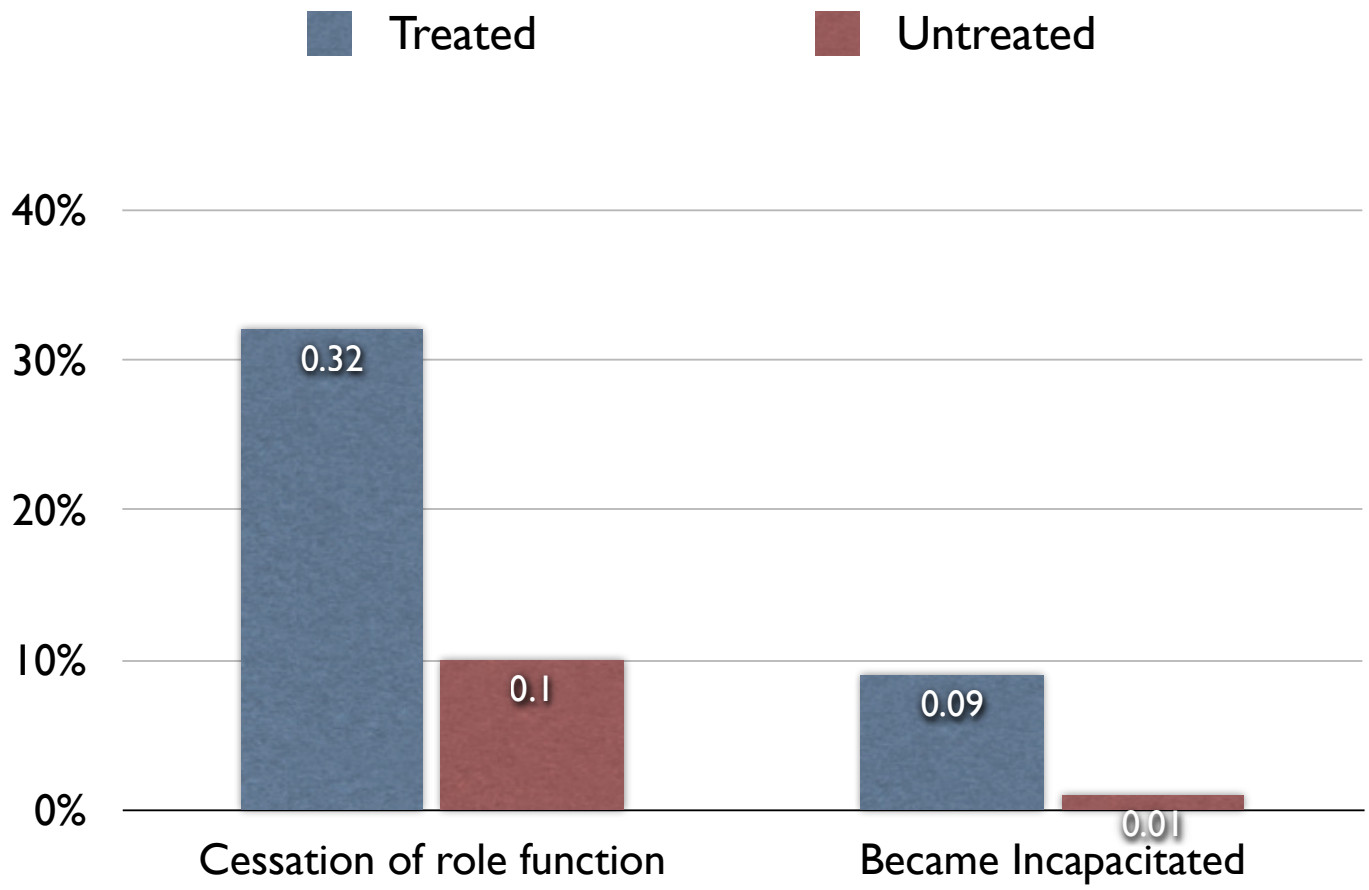
Source: D. Goldberg. "The effects of detection and treatment of major depression in primary care." *British Journal of General Practice* 48 (1998):1840-44.

Canadian Study of Risk of Long-term Disability for Depressed Workers



Source: C Dewa. "Pattern of antidepressant use and duration of depression-related absence from work." *British Journal of Psychiatry* 183 (2003):507-13.

NIMH's Study of Untreated Depression



Source: W. Coryell. "Characteristics and significance of untreated major depressive disorder." *American Journal of Psychiatry* 152 (1995):1124-29.

Antidepressants Lessen the Long-Term Benefits of Exercise

Treatment during first 16 weeks	Percentage of patients in remission at end of 16 weeks	Percentage of patents who relapsed in following six months	Percentage of all patients depressed at end of ten months
Zoloft alone	69%	38%	52%
Zoloft plus exercise	66%	31%	55%
Exercise alone	60%	8%	30%

Source: Babyak, M. "Exercise treatment for major depression." *Psychosomatic Medicine* 62 (2000):633-8.

The STAR*D Trial Confirms That Depression Runs a Chronic Course Today

Findings from the National Institute of Mental Health's STAR*D study, which was the "largest study" of depression ever conducted:

• Only 38% of the patients properly enrolled in the trial remitted during one of the four stages of drug treatment.

• Only 3% of the patients remitted and then stayed well throughout the 12-month followup. The remaining patients either failed to remit, relapsed during the followup, or dropped out.

Conclusion: "Most individuals with major depressive disorders have a chronic course, often with considerable symptomatology and disability even between episodes."

Source: Pigott, E. "Efficacy and effectiveness of antidepressants." *Psychother Psychosom* 79 (2010):267-79.

Tardive Dysphoria

"A chronic and treatment-resistant depressive state is proposed to occur in individuals who are exposed to potent antagonists of serotonin reuptake pumps (i.e. SSRIs) for prolonged time periods. Due to the delay in the onset of this chronic depressive state, it is labeled tardive dysphoria. Tardive dysphoria manifests as a chronic dysphoric state that is initially transiently relieved by -- but ultimately becomes unresponsive to -- antidepressant medication. Serotonergic antidepressants may be of particular importance in the development of tardive dysphoria."

-- Rif El-Mallakh, 2011

Source: El-Mallakh, R. "Tardive dysphoria: The role of long-term antidepressant use in inducing chronic depression. *Medical Hypotheses* 76 (2011): 769-773.

Question Number Four

Are We Creating Bipolar Patients?

The Bipolar Boom

Annual Prevalence in the Pre-Lithium Era

•One in 3000 to one in 10,900

Prevalence Today:

• One in 50 adults

Gateways to Bipolar Today

- Illicit drugs (marijuana, cocaine, hallucinogens, etc.)
- Stimulants and antidepressants
- Expanded diagnostics

The Antidepressant Pathway

In 2004, Yale University investigators reviewed the records of 87,290 patients diagnosed with depression or anxiety between 1997 and 2001, and those treated with an antidepressants converted to bipolar at the rate of 7.7% per year, which was three times greater than those not exposed to the drugs. As a result, 20 to 40% of unipolar depressed patients in the U.S. who stay on antidepressants long-term convert to bipolar illness.

Source: A. Martin. "Age effects on antidepressant-induced manic conversion," *Arch of Pediatrics & Adolescent Medicine* 158 (2002):773-80.

Fred Goodwin, former director of the National Institute of Mental Health, 2005:

"If you create iatrogenically a bipolar patient, that patient is likely to have recurrences of bipolar illness even if the offending antidepressant is discontinued. The evidence shows that once a patient has had a manic episode, he or she is more likely to have another one, even without the antidepressant stimulation."

The Modern Course of Bipolar Illness

- More recurrent episodes and more rapid cycling
- Low-level depression between episodes
- Only 33% enjoy good functional outcomes (compared to 70% to 85% in pre-drug era)
- Long-term cognitive impairment (which wasn't seen in pre-drug era)
- Physical problems related to long-term medication use
- Risk of early death

Carlos Zarate, head of NIMH Mood Disorders Program, 2000:

"In the era prior to pharmacotherapy, poor outcome in mania was considered a relatively rare occurrence. However, modern outcome studies have found that a majority of bipolar patients evidence high rates of functional impairment."

Ross Baldessarini, Harvard Medical School, 2007.

"Prognosis for bipolar disorder was once considered relatively favorable, but contemporary findings suggest that disability and poor outcomes are prevalent, despite major therapeutic advances."

Fred Goodwin, 2008

"The illness has been altered. Today we have a lot more rapid cycling than we described in the first edition [of his book, *Manic Depressive Illness*], a lot more mixed states than we described in the first edition, a lot more lithium resistance, and a lot more lithium treatment failure than we described in the first edition. The illness is not what Kraepelin described any more."

The Transformation of Outcomes for Major Mental Disorders in the Modern Era

Summary of long-term outcomes literature

• Research shows that antipsychotics worsen the long-term course of schizophrenia. The drugs lower recovery rates, and cause brain changes associated with increased biological vulnerability to psychosis, functional impairment, and long-term cognitive decline.

• Depression has been transformed from an episodic disorder into a chronic illness, with much higher disability rates

• Use of illicit drugs, stimulants and antidepressants have helped create a 100-fold increase in the prevalence of bipolar illness (in U.S.)

• Functional outcomes for bipolar illness have dramatically deteriorated in modern era.

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.

"The majority of mental illnesses, especially the most severe, are largely self-limiting in nature if the patient is not subjected to a demeaning experience or loss of rights and liberties."

-- Samuel Bockoven, 1975