

Optimal Treatment of Psychotic Disorders: Clozapine/Engagement/Community

Dr. Robert Laitman

March 16, 2022



Housekeeping Information



Participant microphones will be muted at entry



If you have questions during the event, please use the chat



This session is being recorded and it will be available by the next business day.



If you have questions after this session, please e-mail: newengland@mhttcnetwork.org.

Acknowledgment

Presented in 2022 by the Mental Health Technology Transfer Center (MHTTC) Network.

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At the time of this publication, Miriam E. Delphin-Rittmon, Ph.D, served as Assistant Secretary for Mental Health and Substance Use in the U.S. Department of Health and Human Services and the Administrator of the Substance Abuse and Mental Health Services Administration.

The opinions expressed herein are the view of TTC Network and do not reflect the official position of the Department of Health and Human Services (DHHS), SAMHSA. No official support or endorsement of DHHS, SAMHSA, for the opinions described in this document is intended or should be inferred.

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Presented 2022

The MHTTC Network uses affirming, respectful and recovery-oriented language in all activities. That language is:

**STRENGTHS-BASED
AND HOPEFUL**

**INCLUSIVE AND
ACCEPTING OF
DIVERSE CULTURES,
GENDERS,
PERSPECTIVES,
AND EXPERIENCES**

**HEALING-CENTERED AND
TRAUMA-RESPONSIVE**

**INVITING TO INDIVIDUALS
PARTICIPATING IN THEIR
OWN JOURNEYS**

**PERSON-FIRST AND
FREE OF LABELS**

**NON-JUDGMENTAL AND
AVOIDING ASSUMPTIONS**

**RESPECTFUL, CLEAR
AND UNDERSTANDABLE**

**CONSISTENT WITH
OUR ACTIONS,
POLICIES, AND PRODUCTS**

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.

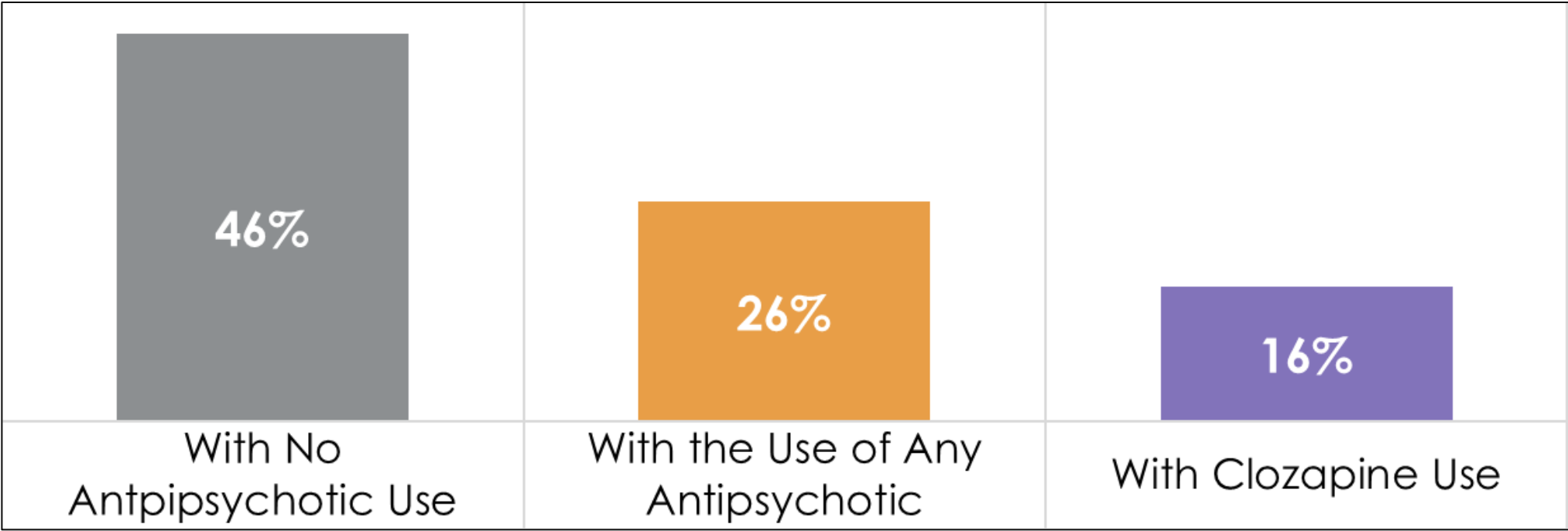


Major Benefit: Lowers Risk of Death

- 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

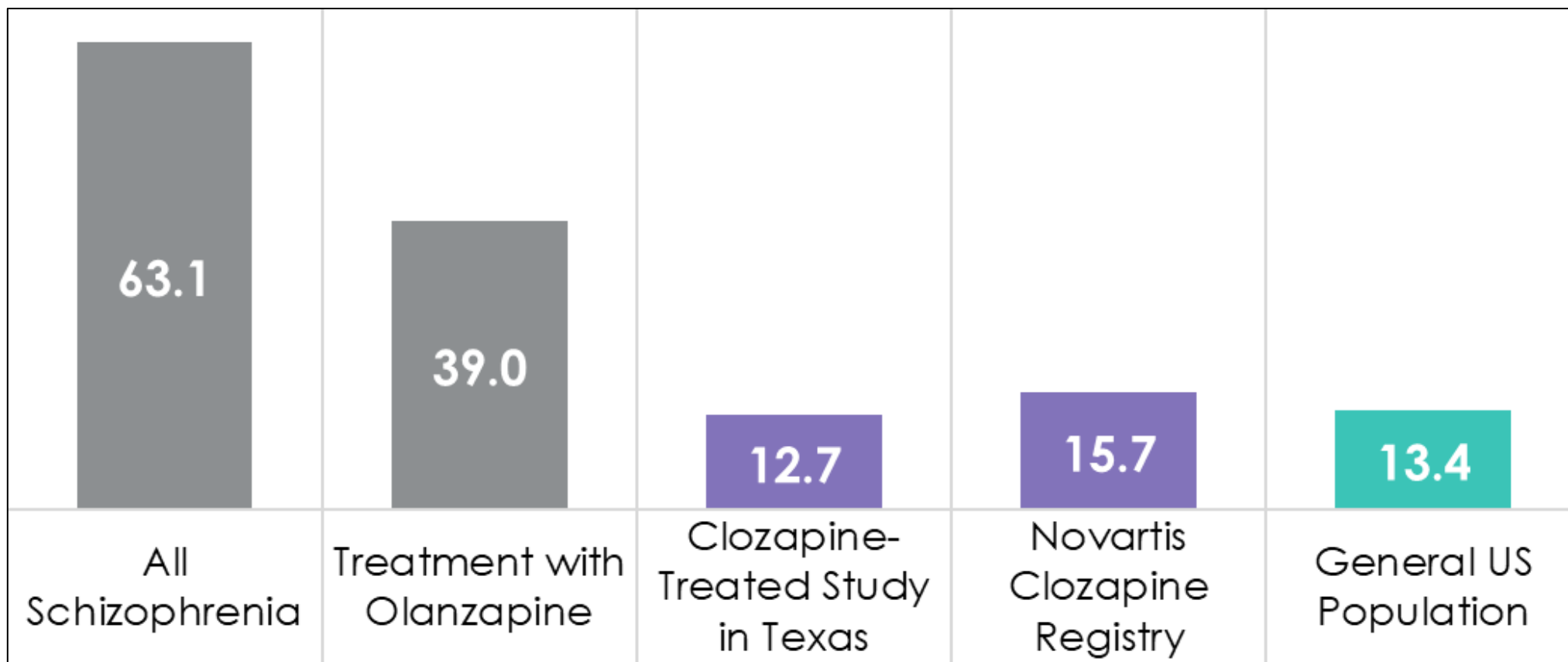


SCHIZOPHRENIA 20-YEAR MORTALITY RATE

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



Reduced Suicide Rate

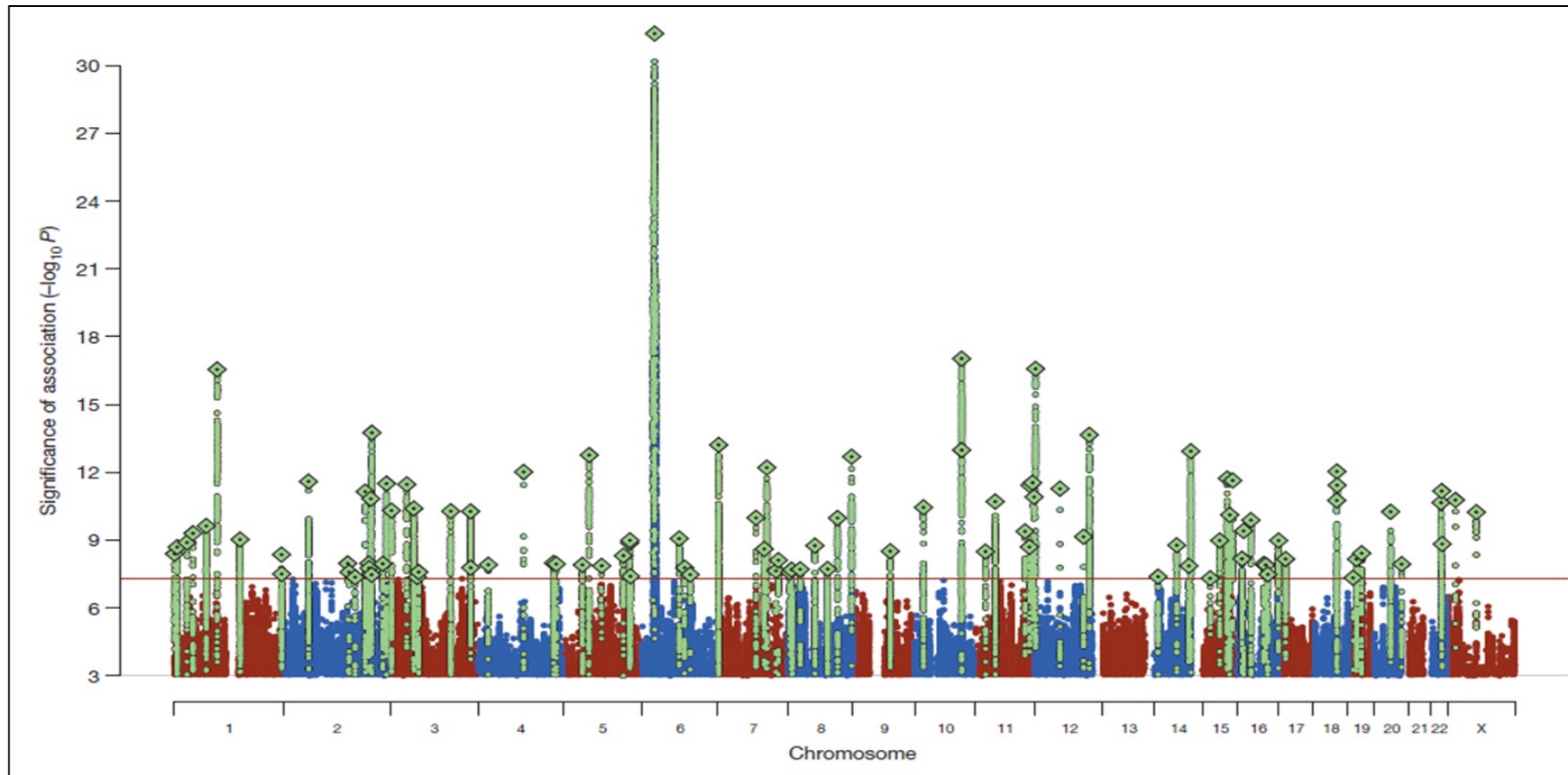


CLOZAPINE REDUCES SUICIDE RATE IN PATIENTS WITH SCHIZOPHRENIA

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.



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.

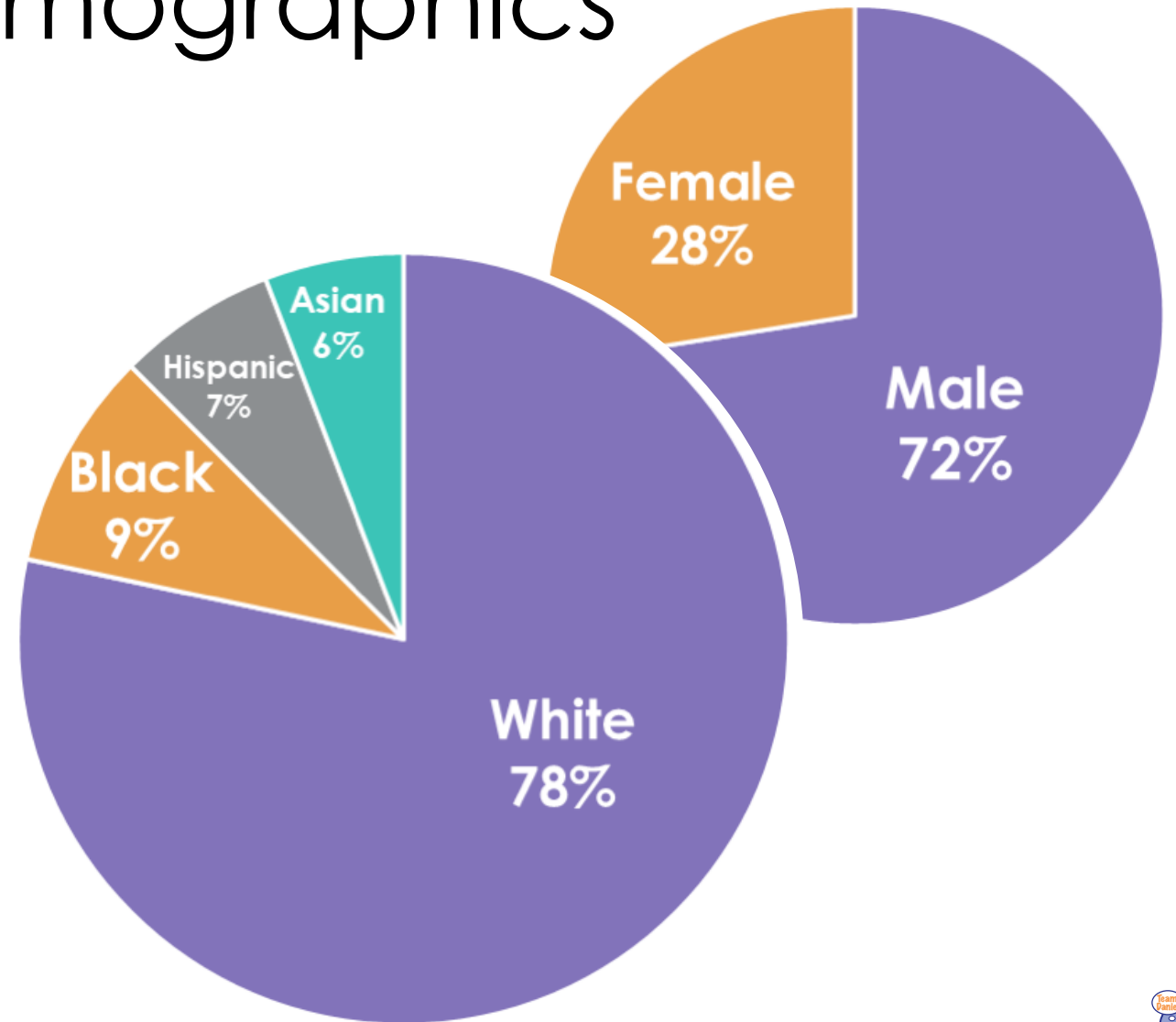


Our Demographics

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.

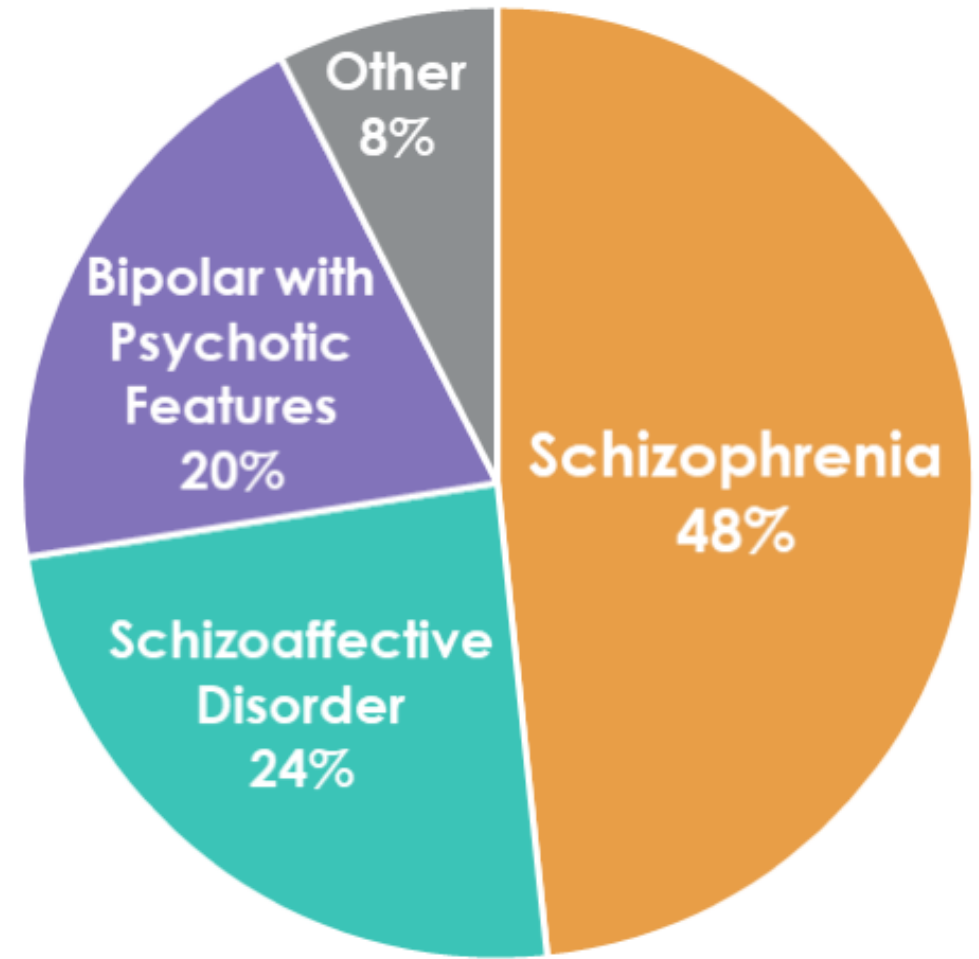


Our Demographics

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.



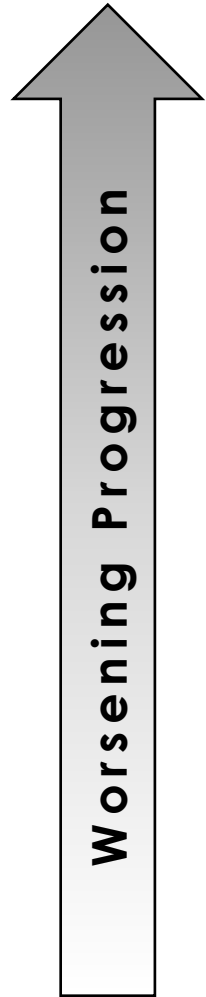
Clozapine First

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**.



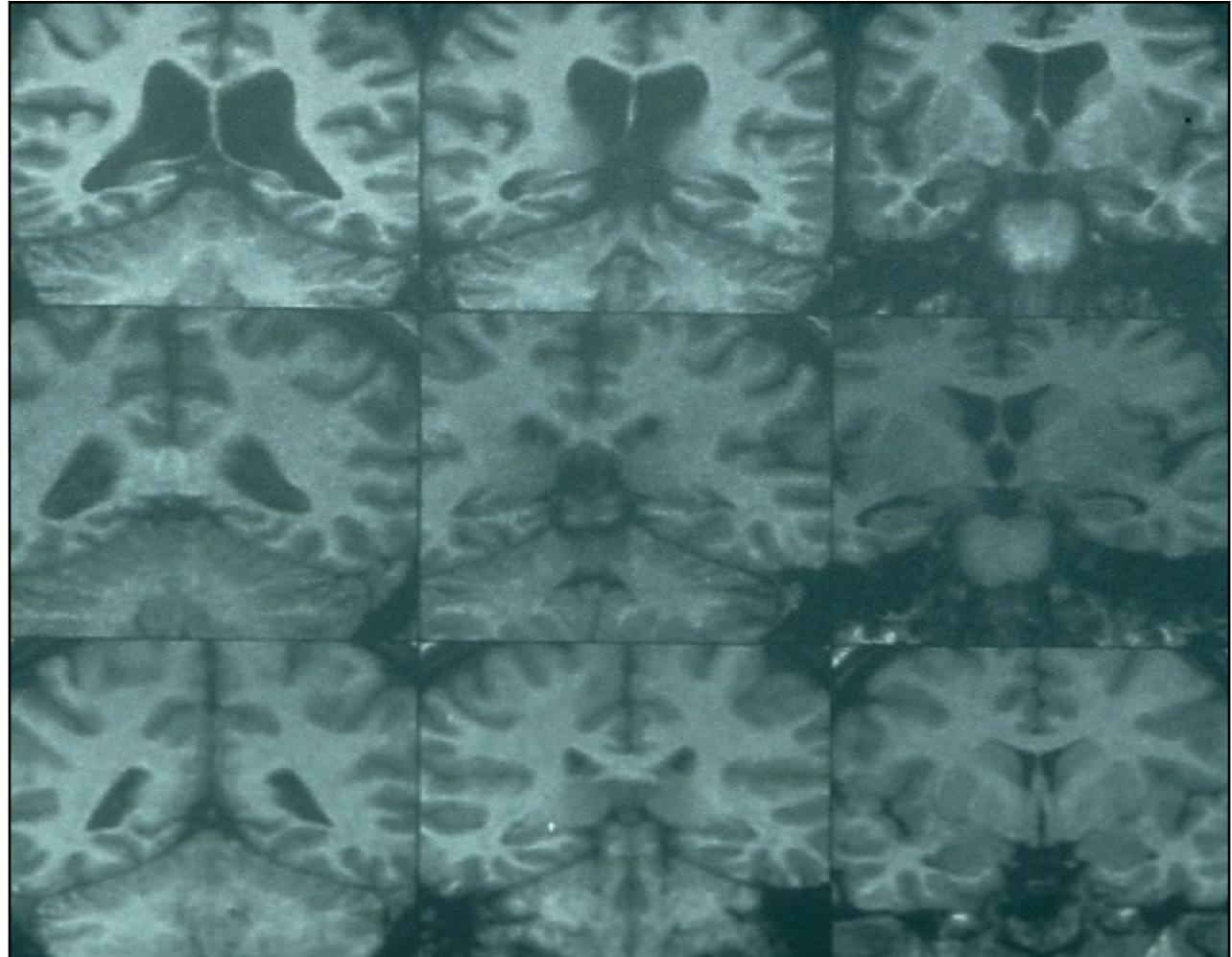
PROGRESSIVE MRI CHANGES OVER THREE RELAPSES IN A MALE WITH SCHIZOPHRENIA



After 8 Relapses

After 3 Relapses

First psychotic episode



Henry Nasrallah M.D., personal files



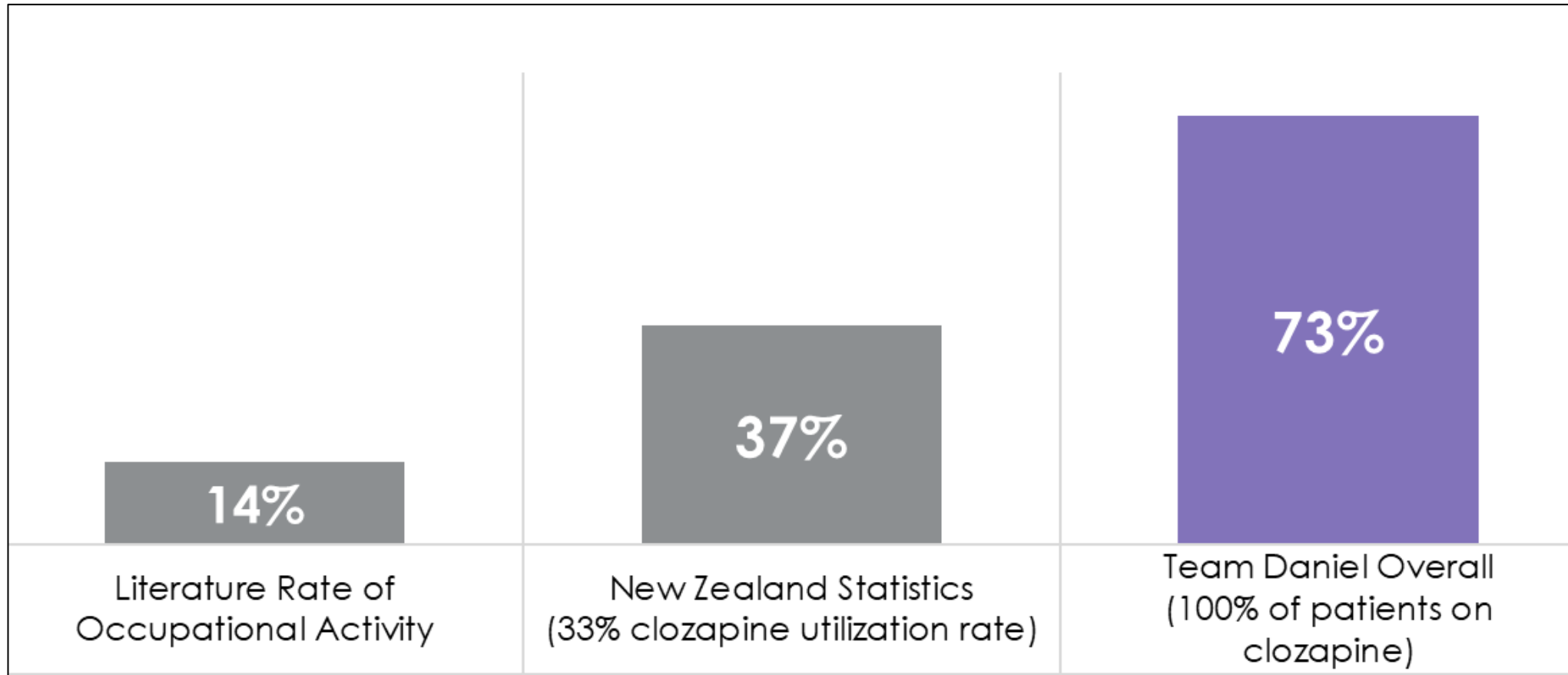
Our Meaningful Recovery

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

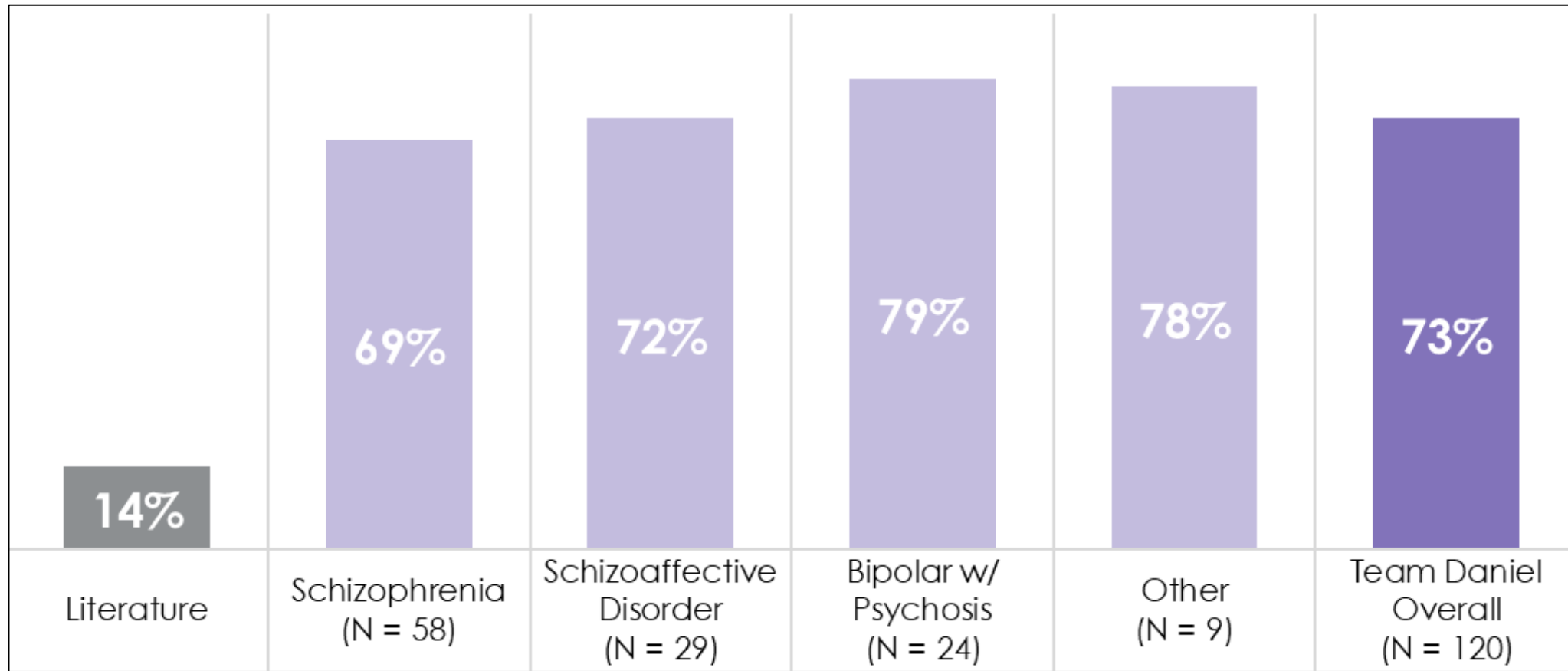


OCCUPATIONAL RATE OF ACTIVITY ON CLOZAPINE

N = 120 Patients on an Optimized Clozapine Regimen



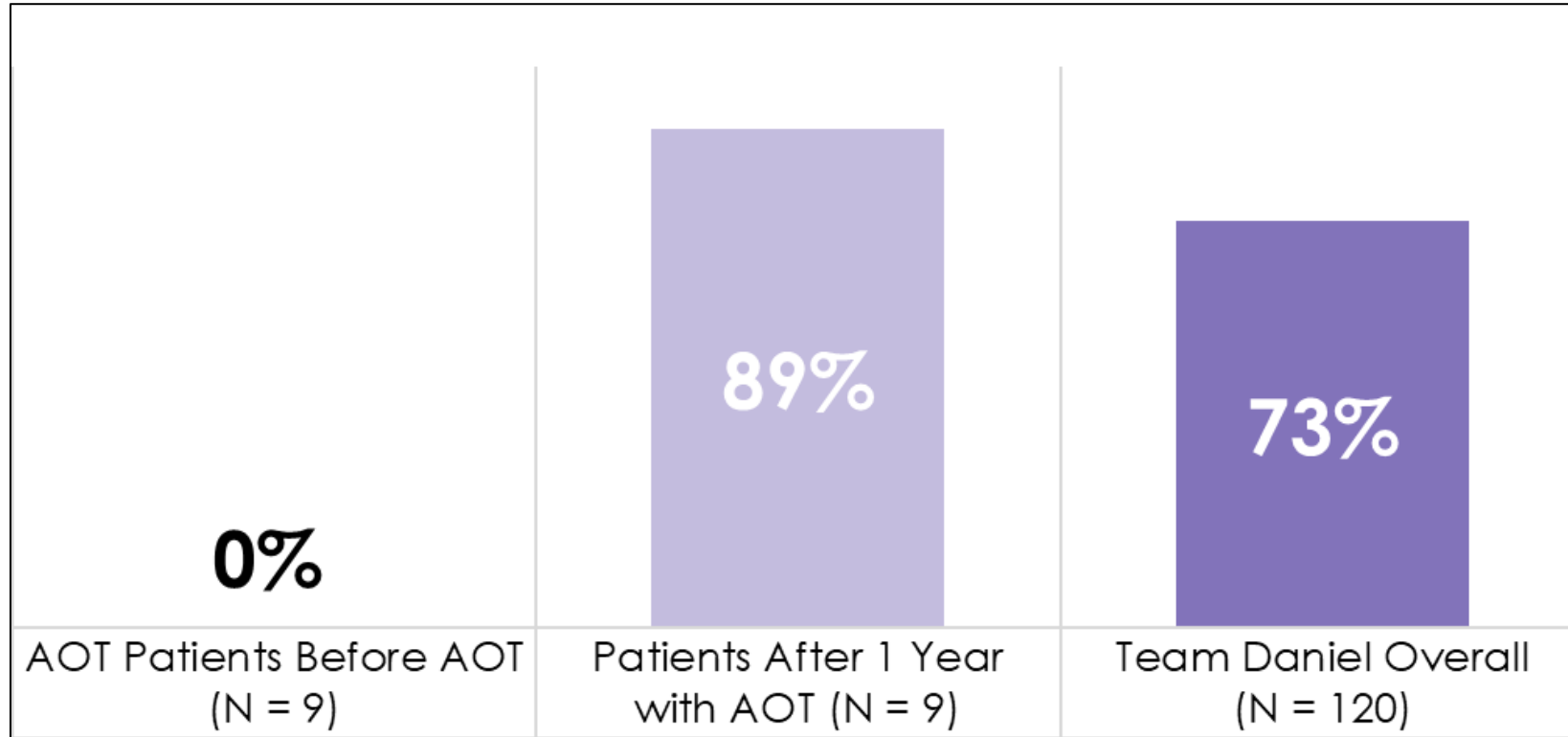
Meaningful Recovery By Diagnosis



RATE OF MEANINGFUL RECOVERY BY DIAGNOSIS



AOT Saves Lives and Livelihoods



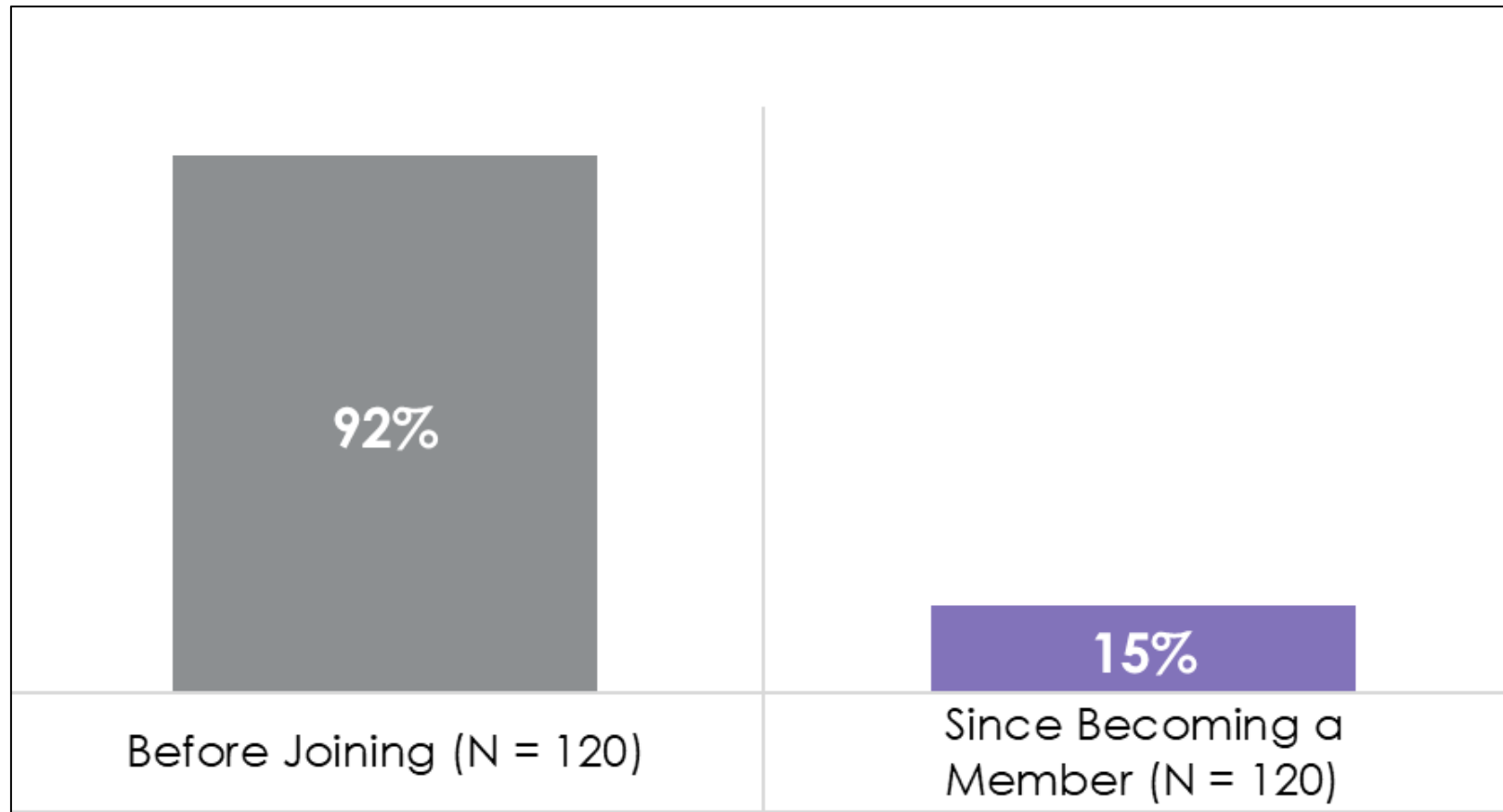
**100% Significant Improvement in Quality of Life.
No hospitalizations!**

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



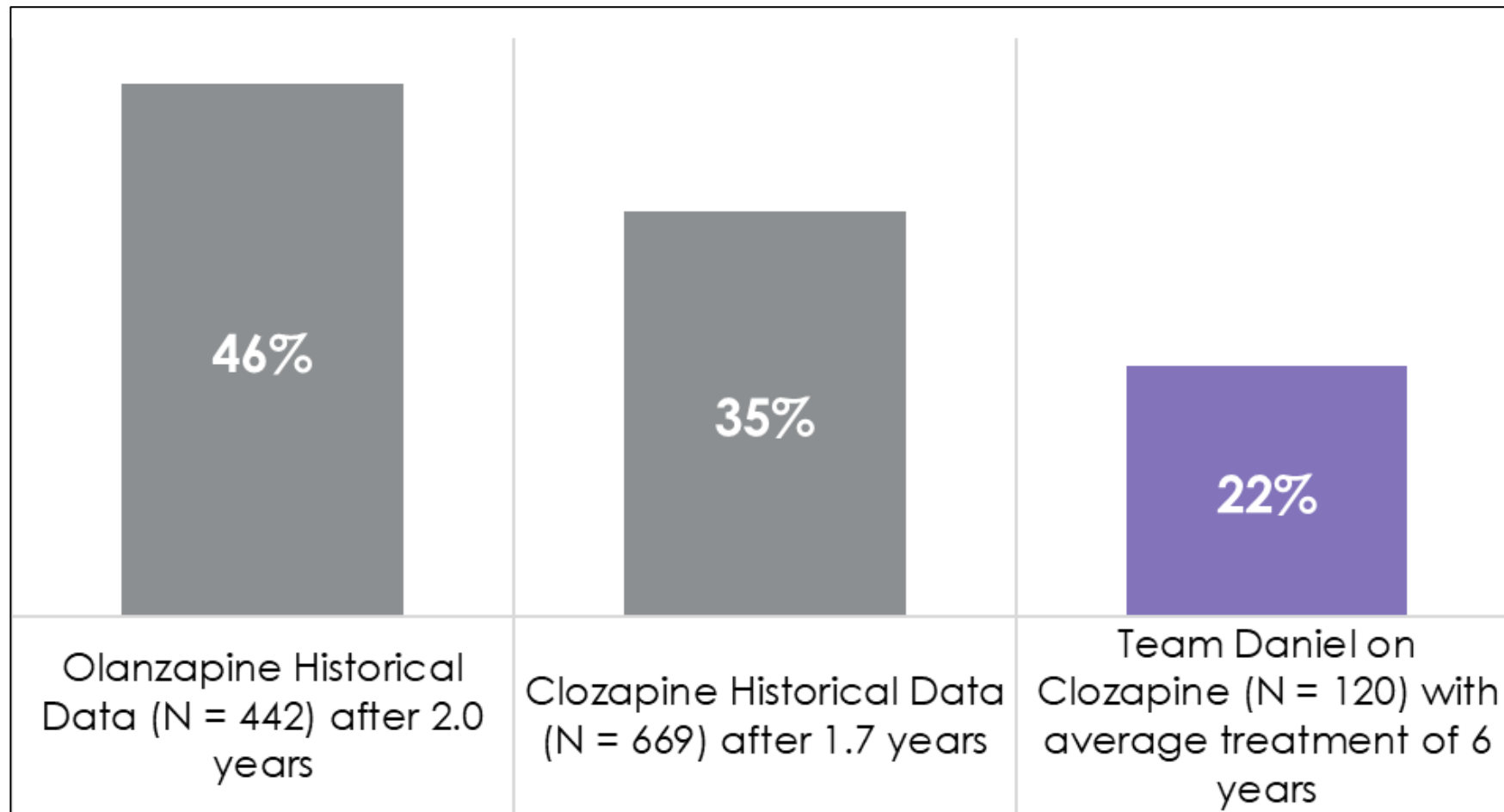
PATIENTS WITH ONE OR MORE HOSPITALIZATIONS

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



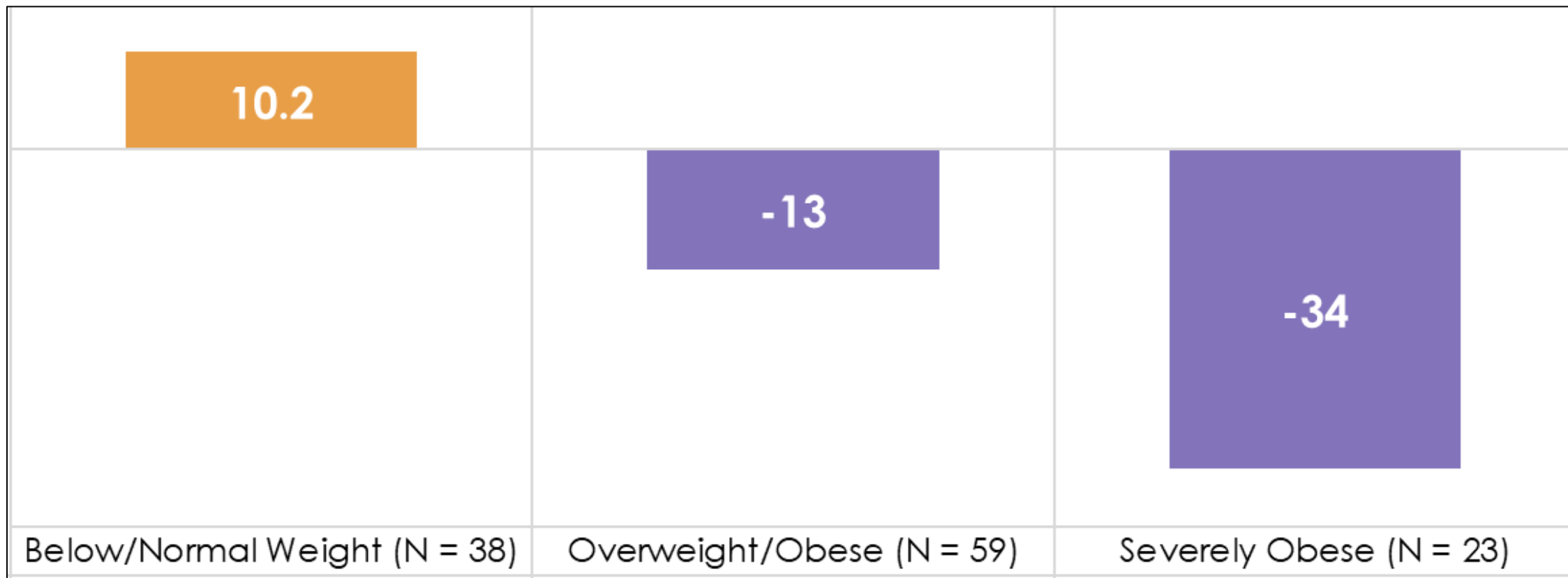
Less Weight Gain



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



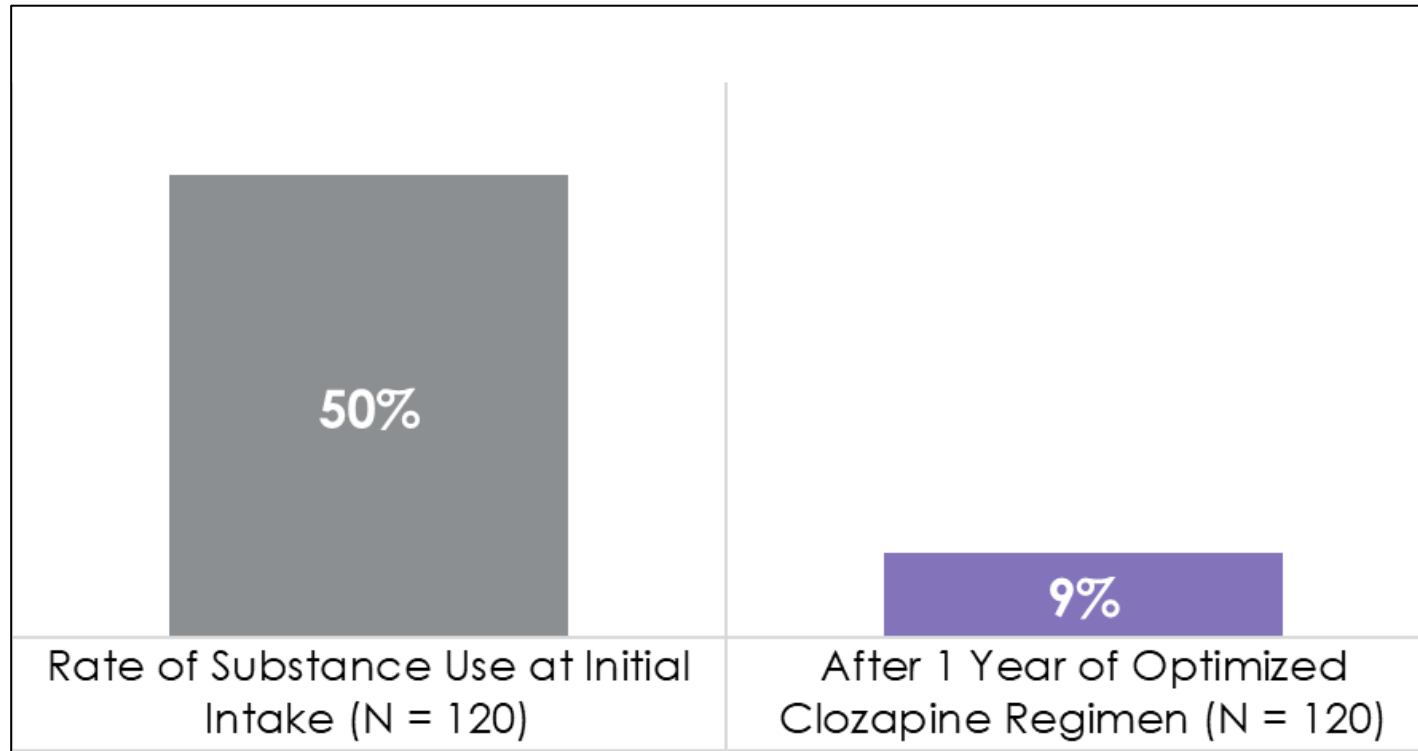
Impressive Weight Change



TEAM DANIEL ON CLOZAPINE AVERAGE WEIGHT CHANGE (LB)



Recovery Rate Unprecedented



82% Recovery from Substance Use

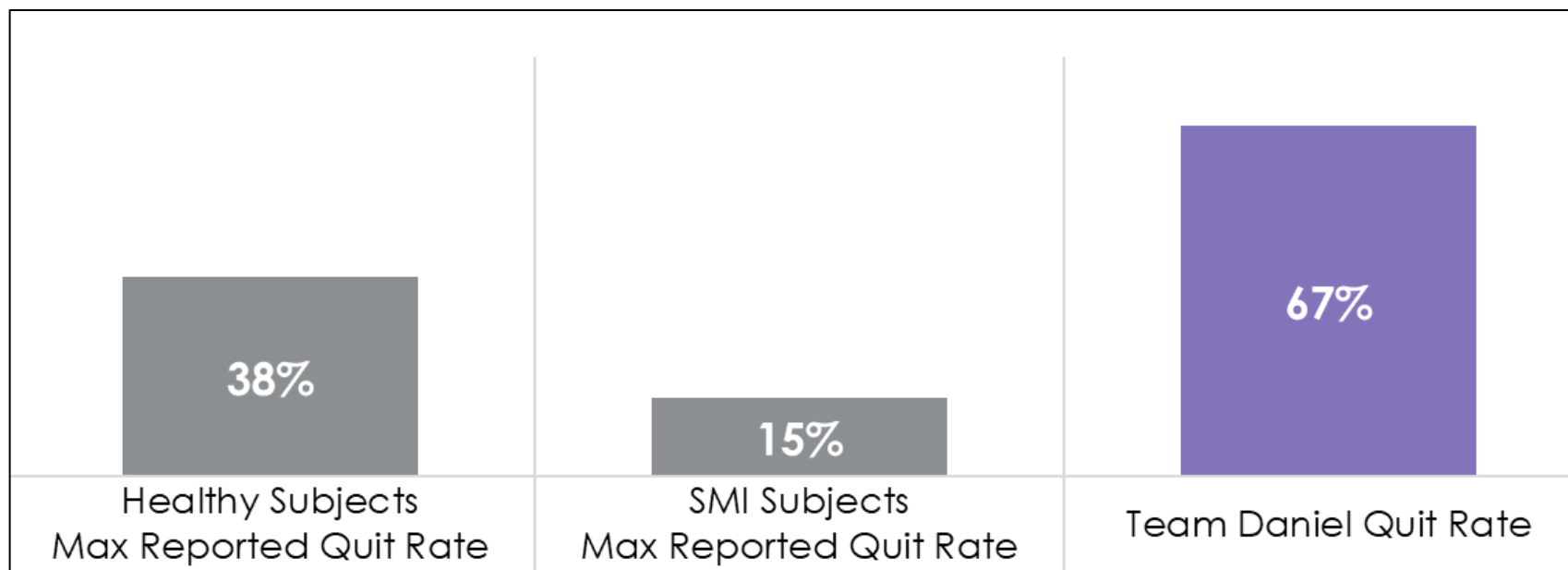
82% Recovery from Cannabis Use Alone

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	17	5 due to Covid-19 2 patients hospitalized High rate of detection
Seizures	6	2 patients of Asian descent 1 abruptly stopped smoking 2 patients hospitalized
Lithium Toxicity	1	Resolved with lowering lithium dose The patient was hospitalized
Cardiomyopathy	1	This occurrence in an elderly transplant patient is our only case of discontinuing clozapine due to adverse effects*
Suicide	1	Tragic and unexpected*
Stevens-Johnsons Syndrome	1	Discontinued Lamotrigine
<ul style="list-style-type: none"> • Agranulocytosis • Embolus • Myocarditis 	0	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

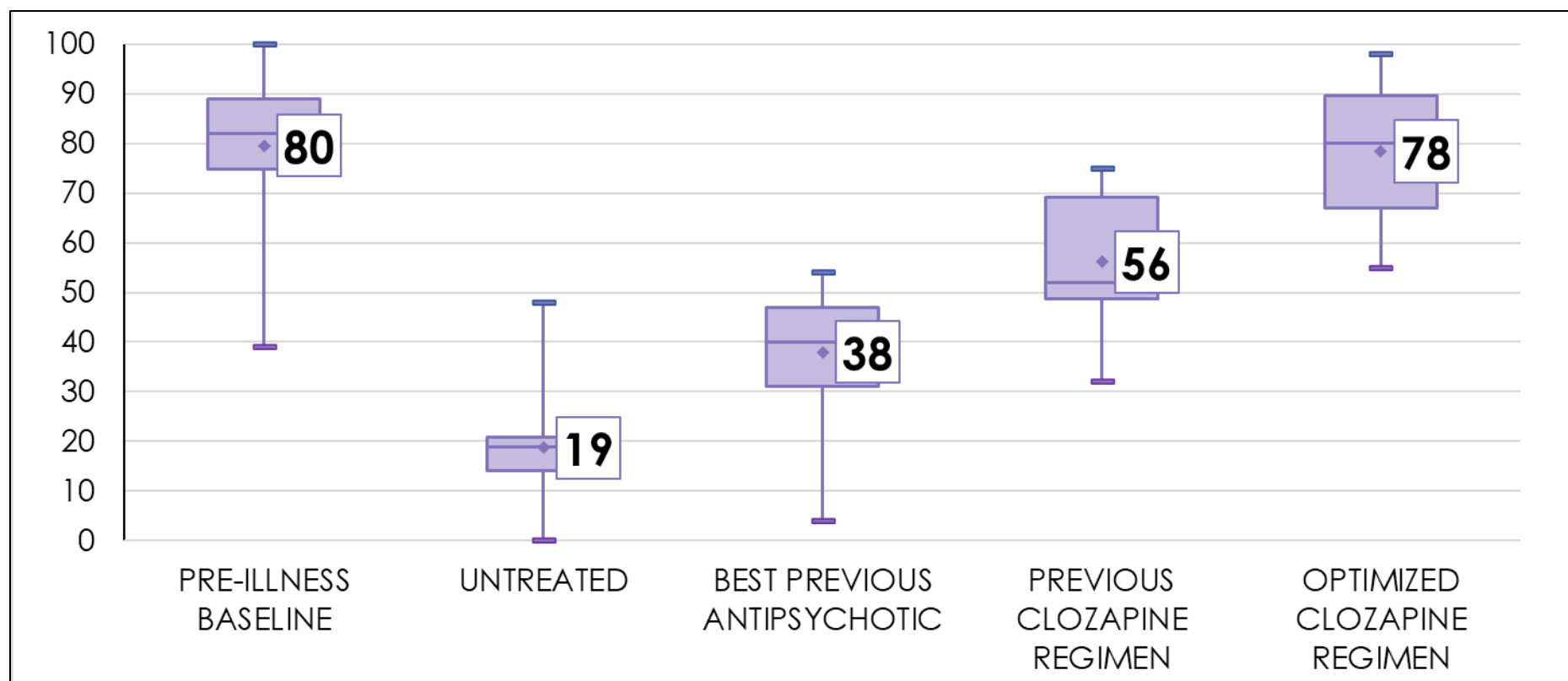


MORE OBSTACLES AND CHALLENGES (N=120)

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

