

Robert Laitman, M.D. *of*  
**TEAM DANIEL**  
*presents*

# Optimal Treatment of Psychotic Disorders: Clozapine/Engagement/Community



**TEAM DANIEL**  
*Running for Recovery  
from Mental Illness*

# Our Daniel



1993



2019



# Clozapine: An Historical Perspective

**Clozapine has always challenged the mental health system**

**1953:** FDA approved first Pharma “Blockbuster” Thorazine.

**1958:** Clozapine Synthesized by Schmutz.

**1960:** Clozapine was patented; patients and family loved it.

Unfortunately, psychiatry avoided clozapine; most were preoccupied with the dopamine model for psychosis.

**1989:** Clozapine was FDA approved but held to an unprecedented standard.

- Demonstrated marked improvement in treatment refractory population when compared to standard of care.
- Sandoz bundled clozapine with the required blood monitoring; significantly increasing costs.
- Clozapine was heavily restricted and rationed.



# Clozapine Risks

- Agranulocytosis - Dangerously low neutrophils (white blood cells)
- Seizures
- Intractable weight gain in over 80% and diabetes
- Unremitting sedation
- Drooling
- Intractable constipation
- Myocarditis and heart failure
- Rebound psychosis if withdrawn
- Venous Thromboembolism (VTE)
- Pulmonary Infection



# Clozapine Benefits

- FDA indicated for treatment-resistant schizophrenia, however:  
**IT IS THE MOST EFFECTIVE MEDICATION IN ALL SETTINGS.**
- Reduces suicide (FDA indicated).
- Reduces violent behavior.
- Reduces substance abuse
- Allows patients to robustly participate and succeed in physical, social and cognitive rehabilitation.
- Best acceptance, lowest discontinuation, and best survival.

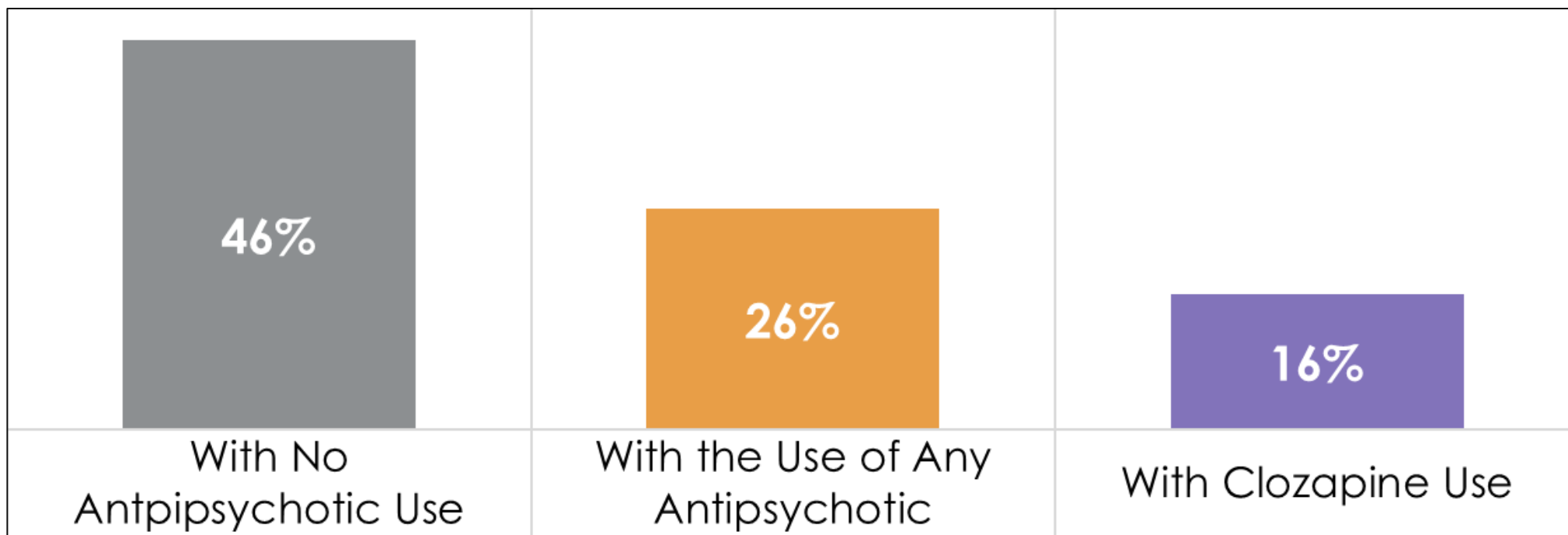


# Major Benefit: Lowers Risk of Death

- First year of psychotic illness the risk of death **24 to 89 times** the general population aged 16-30.
- Suicide risk in psychotic spectrum illness:
  - 50% attempt, 10% completion (3-5 % in the first year).
  - Clozapine reduces this risk by 80-90% compared to other antipsychotics.
  - **380 to 900 more survive for every 10,000 treated with clozapine.**
- Agranulocytosis risks, for comparison:
  - Only 0.3% to 0.8% occurrence, with overall mortality of 1 to 2.5 per 10,000.
  - 90- 95% of this risk occurs in the first 18 weeks.
  - After 6 months the risk of death is no more than other antipsychotics.
  - Context: Iceland does not monitor; 1/10 of this 2/10,000.
- Psychosis cuts life short by 20-25 years, mostly due to cigarette and drug use.
  - Clozapine significantly reduces smoking and substance use disorders.



# Live Longer on Clozapine

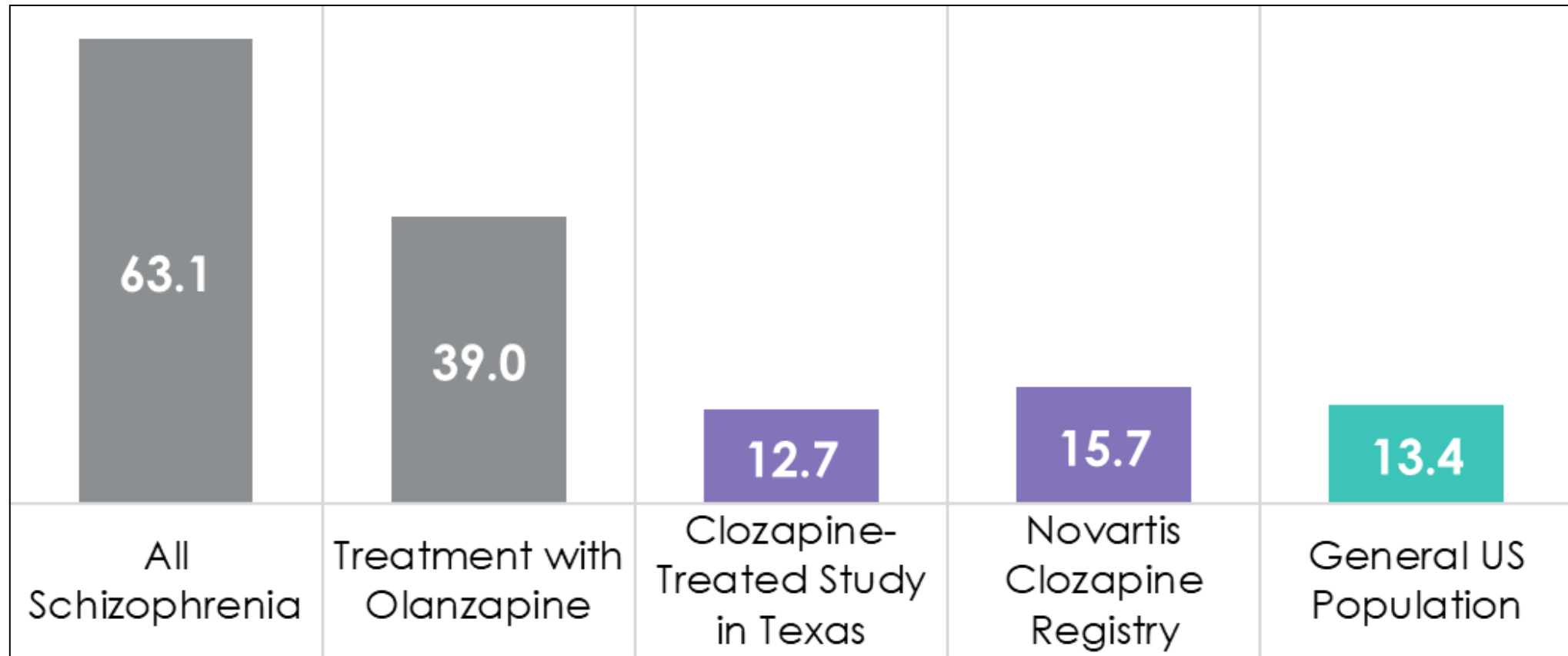


## **SCHIZOPHRENIA 20-YEAR MORTALITY RATE**

A Finish 20-Year Study of >62,000 patients



# Reduced Suicide Rate



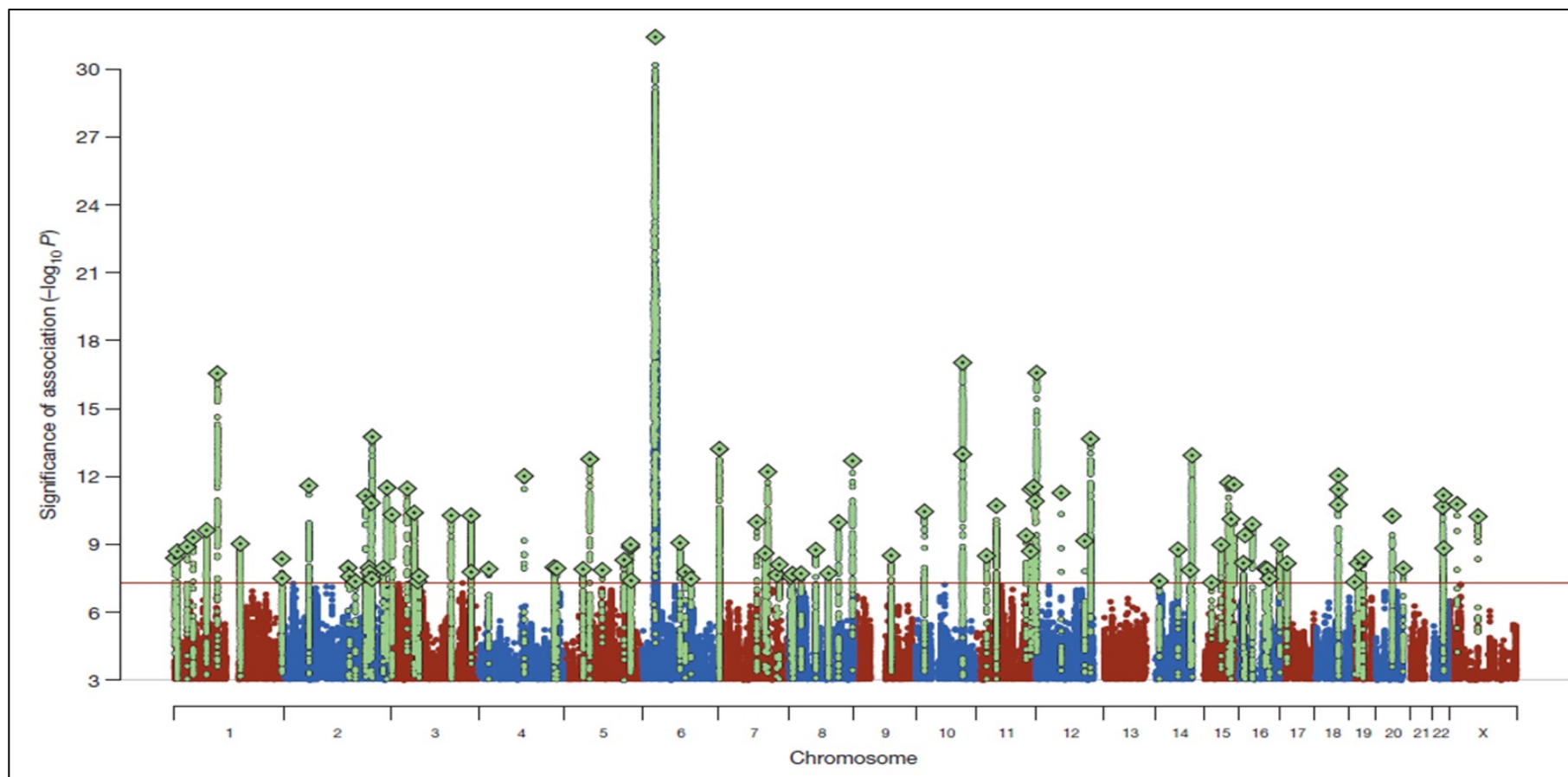
**CLOZAPINE REDUCES SUICIDE RATE IN PATIENTS WITH SCHIZOPHRENIA**

Annual Suicides Per 100,000





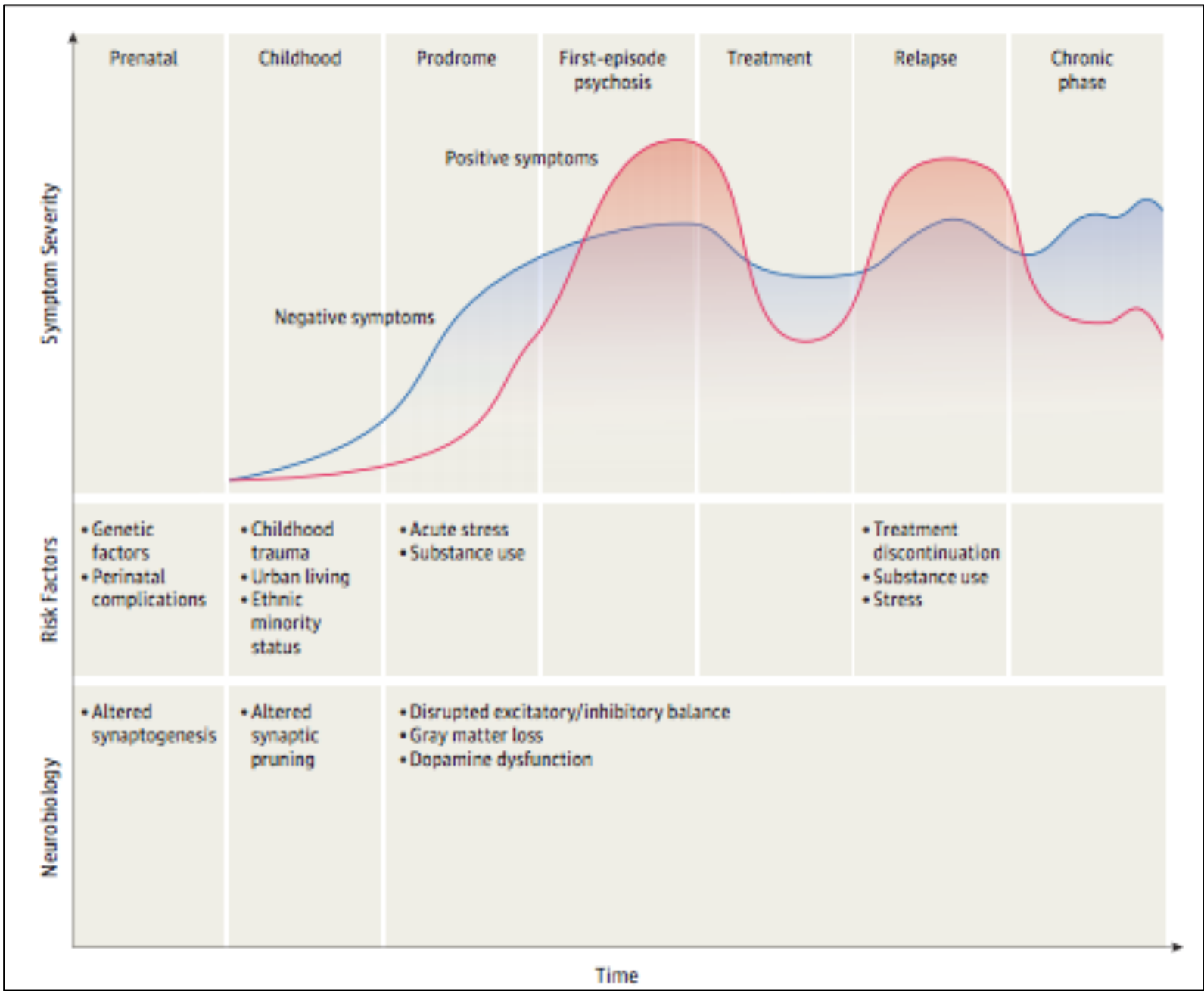
# Pruning C4A & Schizophrenia



## **SCHIZOPHRENIA RISK ASSOCIATED WITH 108 GENOMIC REGIONS**

Schizophrenia Working Group of the Psychiatric Genomics Consortium. *Nature* 2014;511(7510):421–427.





# THE CLINICAL COURSE OF SCHIZOPHRENIA

Schizophrenia—An Overview  
Robert A. McCutcheon, MRCPsych;  
Tiago Reis Marques, PhD;  
Oliver D. Howes, PhD  
Published online October 30, 2019.



# Clinical Features of Psychosis



Maguire 2002



# The TEAM DANIEL Family

**Our Cohort:** A cohort of **120** patients that have received a clozapine-centered treatment approach for 1 year or longer, currently the subjects of an in-depth patient characterization study.

**Family:** Another **40+** (and counting) patients in earlier phases of their clozapine journey, with less than 1 year of treatment.

**Extended Family:** Over **100** more families following the clozapine-centered approach through consultation or co-following with Dr. Robert Laitman and Dr. Ann Mandel and unfortunately those that have left us due to a lack of engagement.



# The TEAM DANIEL Family -2

## Patient Utilization Statistics

**53%** came to the practice to **initiate** clozapine.

- Previous providers could not- or would not- prescribe clozapine.

**47%** came to the practice **already on** clozapine.

- Still suffering from psychosis symptoms.
- Enduring intolerable side effects.
- Still not recovered to pre-illness baseline functioning and well-being.
- Previous providers unwilling to re-challenge after prior adverse effect.

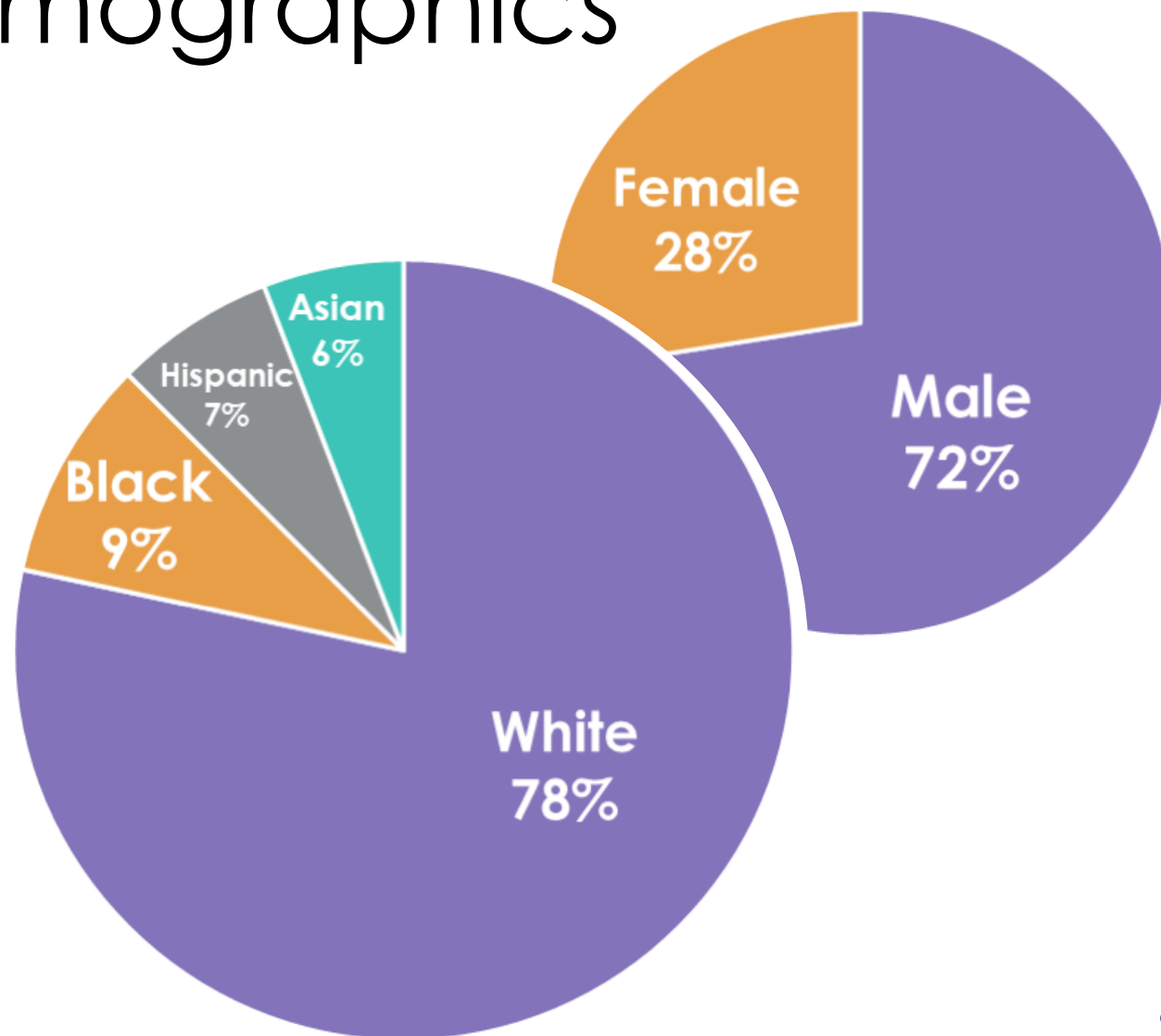


# Our Demographics

## TEAM DANIEL Profile Statistics

- Average age: **34 years old**
- Youngest: **17**
- Oldest: **75**
- Longest patient on clozapine: **31 years** (and counting)

All genetic profiles, backgrounds and ethnicities respond better to clozapine than any other antipsychotic.  
Asians, females and non-smokers may respond to lower dosages, on average.

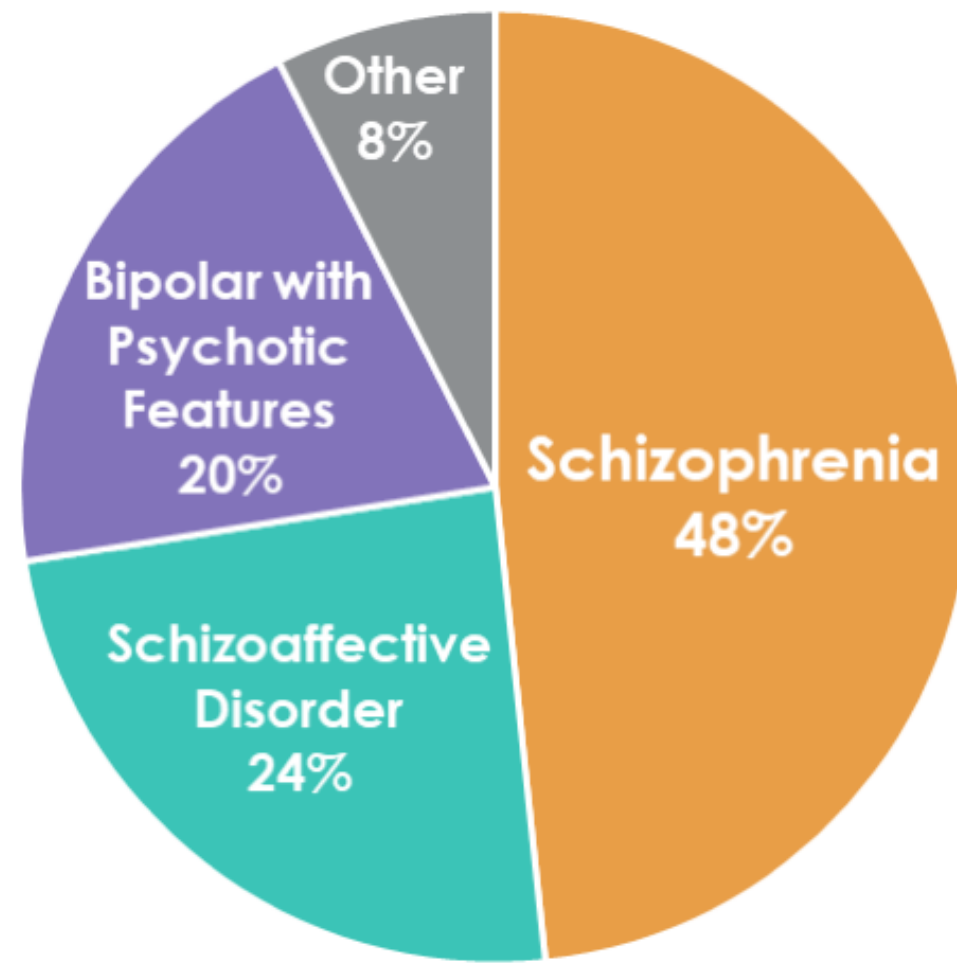


# Our Demographics

## Compelling Statistics

- **4** of the **120** Team Daniel cohort patients are no longer on clozapine due to their psychiatric condition resolving.
- **59%** characterized with anosognosia (poor insight).
- **9** patients on Assisted Outpatient Treatment (AOT).

Clozapine can be used for drug-induced psychosis, borderline personality disorder, severe insomnia, depressive disorder with psychosis, and other conditions.



# The Practice

## Not Every Patient is Still With Us...

- **18** Refused or never started treatment; unable to obtain an AOT.
- **10** Discontinued treatment or transitioned to other medications.
  - Other antipsychotic, mood stabilizer or cognition medications.
  - 1 due to clozapine adverse effect: cardiomyopathy in an elderly transplant patient.
- **2** Deaths
  - 1 elderly patient
  - 1 suicide
- **20** Lost to follow up or transferred to another practice.
- **4** Dismissed from practice.





# How is TEAM DANIEL Different?

- We use **Clozapine First**... NOT as a last resort!
- We believe patients have a **Right to Be Well** and encourage the use of LEAP and if needed court-ordered Assisted Outpatient Treatment (AOT).
- We do not tolerate side effects, including weight gain, and we aggressively use **adjunctive medications, ultra-slow titrations, diet and exercise** to treat and prevent them.
- Our goal is **Meaningful Recovery** and returning patients to their pre-illness baseline level of functioning and well-being.
- We promote a sense of **community** and engage and communicate with the patient's **Family**. After learned helplessness and hopelessness we restore optimism.



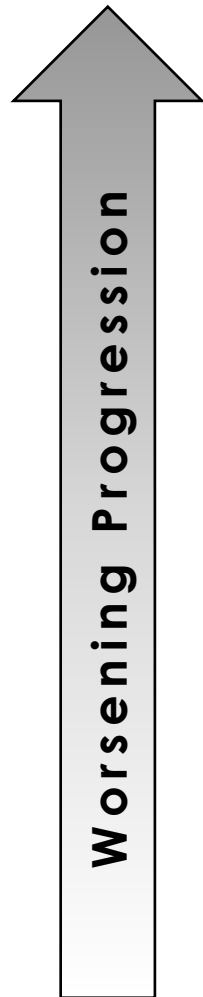
# Clozapine First

**This is what we believe. Why? Change the disease!**

- Early treatment leads to best outcomes: Including survival.
- Shorten the duration of untreated psychosis (DUP) by early treatment with clozapine; the earlier it is used the better.
- Better compliance and faster and more robust recovery.
- Decrease early suicide (24X increased mortality the first year).
- Decrease early aggression (12% serious violence.)
- Superior in adherence, quality of life, and patient satisfaction.
- Reduces drug and cigarette abuse.
- Patients respond better to psychosocial support.
- Patients achieve robust **Meaningful Recovery**.



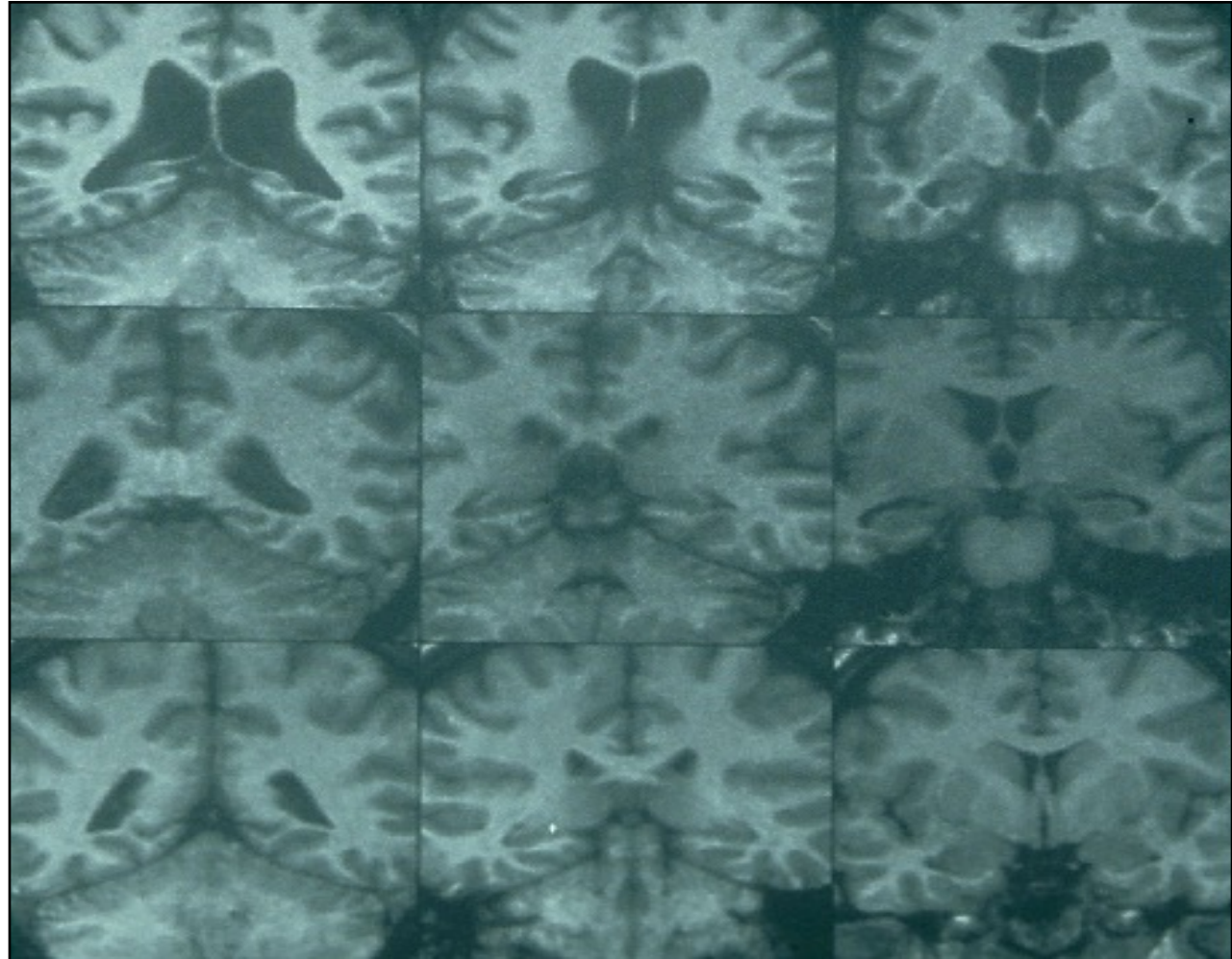
## PROGRESSIVE MRI CHANGES OVER THREE RELAPSES IN A MALE WITH SCHIZOPHRENIA



After 8 Relapses

After 3 Relapses

First psychotic episode



Henry Nasrallah M.D., personal files



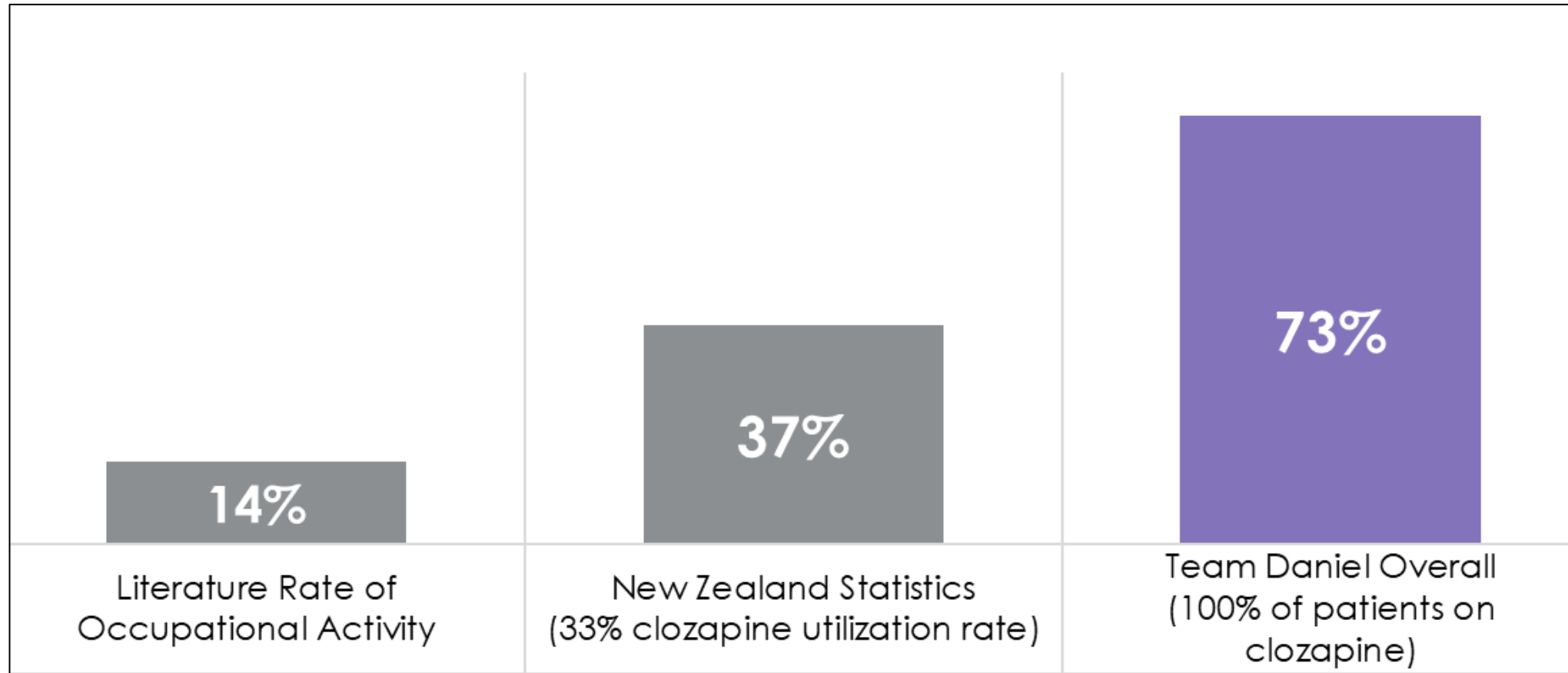
# Our Meaningful Recovery

**With TEAM DANIEL it means achieving any of the following:**

- Employed for 20 hours per week or more.
- Attending school full-time, or part-time with other activities.
- Responsibly maintaining a homemaker and/or parenting role.
- Successfully participating in a vocational rehabilitation program.
- Successfully engaged in consistent volunteer activity for 20 hours per week or more.



# Meaningful Rate of Recovery

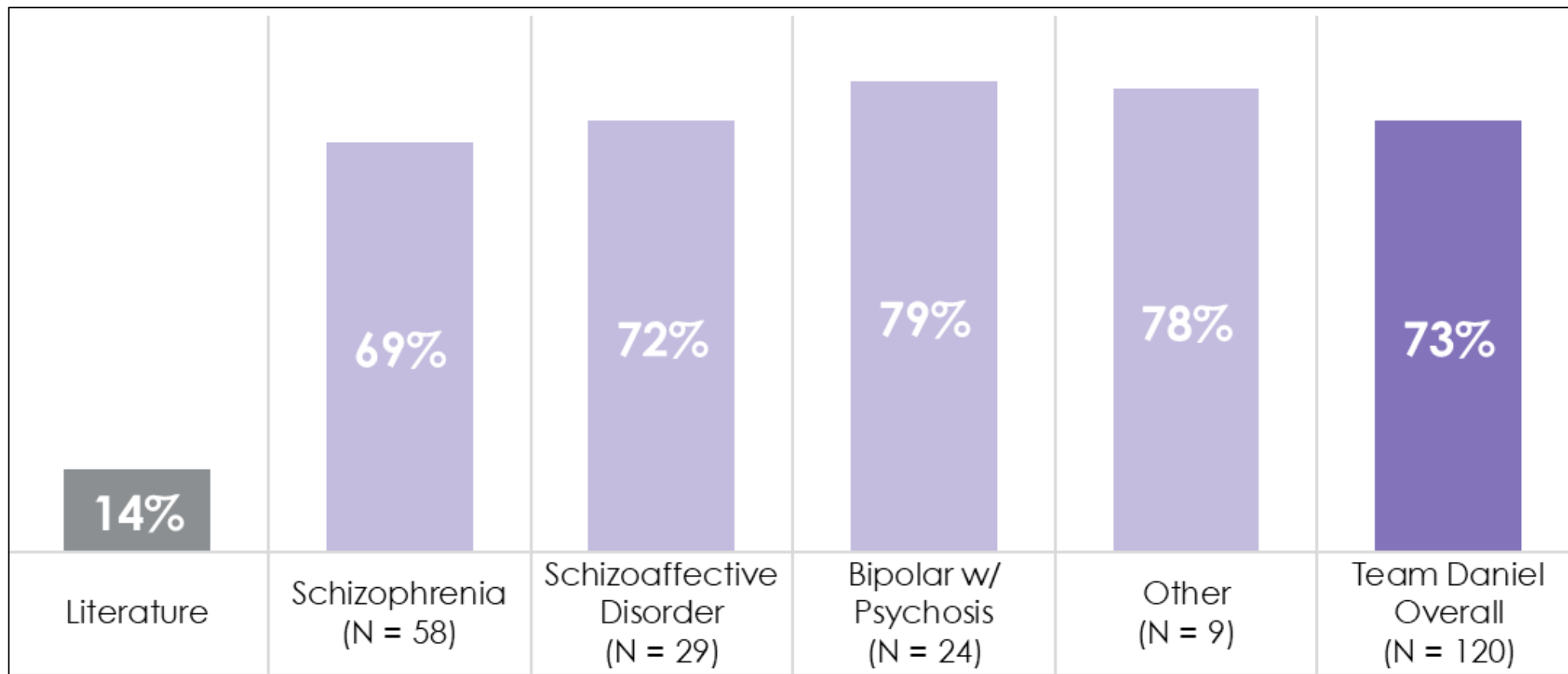


## OCCUPATIONAL RATE OF ACTIVITY ON CLOZAPINE

N = 120 Patients on an Optimized Clozapine Regimen



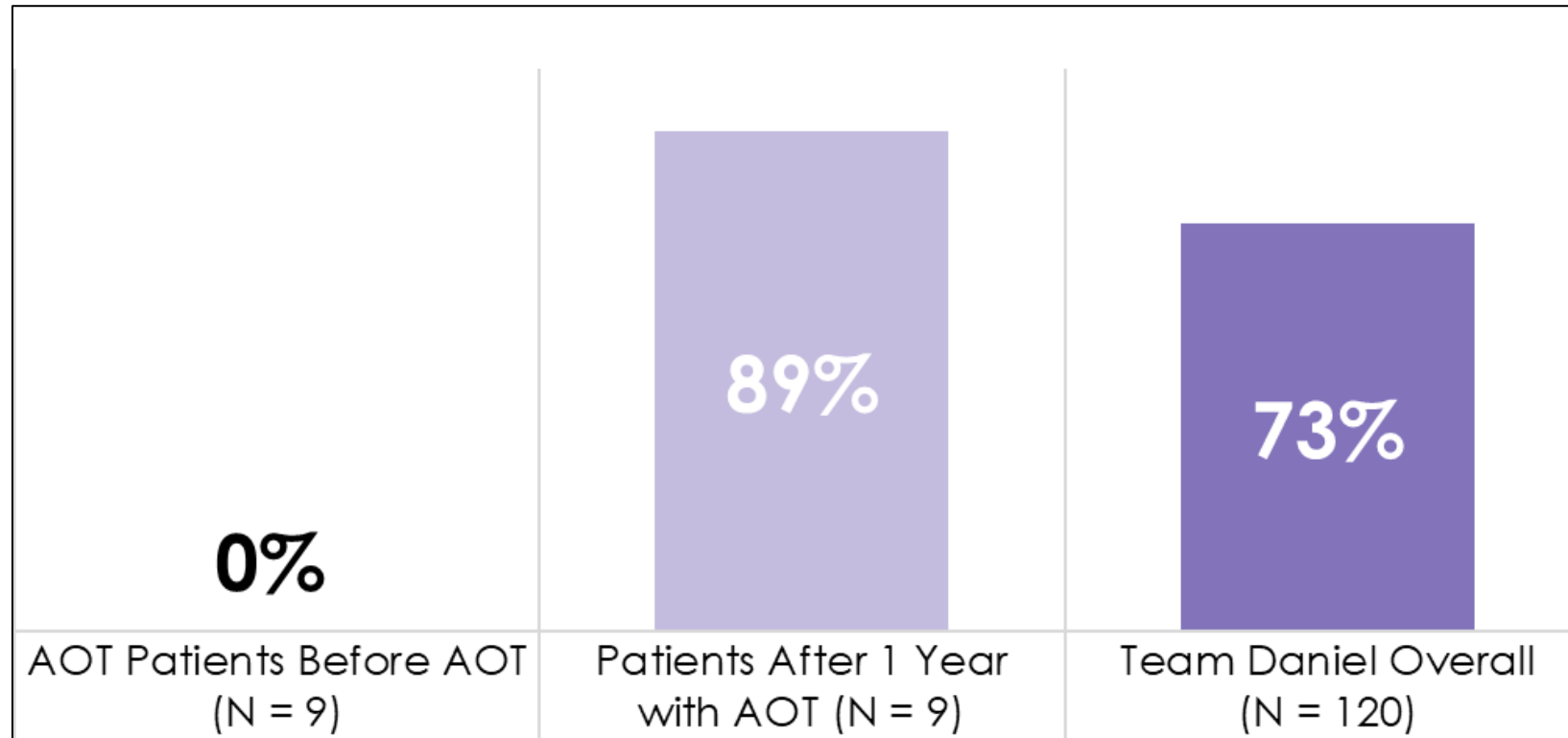
# Meaningful Recovery By Diagnosis



**RATE OF MEANINGFUL RECOVERY BY DIAGNOSIS**



# AOT Saves Lives and Livelihoods



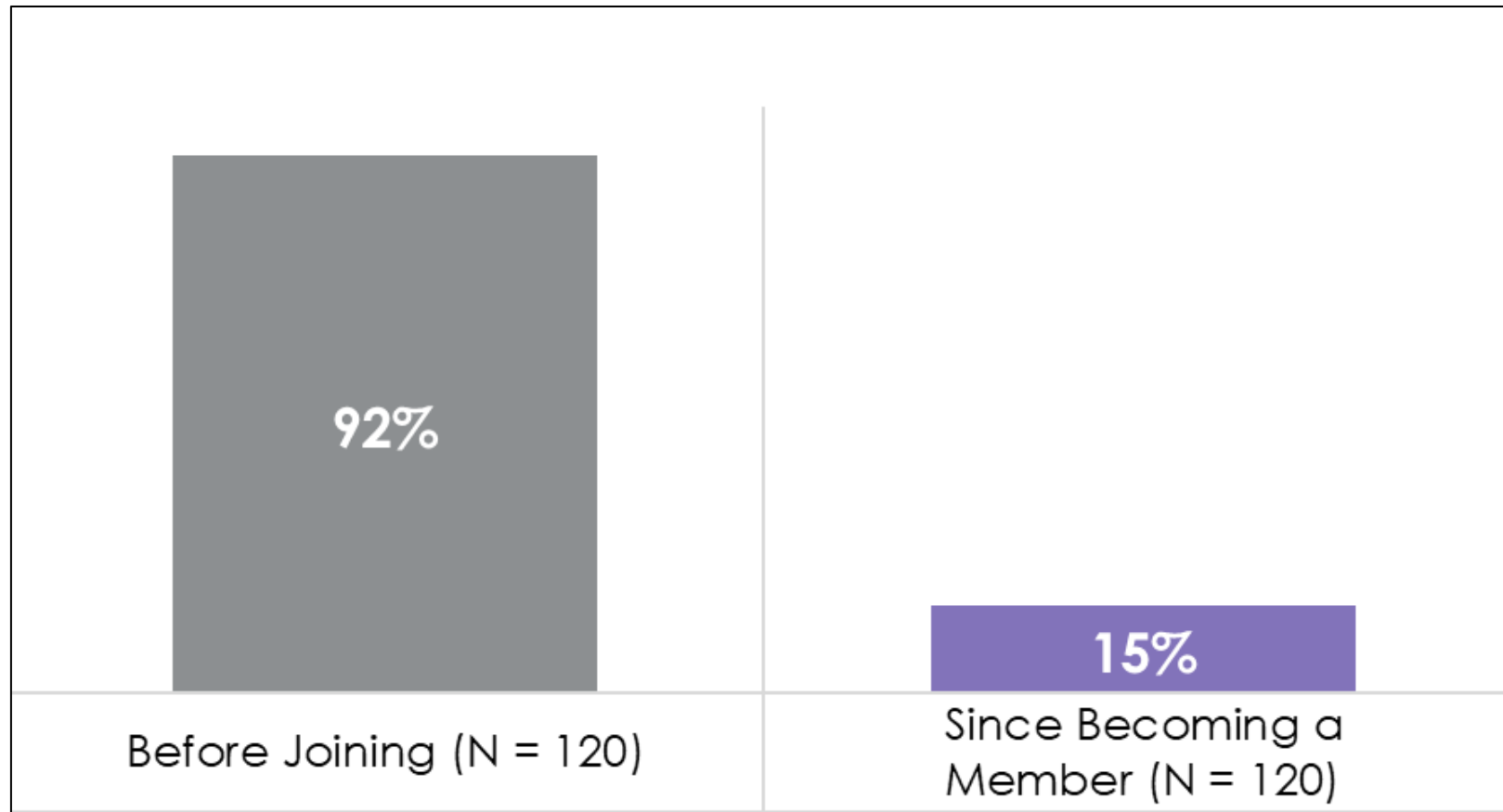
**100% Significant Improvement in Quality of Life.  
No hospitalizations!**

## MEANINGFUL RECOVERY WITH ASSISTED OUTPATIENT TREATMENT (AOT)

Depending on the location, "AOT" may be called "**COT**" for Court Ordered Treatment or "**MOT**" for Mandatory Outpatient Treatment. Although definitions and enforcement vary widely, the intent is court-mandated participation in treatment, with hospitalization enforced for non-compliance.



# 85% Never See Hospital Again



**PATIENTS WITH ONE OR MORE HOSPITALIZATIONS**

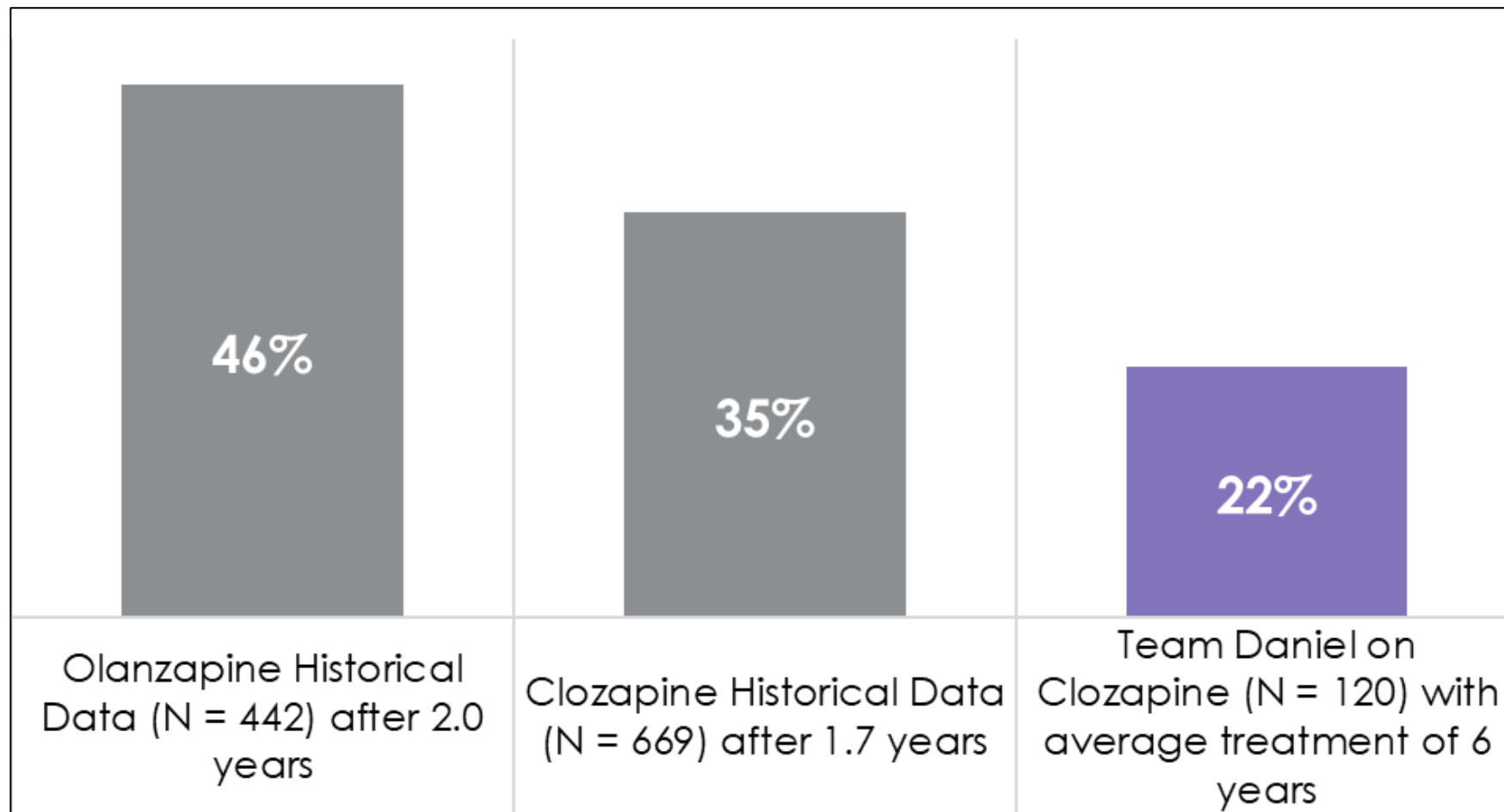
## **18 Hospitalizations:**

- 9** Patients for mental health
- 1** For substance use
- 4** For adverse effect:
  - 2** Seizures
  - 1** Pneumonia
  - 1** Lithium toxicity
- 3** For medical reasons
- 1** Age-related decline





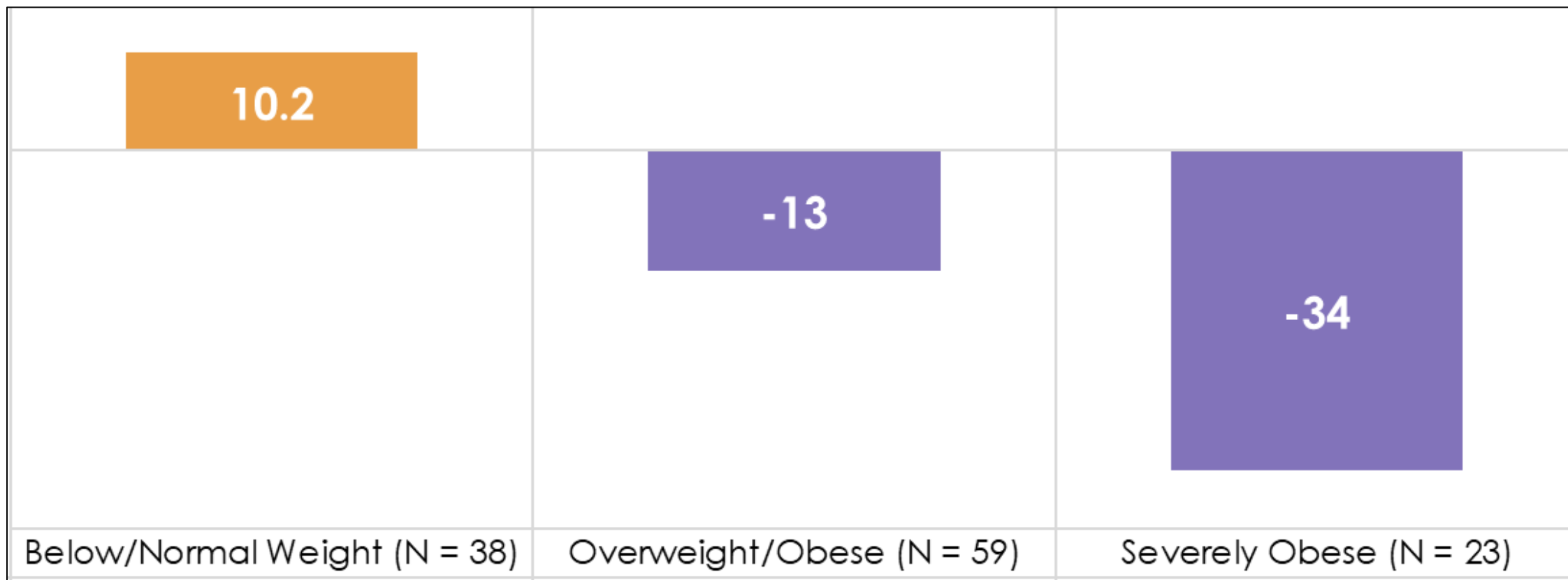
# Less Weight Gain



**PROPORTION OF PATIENTS WITH MORE THAN 7% INCREASE IN BODY WEIGHT**



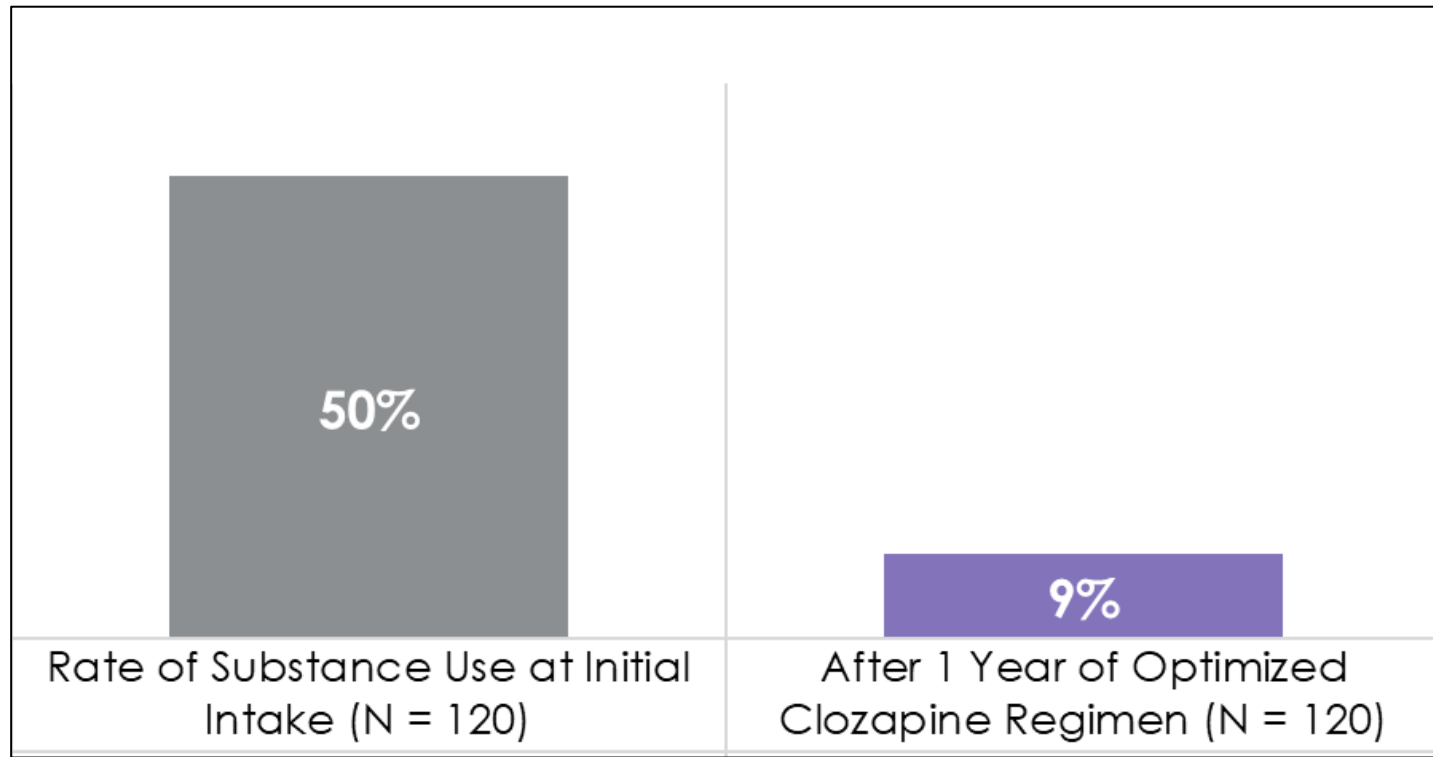
# Impressive Weight Change



**TEAM DANIEL ON CLOZAPINE AVERAGE WEIGHT CHANGE (LB)**



# Recovery Rate Unprecedented



**82% Recovery from Substance Use**

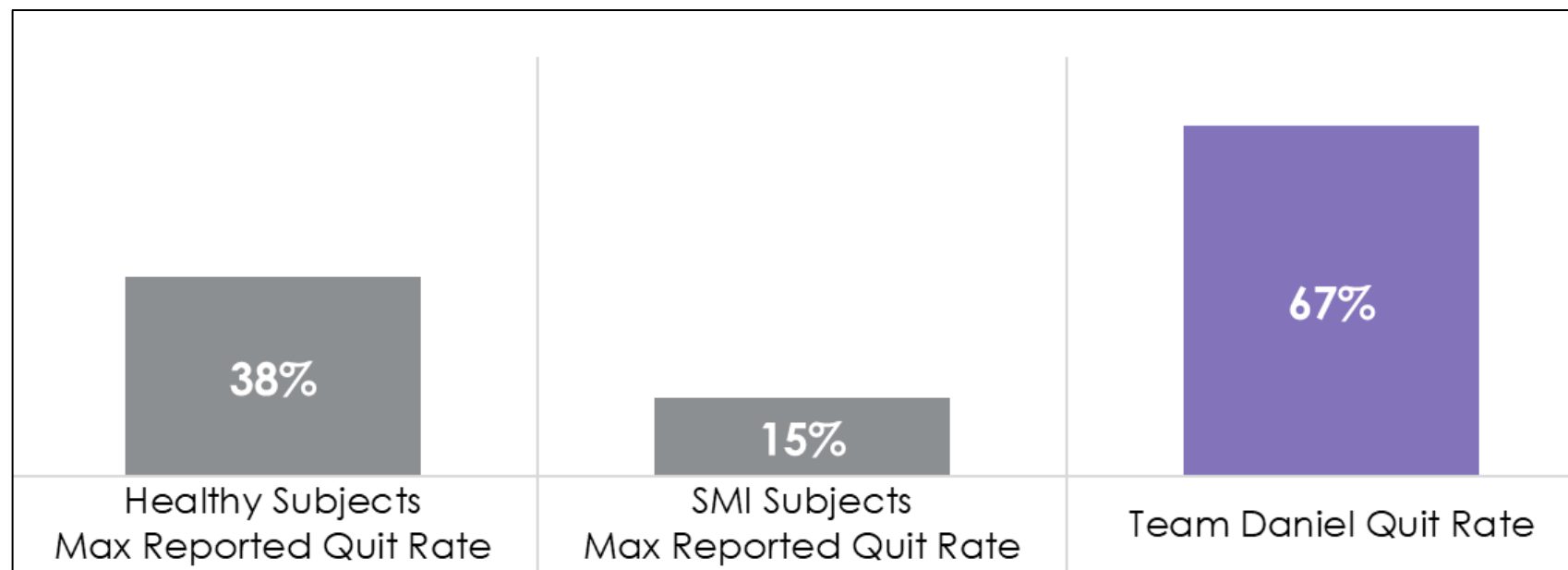
**82% Recovery from Cannabis Use Alone**

## **RATE OF SUBSTANCE USE DISORDER**

Cannabis was the primary drug in 85% of patients



# Cessation Rate Beats The Odds



**31 of 46 Smokers Quit**

Most used  
combination therapy:

84% Chantix

42% NRT

55% Bupropion

## **RATE OF TOBACCO CESSATION**

(N=46 Team Daniel Smokers)



## TEAM DANIEL NOTABLE ADVERSE EVENTS (N=120)\*

Pneumonia	<b>17</b>	<b>5</b> due to Covid-19 <b>2</b> patients hospitalized High rate of detection
Seizures	<b>6</b>	<b>2</b> patients of Asian descent <b>1</b> abruptly stopped smoking <b>2</b> patients hospitalized
Lithium Toxicity	<b>1</b>	Resolved with lowering lithium dose The patient was hospitalized
Cardiomyopathy	<b>1</b>	This occurrence in an elderly transplant patient is our only case of discontinuing clozapine due to adverse effects*
Suicide	<b>1</b>	Tragic and unexpected*
Stevens-Johnsons Syndrome	<b>1</b>	Discontinued Lamotrigine
<ul style="list-style-type: none"> <li>• Agranulocytosis</li> <li>• Embolus</li> <li>• Myocarditis</li> </ul>	<b>0</b>	No cases observed in hundreds of patients among the Team Daniel cohort and extended family

\*The suicide death and cardiomyopathy patient are not included among the 95 patients being characterized in the Team Daniel cohort

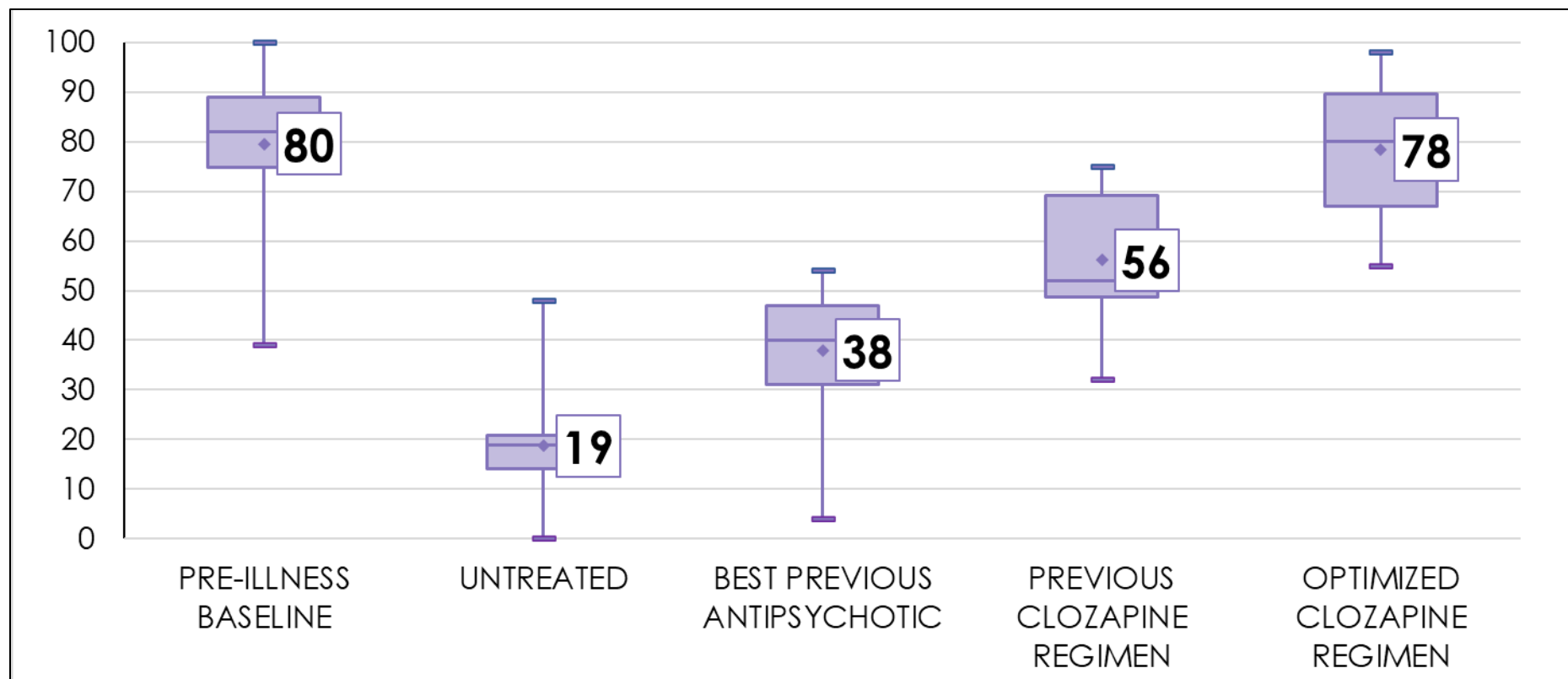


## MORE OBSTACLES AND CHALLENGES (N=120)

Neutropenia	<b>4</b>	<b>3</b> resolved after 1 instance <b>1</b> resolved with lithium
Substantial Weight Gain	<b>11</b>	<b>7</b> cases are tied to poor compliance with weight control medications <b>3</b> New to the weight control regimen
Severe orthostasis	<b>2</b>	Improved with fludrocortisone
Severe secondary narcolepsy	<b>2</b>	Using various strategies (splitting the dose, medications)
Urinary difficulties	<b>3</b>	Improved with desmopressin
Movement Disorders	<b>1</b>	<b>1</b> rare case of clozapine-related dystonia observed at a very high dose, resolved with lowering dose <b>3</b> patients with tardive dyskinesia from previous antipsychotic use resolved with clozapine



# Our Patients Return to Baseline



## GLOBAL ASSESMENT OF FUNCTIONING SCORES

Preliminary Data (N=14)

**TEAM DANIEL**  
Returns to Baseline  
Functioning &  
Well-being

