

# Psychosis 101



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*Promoting Innovation. Restoring Lives.*

This material provided by the Best Practices in Schizophrenia Treatment (BeST) Center, Department of Psychiatry, Northeast Ohio Medical University.

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# Best Practices in Schizophrenia Treatment (BeST) Center at NEOMED

- **The BeST Center's mission:**

- Promote recovery and improve the lives of as many individuals with schizophrenia as quickly as possible
- Accelerate the use and dissemination of effective treatments and best practices
- Build capacity of local systems to deliver state-of-the-art care to people affected by schizophrenia and their families

- **The BeST Center offers:**

- Training
- Consultation
- Education and outreach activities
- Services research and evaluation

- **The BeST Center was established:**

- Department of Psychiatry, Northeast Ohio Medical University in 2009
- Supported by Peg's Foundation and other private foundations and governmental agencies

# Reasons for this talk

- Psychosis is often misunderstood
- Psychosis is common
- Recognition and treatment of psychosis is important

# What is psychosis?

- A family of medical illnesses that
- Affect neurological functions related to the
- Processes that convert raw sensory data to finished-product perception



# What are the outputs from the brain?

- Perception
- Language
- Sense of self
- Recognition of others
- Emotions
- Empathy
- Behavior
- Thought

# The brain's major task is INTEGRATION



- Imponderably large on/off data from every nerve cell within the body
- Integrated seamlessly to
- Construct an internal representation of the inner and outer worlds to
- Promote the survival of the organism

# The integration tasks are demanding and complex

- Energy demands of the brain testify to the complexity of constructing and continually refreshing these virtual realities that we perceive as real
  - The brain accounts for only 3% of the body's weight
  - Yet the brain burns 20% of the body's calories
- The more complex the system/task, the greater the opportunities for errors





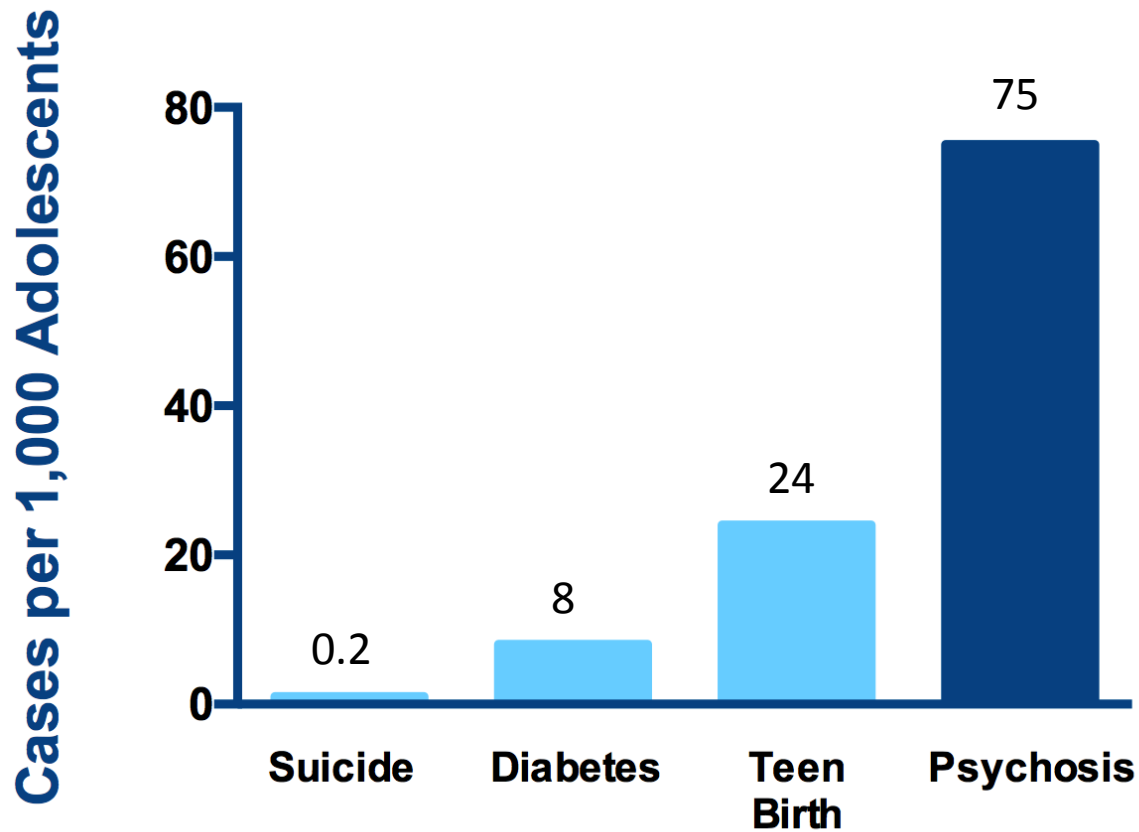
# What is psychosis?

- “osis” - medical term for abnormality without evidence of inflammation
- “**psyche**” - antiquated term for the **integrated outputs of the brain** (perception, thought, memory, emotion, self-concept, etc)
- Errors in the brain’s integrative functions lead to misperceptions or abnormal perceptions.
- These often take the form of paranoia, illogical ideas, hallucinations, disorganized speech, unusual behavior.
- **Better, more accurate term is Integration Disorder**; this term is used in Japan
- This is neurological disorder (psychiatry is the branch of neurology that focuses on higher-order, integrative brain processes)

# Psychosis: more common than most people imagine

- Not surprising considering the extreme complexity of the brain's integrative functions.
- **“30% of adolescents may experience psychotic symptoms during their development”** Newbury J. et al. (2016) Why are children in urban neighborhoods at increased risk for psychotic symptoms? *Schizophrenia Bulletin* 24:1372-1383.
- **75 per 1,000 adolescents experience at least one feature of psychosis in any given year.** Kelleher, I., Connor, D., Clarke, M.C., Devlin, N., Harley, M., and Cannon, M. (2012). Prevalence of psychotic symptoms in childhood and adolescence: a systematic review and meta-analysis of population-based studies. *Psychol Med* 42, 1857–1863.

# Speaking of psychosis in adolescents...



# Data sources

## **Annual risk of suicide in adolescents: 0.2 per 1,000 individuals**

Hawton, K., et al. (2012). Self-harm and suicide in adolescents. *The Lancet* 379, 2373–2382.

## **Annual risk of diabetes, any type: 8 per 1,000 individuals**

Demmer, R.T., et al. (2013). Prevalence of diagnosed and undiagnosed type 2 diabetes mellitus among US adolescents: results from the continuous NHANES, 1999-2010. *Am. J. Epidemiol.* 178, 1106–1113.

## **Annual risk of teen birth: 24 per 1,000**

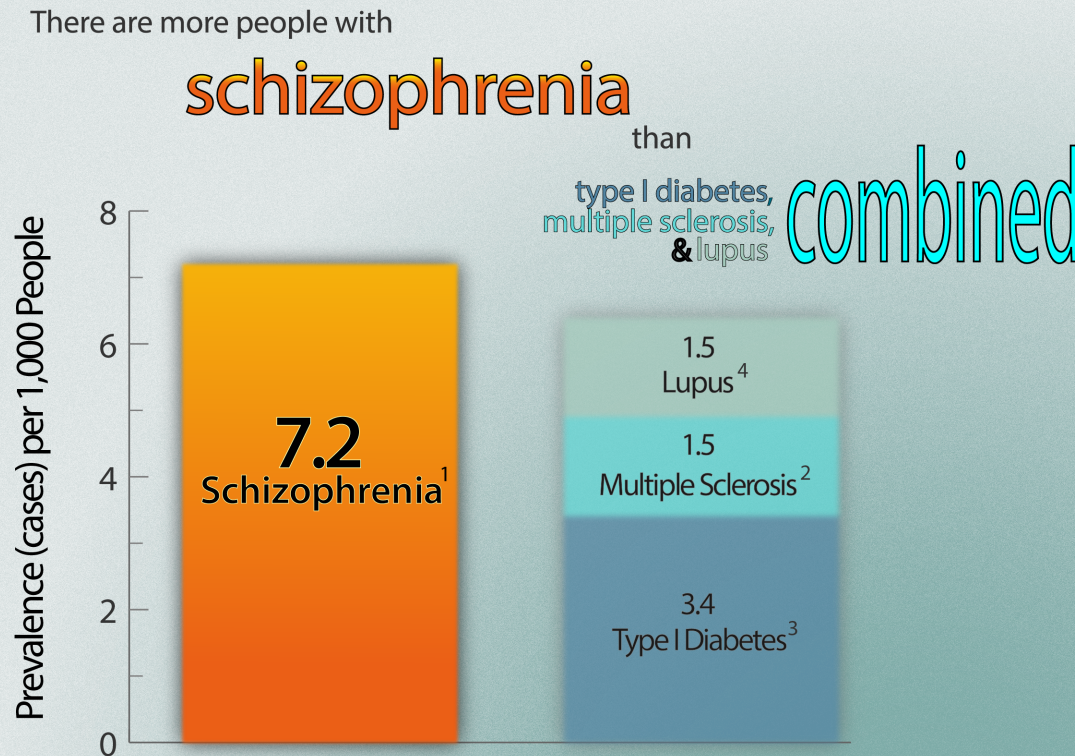
Trends in teen pregnancy and childbearing: teen births

<https://www.hhs.gov/ash/oah/adolescent-development/reproductive-health-and-teen-pregnancy/teen-pregnancy-and-childbearing/trends/index.html>

## **Annual risk of psychosis in adolescence: 75 per 1,000**

Kelleher, I., et al. (2012). Prevalence of psychotic symptoms in childhood and adolescence: a systematic review and meta-analysis of population-based studies. *Psychol Med* 42, 1857–1863.

# Schizophrenia is more common than: lupus, multiple sclerosis, and type 1 diabetes - combined



#### Sources

<sup>1</sup> McGrath, J., Saha, S., Chant, D., and Welham, J. (2008). Schizophrenia: A Concise Overview of Incidence, Prevalence, and Mortality. *Epidemiol Rev* 30, 67–76.

<sup>2</sup> Dilokthornsakul, P., Valuck, R.J., Nair, K.V., Corboy, J.R., Allen, R.R., and Campbell, J.D. (2016). Multiple sclerosis prevalence in the United States commercially insured population. *Neurology* 86, 1014–1021.

<sup>3</sup> Menke, A., Orchard, T.J., Imperatore, G., Bullard, K.M., Mayer-Davis, E., and Cowie, C.C. (2013). The Prevalence of Type 1 Diabetes in the United States. *Epidemiology* 24, 773–774.

<sup>4</sup> CDC Lupus Facts <https://www.cdc.gov/lupus/facts/detailed.html>

# Psychotic disorders are the most common problem that nobody talks about

# Without ongoing, science-informed public health information about psychotic disorders, fear and prejudice fills the void

Common misconceptions about schizophrenia:

- It involves splitting of the mind
- It is like multiple personalities
- People with schizophrenia are dangerous
- Medications for schizophrenia are harsh, dangerous
- Hardly anyone recovers from it

Realities about schizophrenia:

- There is no splitting of the mind, nor of the personality
- It's a neurological condition that affects the processing and integration of nerve cell activity
- Most people with schizophrenia are polite and kind
- The majority of people with schizophrenia can recover with the right kind of treatment
- The right kind of treatment does not involve hard-to-tolerate medications

# Psychosis vs Schizophrenia

Psychosis is a symptom

- Arises when one or more factors affect integrative activity of the brain

Psychosis has many possible causes

Schizophrenia encompasses those cases where:

- Psychosis is persistent or recurrent
- Not better explained by other psychiatric or medical conditions
- In other words, schizophrenia is a diagnosis of exclusion
- Within the schizophrenia category are probably multiple diseases



# Some causes of psychosis

Addison's disease	Adrenomyeloneuropathy	Celiac disease	Cerebral cysts and abscesses
Cerebral malaria	Cerebrovascular lesions	Chromosomal disorders	Cranial trauma
Cushing's disease	Encephalitis and its sequelae	Fabry's disease	Familial basal ganglia calcification
GM2 gangliosidosis	Hartnup disease	Hashimoto's encephalopathy	HIV
Homocystinuria (MTHFR reductase deficiency)	Huntington's disease	Hydrocephalus	Hyperparathyroidism
Hyperthyroidism	Hypoparathyroidism	Hypopituitarism	Hypothyroidism
Kartagener's syndrome	Klinefelter's syndrome	Metachromatic leukodystrophy	Narcolepsy
Neurosyphilis	NMDA receptor antibody encephalitis	Occult hydrocephalus	Oculocutaneous albinism
Pellagra	Pernicious anemia	Pick's disease	Porphyrias
Prenatal static encephalopathy	Rheumatic chorea	Schilder's cerebral sclerosis	Sheehan's syndrome
Subarachnoid hemorrhage	Systemic lupus erythematosus	Tourette syndrome	Toxicity (drugs, medications, heavy metals)
Tuberous sclerosis	Tumors of the brain	Velocardiofacial syndrome	Vitamin A deficiency
Vitamin B12 deficiency	Vitamin D deficiency	Wilson's disease	Zinc deficiency

A complete medical evaluation is necessary to rule out treatable medical illnesses that may cause psychosis

# Medical causes of schizophrenia-like symptoms

**6% to 12% of people initially thought to have schizophrenia may actually have an undetected medical disease as the cause of their symptoms.**

- Coleman, M., and Gillberg, C. (1997). A biological approach to the schizophrenia spectrum disorders. *J Neuropsychiatry Clin Neurosci* 9, 601–605.
- Falkai, P. (1996). Differential diagnosis in acute psychotic episode. *Int Clin Psychopharmacol* 11 Suppl 2, 13–17
- Johnstone, E.C., Macmillan, J.F., and Crow, T.J. (1987). The occurrence of organic disease of possible or probable aetiological significance in a population of 268 cases of first episode schizophrenia. *Psychol Med* 17, 371–379.
- Johnstone, E.C., Cooling, N.J., Frith, C.D., Crow, T.J., and Owens, D.G. (1988). Phenomenology of organic and functional psychoses and the overlap between them. *The British Journal of Psychiatry* 153, 770–776.

# Within schizophrenia are many illnesses

Reminder: Schizophrenia is characterized by persistent or recurring psychosis that can't be better explained by some other psychiatric diagnosis or medical condition.

Within this category are several illnesses\*

- Dopamine psychosis
- Glutamate psychosis
- Inflammatory psychosis
- Other psychoses

\*These categories of schizophrenia are not yet recognized by the APA, but are clearly emerging within the medical research community

# Not all schizophrenias are the same

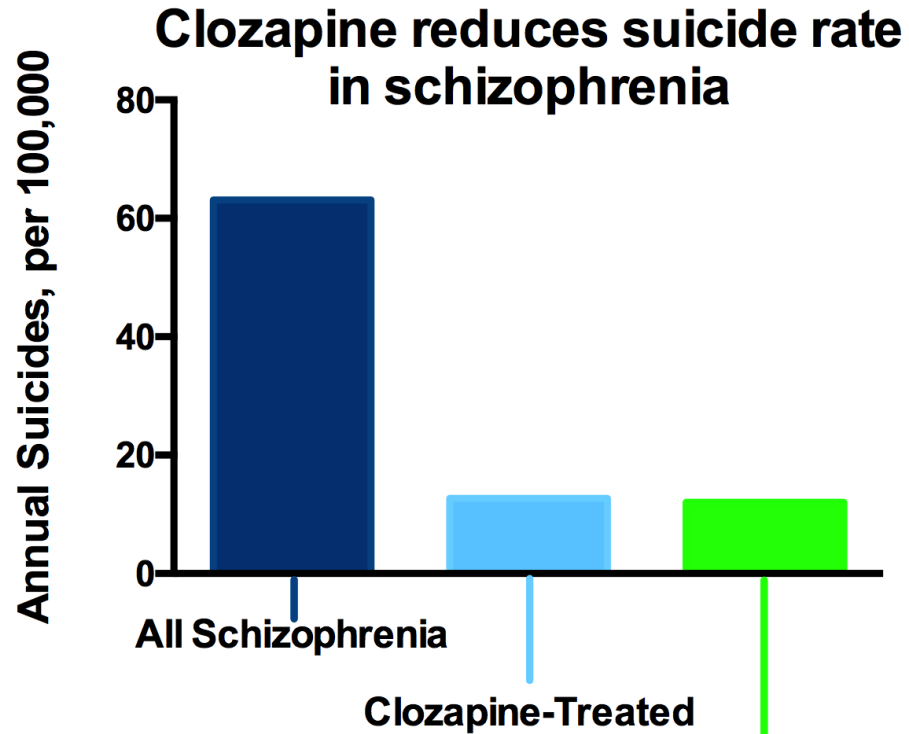
- Every first-line antipsychotic medication is designed to reduce dopamine signals within the brain. They are appropriate for treating people with the ‘dopamine psychosis’ type of schizophrenia.
- These medications don’t work for people with “normal dopamine psychosis.”
  - Dopamine reduction is irrelevant, possibly harmful in normal dopamine psychosis
  - Minimal likelihood of benefit
  - Full risk of side effects/adverse events

# Treatment of normal dopamine schizophrenia

- Ordinary antipsychotic medications are ineffective in normal dopamine schizophrenia
- Clozapine is effective in about 60% of patients with normal dopamine schizophrenia
- Clozapine also reduces suicide risk
  - It is the only medication with FDA recognized suicide reduction

# Clozapine reduces suicide rates in schizophrenia

- And is the only medication with FDA-approval for suicide reduction



Source: Reid et al., 1998

General Population

# Clozapine use in other countries

(% of people with schizophrenia prescribed clozapine)

Australia	35%
China	30%
England	23%
Sweden	22%
Germany	20%
India	13%
Malaysia	4%
USA	4%

Source: Treatment Advocacy Center. "Clozapine by the numbers" <http://www.treatmentadvocacycenter.org/fixing-the-system/features-and-news/3613-research-weekly-clozapine-by-the-numbers>

# Forcing ineffective medications

- The ethics of forced or coerced treatment rests on the assumption that the forced/coerced treatment will bring about the greater good of restored health.
- Yet the science of psychosis is clear that most of the medications that would be forced (i.e., dopamine signal blockers) are ineffective in the subset of individuals with normal dopamine psychoses.
- Combining dopamine signal blocker meds, giving them at higher doses, or giving them in the form of forced long-acting injection does not make them more effective... just more dangerous.



# Good-practice in schizophrenia treatment

- Early recognition
- Comprehensive medical, neurological, imaging, and neurological examination to detect the 6% to 12% of cases with underlying medical disease
- Don't continue ineffective medications
- Don't change effective medications
- Question original diagnosis when treatment is not working
- Offer clozapine for those cases where two adequately-dosed trials of medication have not worked

# With the right treatment, the majority of patients will recover

Study	Sample Size	Years Followed	% Recovered
Bleuler (1974) Switzerland	208	23	53 - 68%
Hinterhuber (1973) Austria	157	30	75%
Ciampi & Muller (1976) Switzerland	289	37	53%%
Kreditor (1977) Lithuania	115	20	84%
Tsuang et al. (1979) Iowa	200	35	46%
Huber et al. (1979) Germany	502	22	57%
Marinow (1986) Bulgaria	280	20	75%
Harding et al. (1987) Vermont	269	32	62 - 68%
Ogawa et al. (1987) Japan	140	22.5	56%
Desisto et al. (1995) Maine	269	35	49%

Table adapted from Glynn et al (2010) How do some people with schizophrenia thrive?

<https://www.apa.org/practice/leadership/serious-mental-illness/glynn.pdf>

# Change the Cycle!

## Subpar practice

- outdated
- incomplete
- reactive

## Poor outcomes

- poor function
- frequent relapse
- frequent side effects

Reluctance to accept diagnosis  
Reluctance to seek help →  
Patients come in with more  
severe illness, bigger setbacks

Clinicians not motivated nor  
equipped to aim for top-level  
outcomes

Low motivation for  
government/insurance to  
adequately fund up-to-date,  
comprehensive treatment

# Change the cycle!

"Many would now contend that much of the poor outcome in psychosis is an artifact of

- late detection,
- crude and reactive pharmacotherapy,
- sparse psychosocial care, and
- social neglect"

McGorry, P., Alvarez-Jimenez, M., and Killackey, E. (2013). Antipsychotic medication during the critical period following remission from first-episode psychosis: less is more. *JAMA Psychiatry* 70, 898–900.

# What could be possible with current knowledge

Like stroke or heart attack, symptoms of psychosis are widely known, accurately recognized

50% to 70% are in recovery or remission within the first 4 months

New-onset cases receive accurate diagnosis, personalized treatment

85% in recovery or remission within the first 12 months

Reduced use of hospitals, involuntary treatments, psychosis-related incarceration

Public recognition of psychosis, schizophrenia as common, treatable conditions from which recovery is the normal outcome

# The Promise of Early, Evidence-Based Treatment

40% of early-treated patients are ultimately able to either:

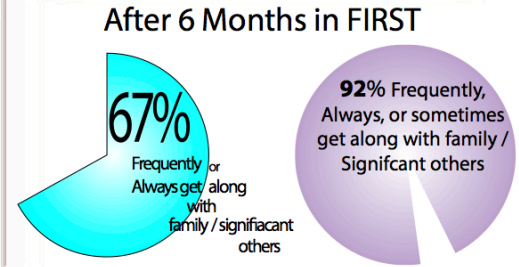
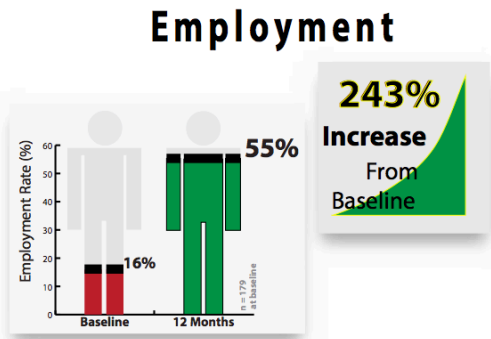
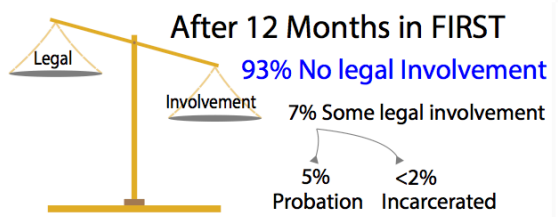
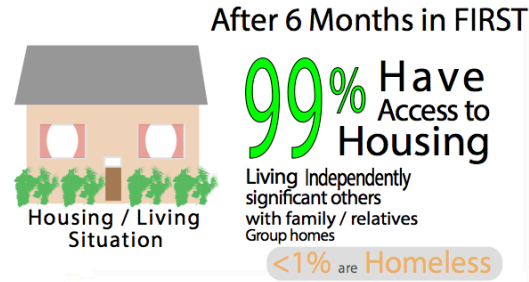
- successfully discontinue medications (20%), or
- be maintained on extremely low doses of medication (20%).

McGorry et al. (2013) *JAMA Psychiatry* 70(9): 898-900.



# BeST Practices in Schizophrenia

Treatment Center



After 6 months in FIRST **Hospitalization rates declined by 88%**. At 12 months only 14% of FIRST clients reported being **hospitalized, a 79.4% decrease** from baseline.

## Education

After 6 Months in FIRST

- 33%** of First Clients are attending: High school, College, or Vocational School
- 17%** of First Clients are attending college (part / full time)
- 34%** of First Clients have high school diploma or GED

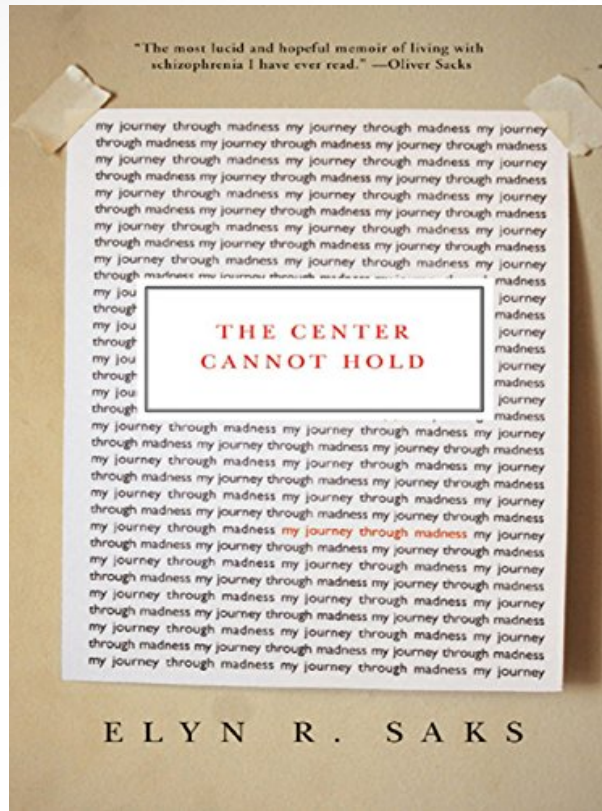
# A Recovery Story

- August 1999. Begins university
- June 2002. Publishes 2 papers in academic journals
- March, 2003. Becomes homeless
- January 2006. Hears voices, experiences hallucinations
- October, 2006. Jailed
- November, 2006. Jailed
- March, 2007. Hospitalized and treated for schizophrenia
- February, 2008. Recovers
- September, 2009. Returns to university
- December, 2011. Graduates with honors.



Bethany Yeiser  
[www.BethanyYeiser.com](http://www.BethanyYeiser.com)

# Another Recovery Story



Elyn Saks  
Orrin B. Evans Professor of Law,  
Psychology, and Psychiatry and the  
Behavioral Sciences

There are many trajectories within the schizophrenias.  
Some of those trajectories end in law school or professorships



# Summary

- Considering the brain's tasks, psychosis is an expected event that anyone can experience.
- Schizophrenia is a group of illnesses, characterized by psychosis, that can't be explained by other medical, neurological, or psychiatric diagnoses.
- Schizophrenias can be caused by: dopamine, glutamate, inflammation, other
- Almost all antipsychotic medications work for the high-dopamine form of schizophrenia; ineffective for normal-dopamine forms
- Clozapine is the only FDA-recognized treatment for the other types of schizophrenia
- With personalized, comprehensive treatment most people with schizophrenia will recover
- Start the right treatment as soon as possible
- Don't continue ineffective treatments - this leads to harm and stigma