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- **Rebound psychosis if withdrawn**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

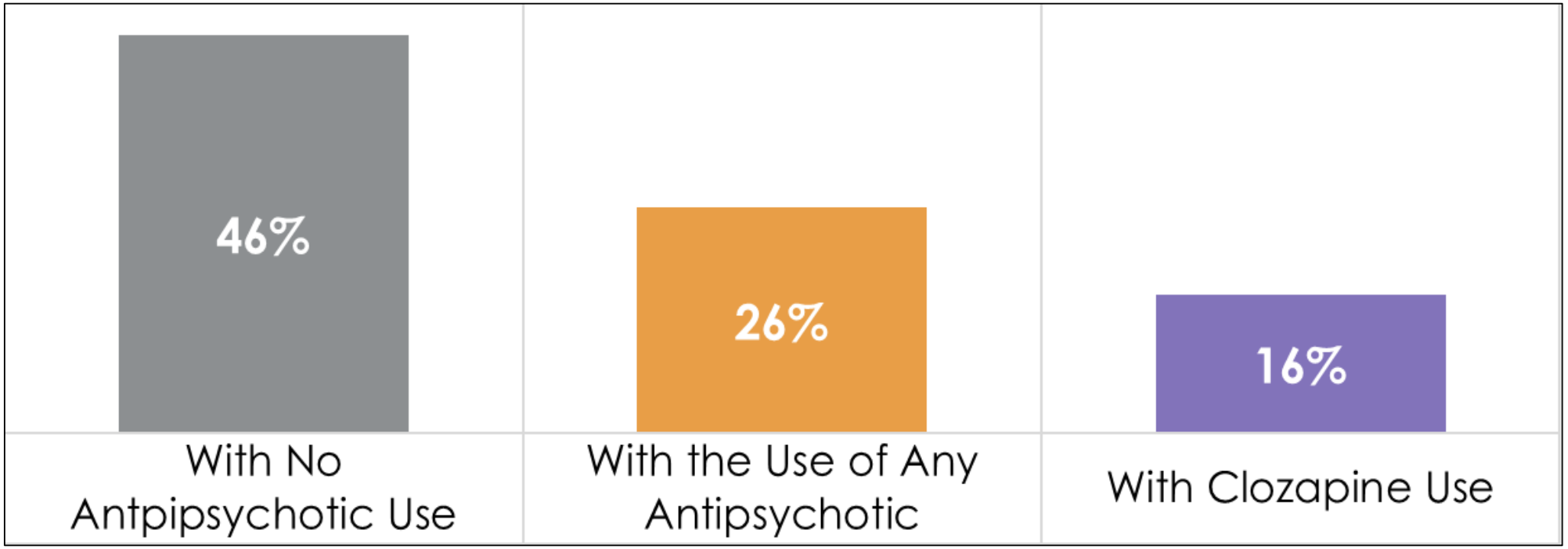
- First year of psychotic illness the risk of death **24 to 89 times** the general population aged 16-30.

- 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 every10,000 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.

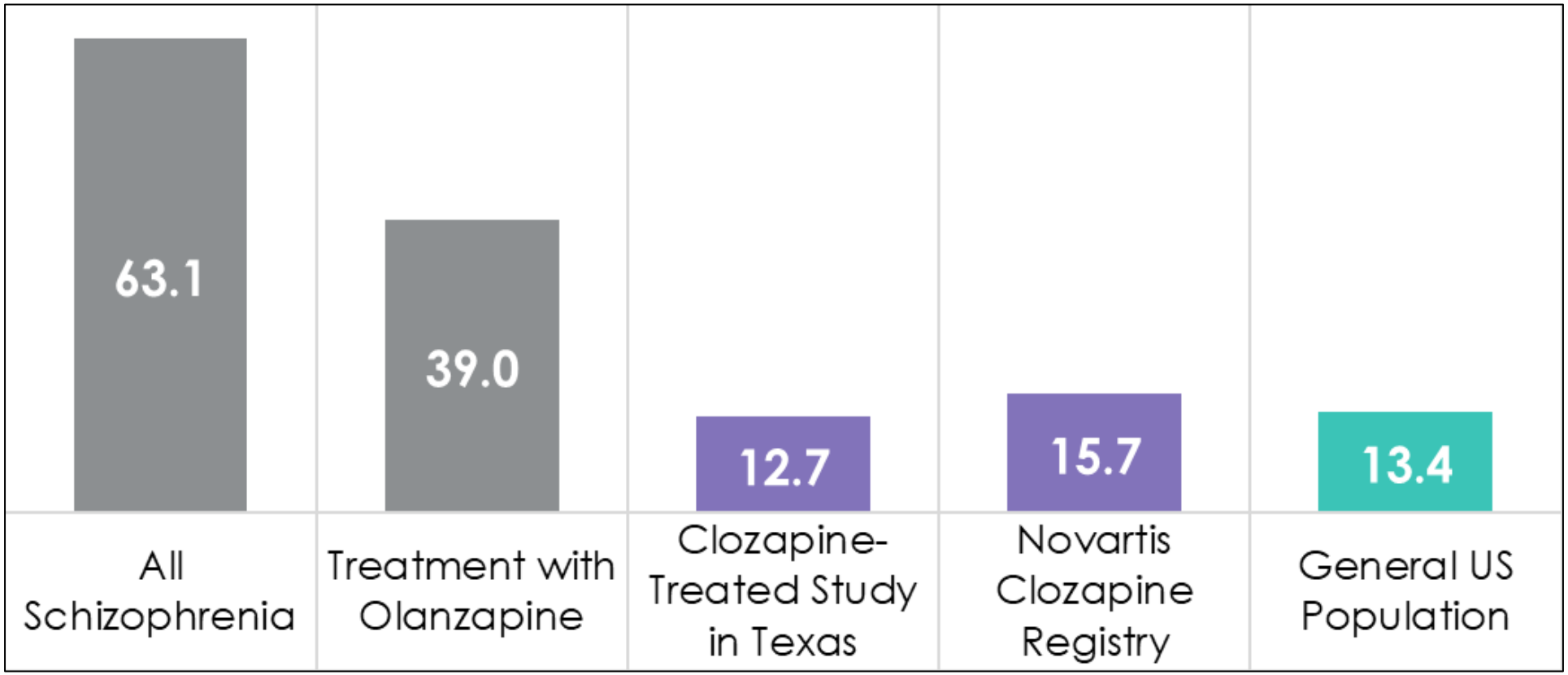
Live Longer on Clozapine



SCHIZOPHRENIA 20-YEAR MORTALITY RATE

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

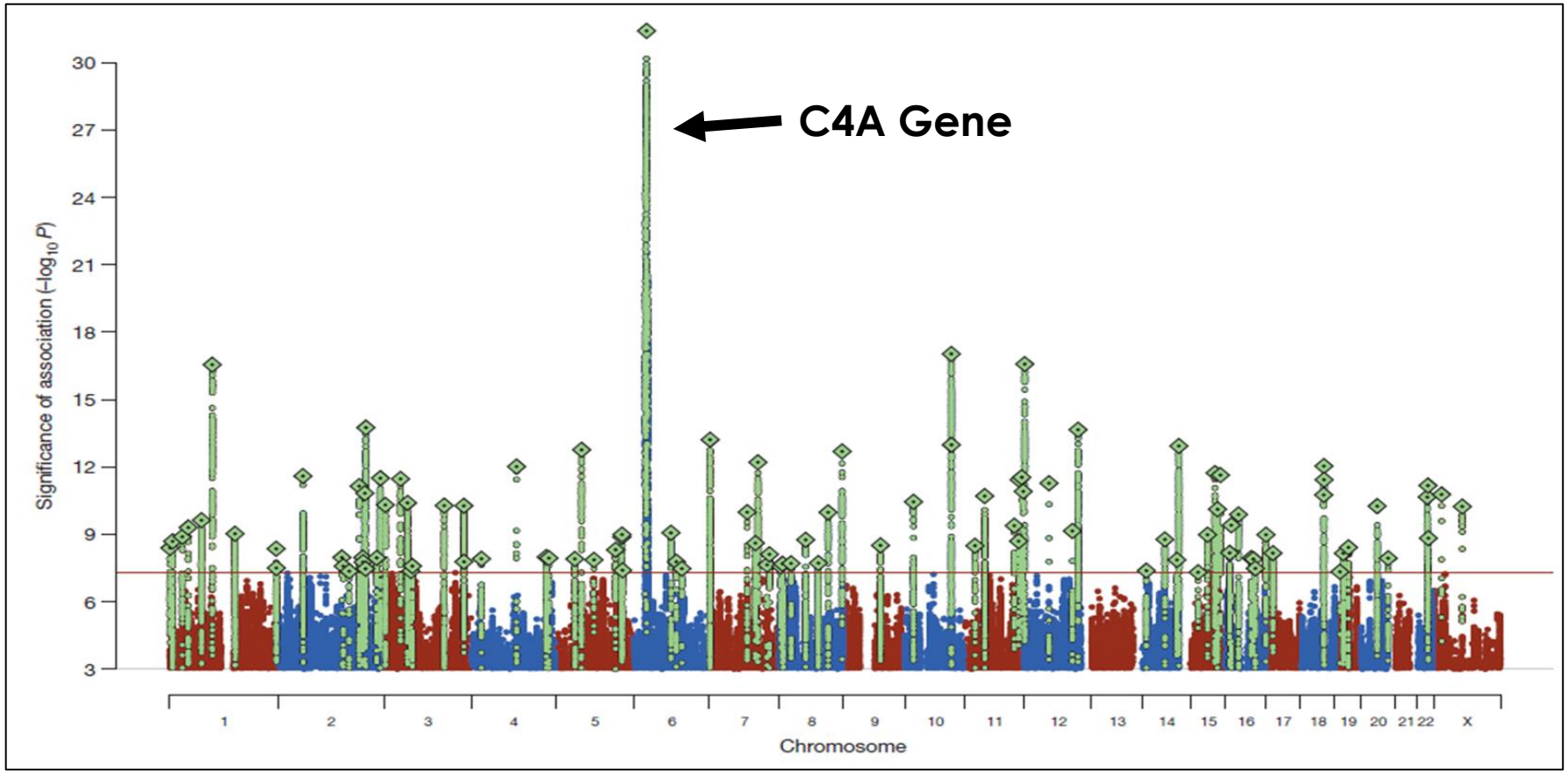
Reduced Suicide Rate



CLOZAPINE REDUCES SUICIDE RATE IN PATIENTS WITH SCHIZOPHRENIA

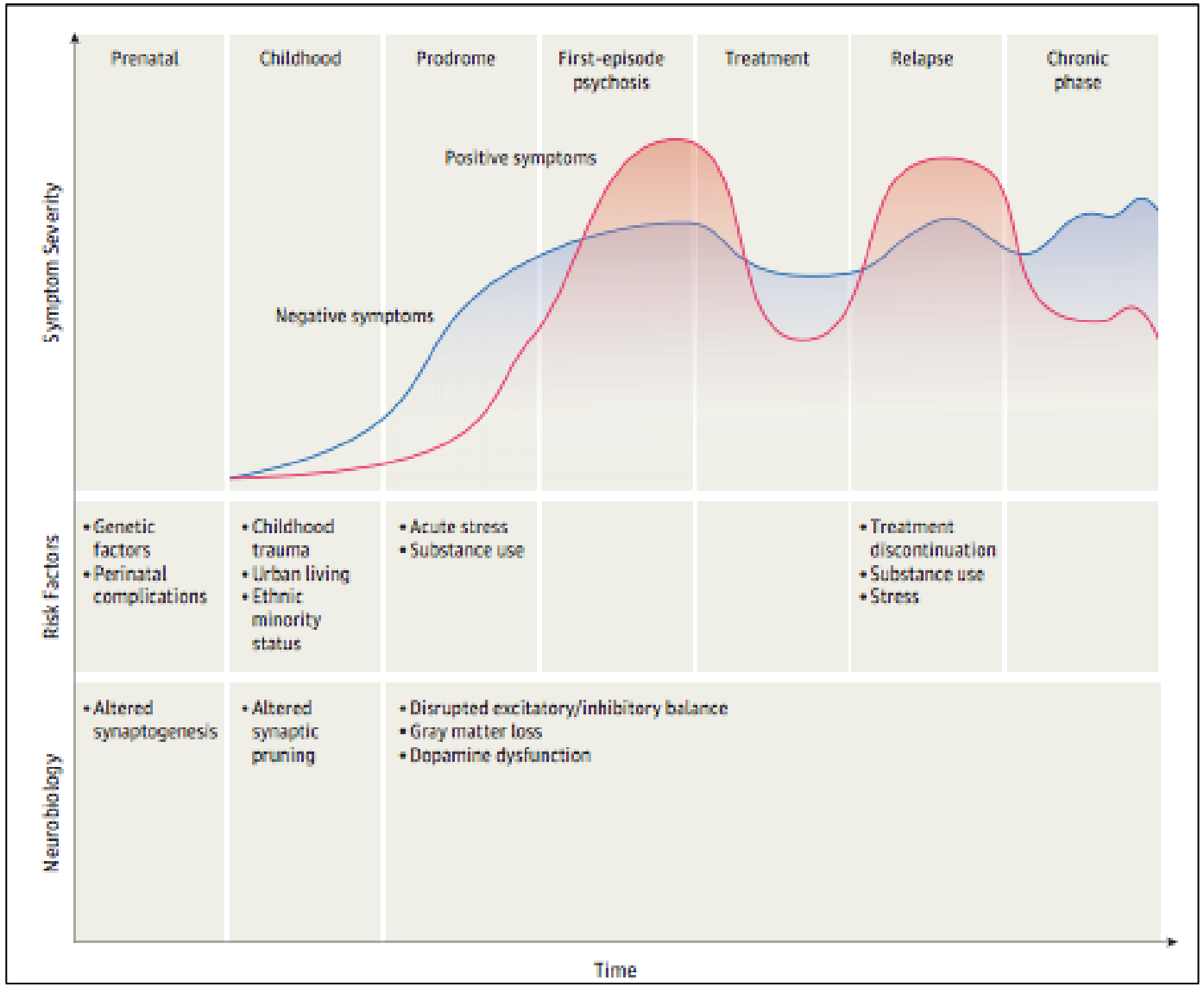
Annual Suicides Per 100,000

Pruning C4A & Schizophrenia



SCHIZOPHRENIA RISK ASSOCIATED WITH 108 GENOMIC REGIONS

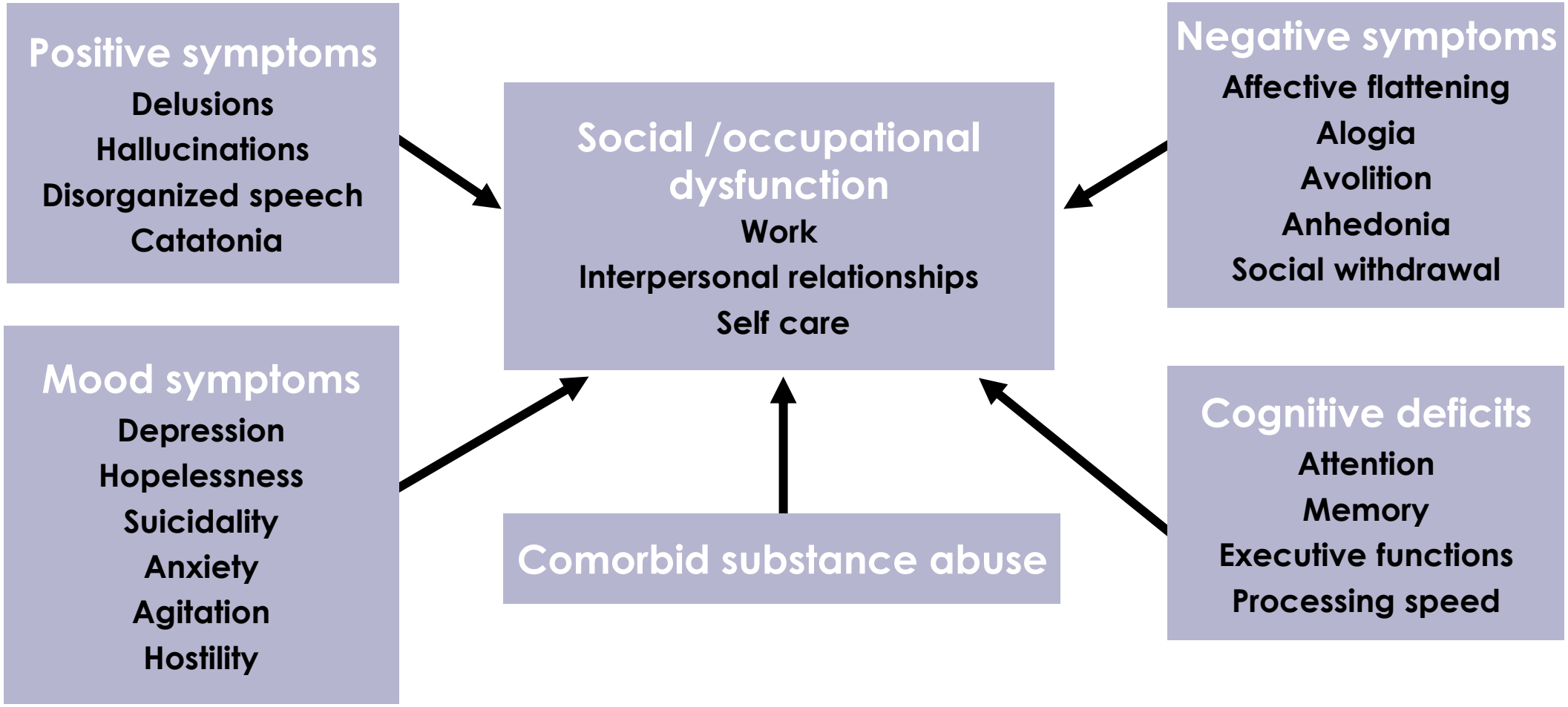
Schizophrenia Working Group of the Psychiatric Genomics Consortium. Nature 2014;511(7510):421–427.



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 **95** 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.

Who is TEAM DANIEL?

Patient Utilization Statistics

52% came to the practice to **initiate** clozapine.

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

48% 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.

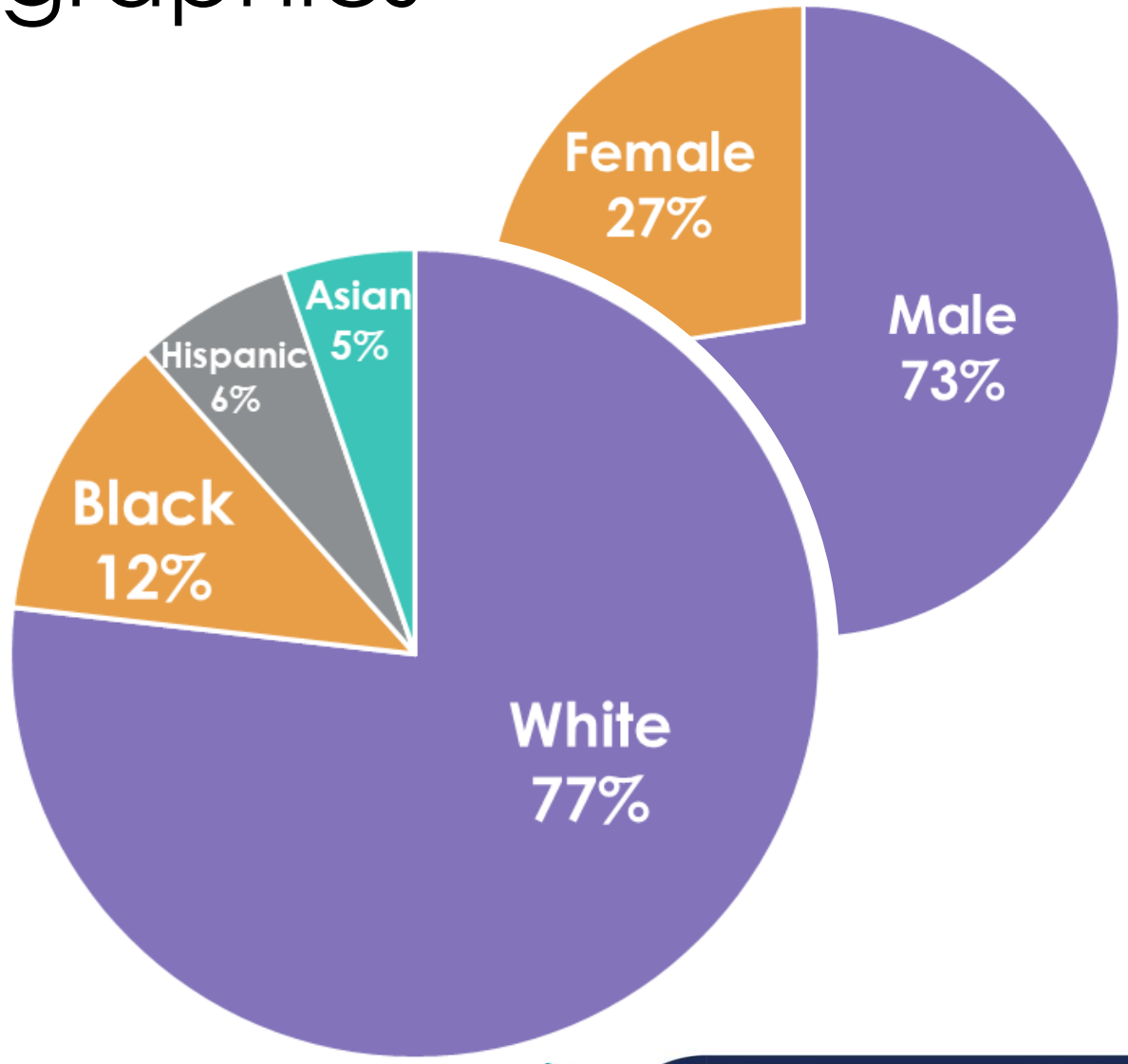
Our Demographics

TEAM DANIEL Profile Statistics

- Average age: **34 years old**
- Youngest: **17**
- Oldest: **74**
- Longest patient on clozapine:
  30 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.

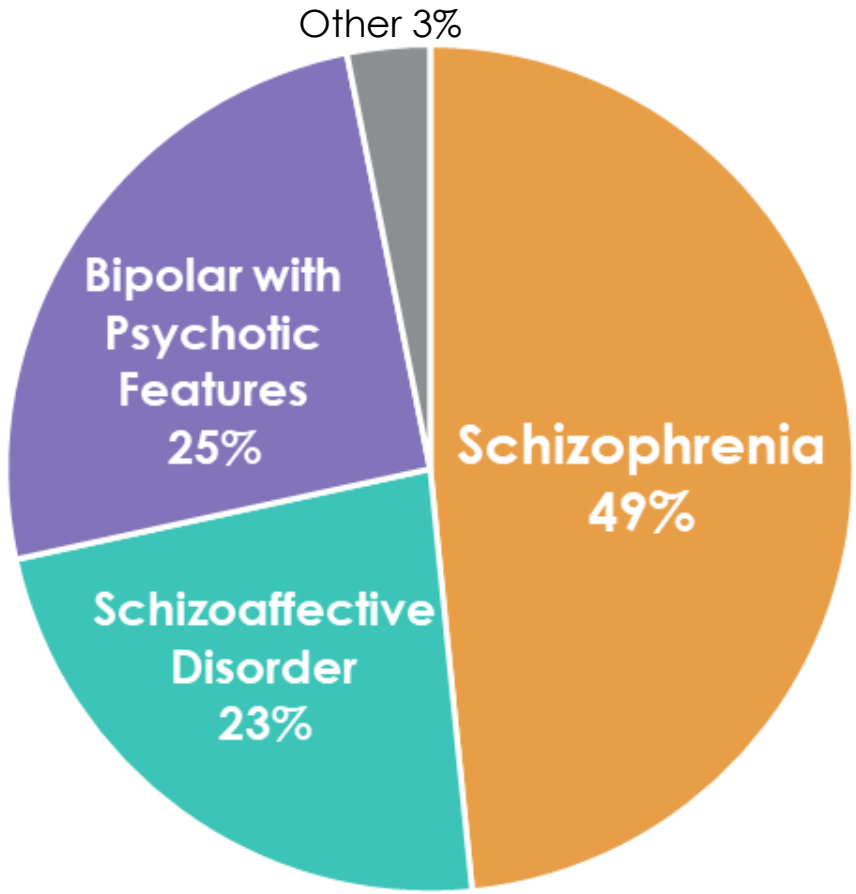


Our Demographics

Compelling Statistics

- **4** of the **95** Team Daniel cohort patients are no longer on clozapine due to their psychiatric condition resolving.
- Two of the 4 received ***clozapine first***!
- **56%** characterized with anosognosia (poor insight).
- **8** 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.



Not Every Success

Not Every Patient is Still With Us…

18 Refused or never started treatment; unable to obtain an AOT.

9 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

12 Lost to follow up or transferred to another practice.

2 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.

Our Goals: Restore

We CAN restore optimal health – body and mind.

Patient has a sense of purpose and self, enabling them to form relationships and be a productive member of their community and society.

Vital individuals with optimal physical functioning.

Pain-free both physically and emotionally enjoying long and fulfilling lives.

The Goal: Meaningful Recovery.

We CAN restore hope – patient and family

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**.

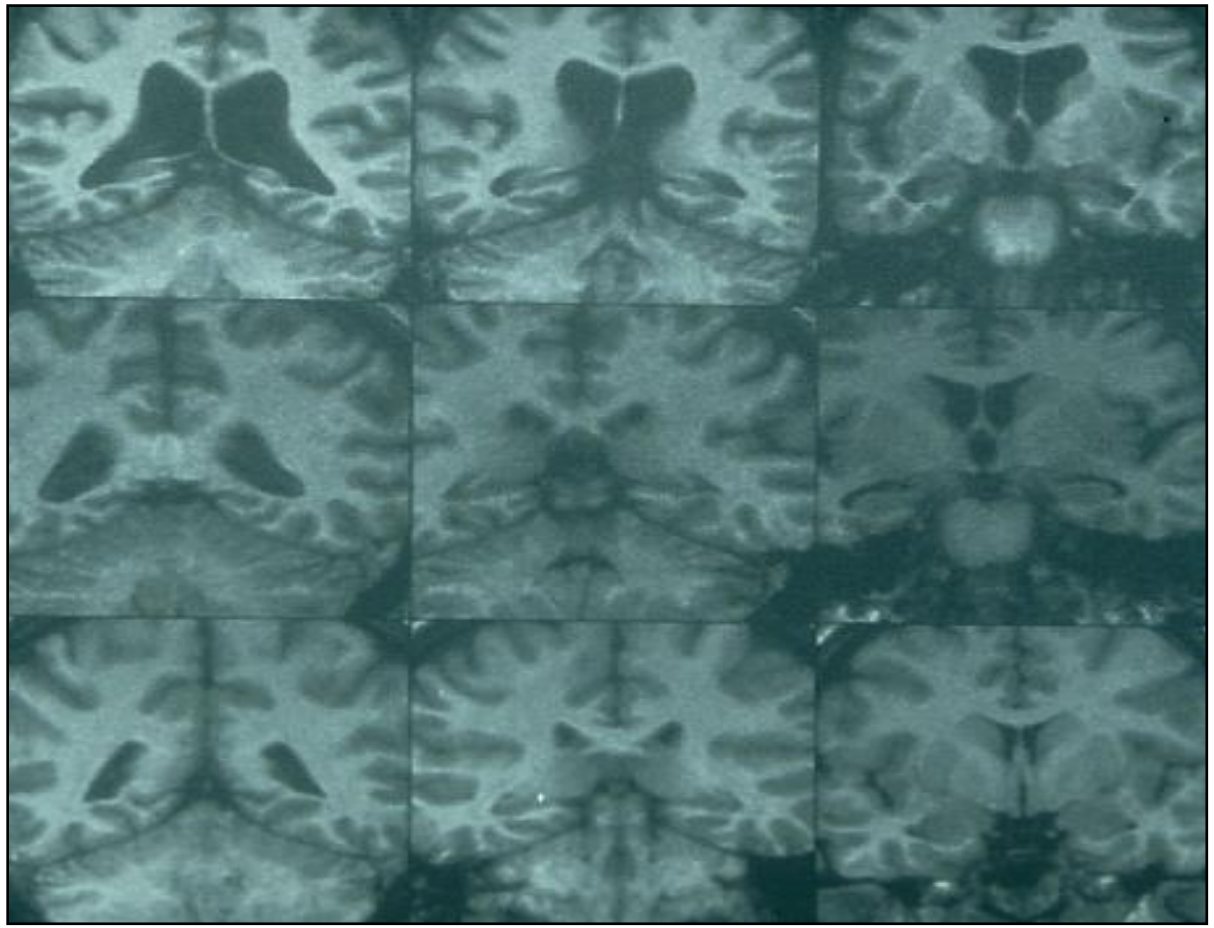
PROGRESSIVE MRI CHANGES OVER THREE RELAPSES IN A MALE WITH SCHIZOPHRENIA

Worsening Progression

After 8 Relapses

After 3 Relapses

First psychotic episode



Nasrallah, HA. personal files

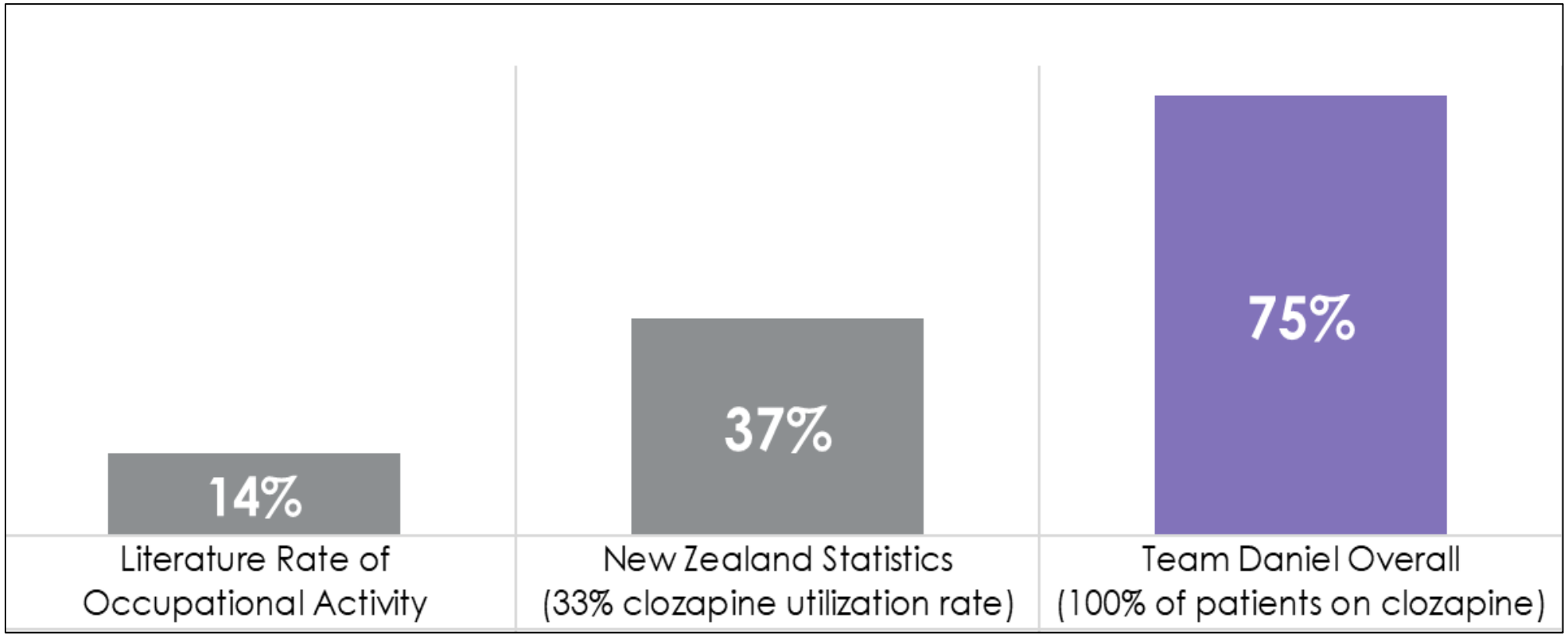
Our Meaningful Recovery

With TEAM DANIEL it means achieving any of the following:

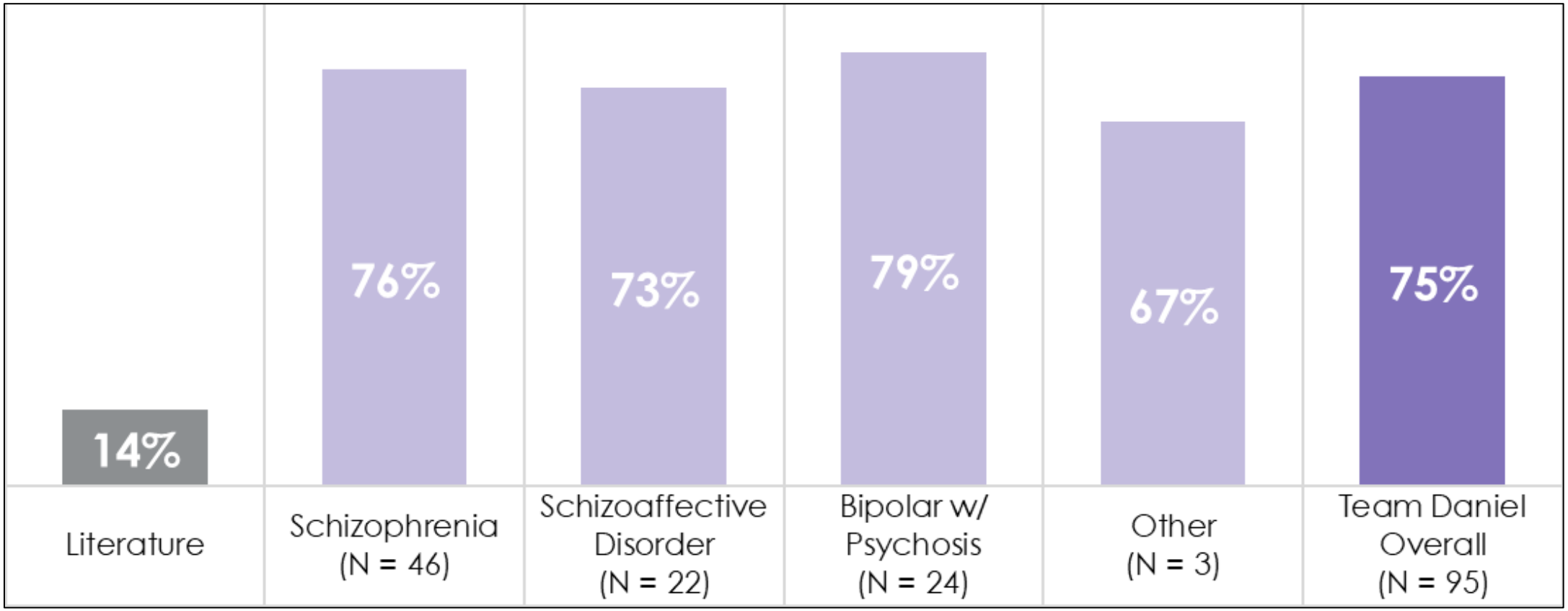
- Employed for 20 hours per week or more.
- Attending school full-time, or part-time with other activities.
- Responsibly maintaining a homemaker and/or parenting role.
- Successfully participating in a vocational rehabilitation program.
- Successfully engaged in consistent volunteer activity for 20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

RATE OF MEANINGFUL RECOVERY

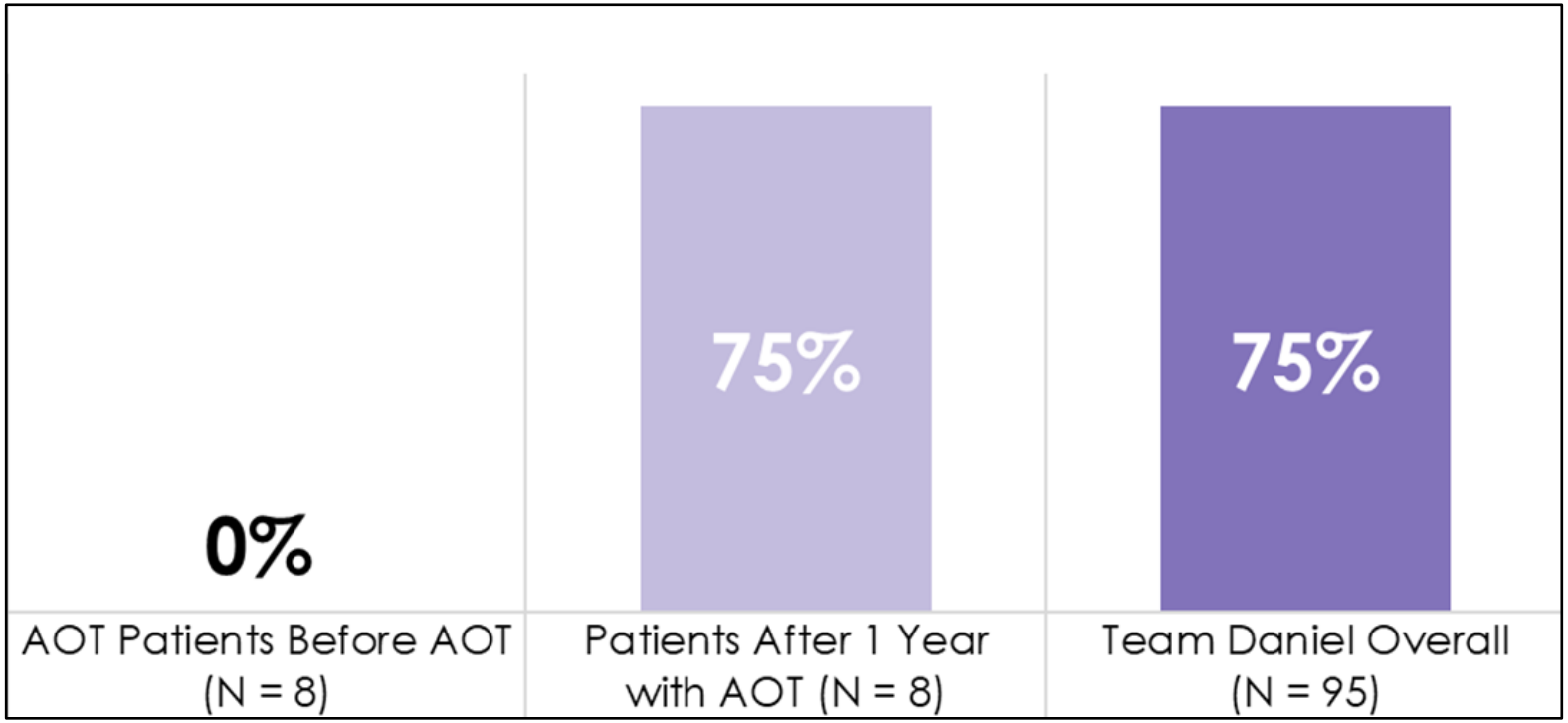
N = 95 Patients on an Optimized Clozapine Regimen



RATE OF MEANINGFUL RECOVERY BY DIAGNOSIS



AOT Saves Lives and Livelihoods

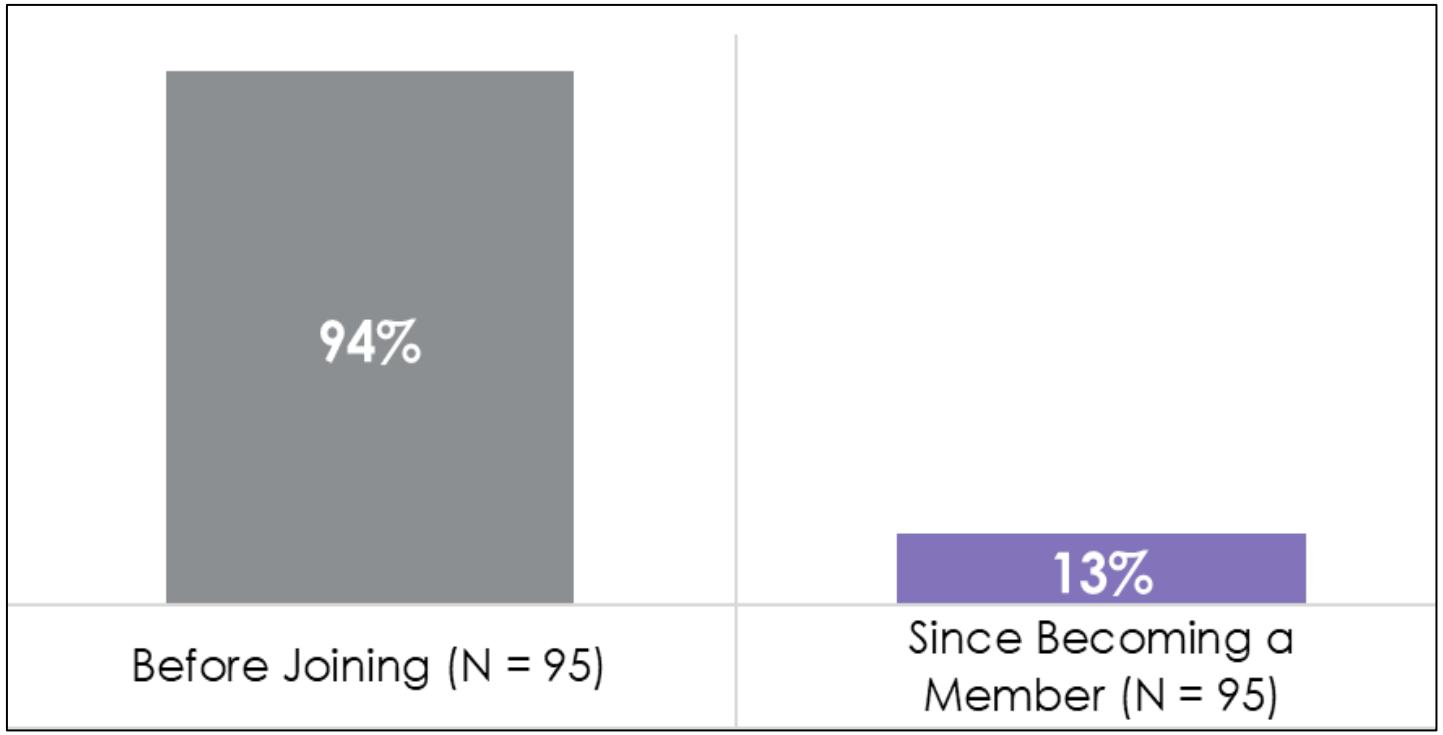


100% Significant Improvement in Quality of Life

No hospitalizations!

MEANINGFUL RECOVERY WITH ASSISTED OUTPATIENT TREATMENT (AOT)

87% Never See Hospital Again



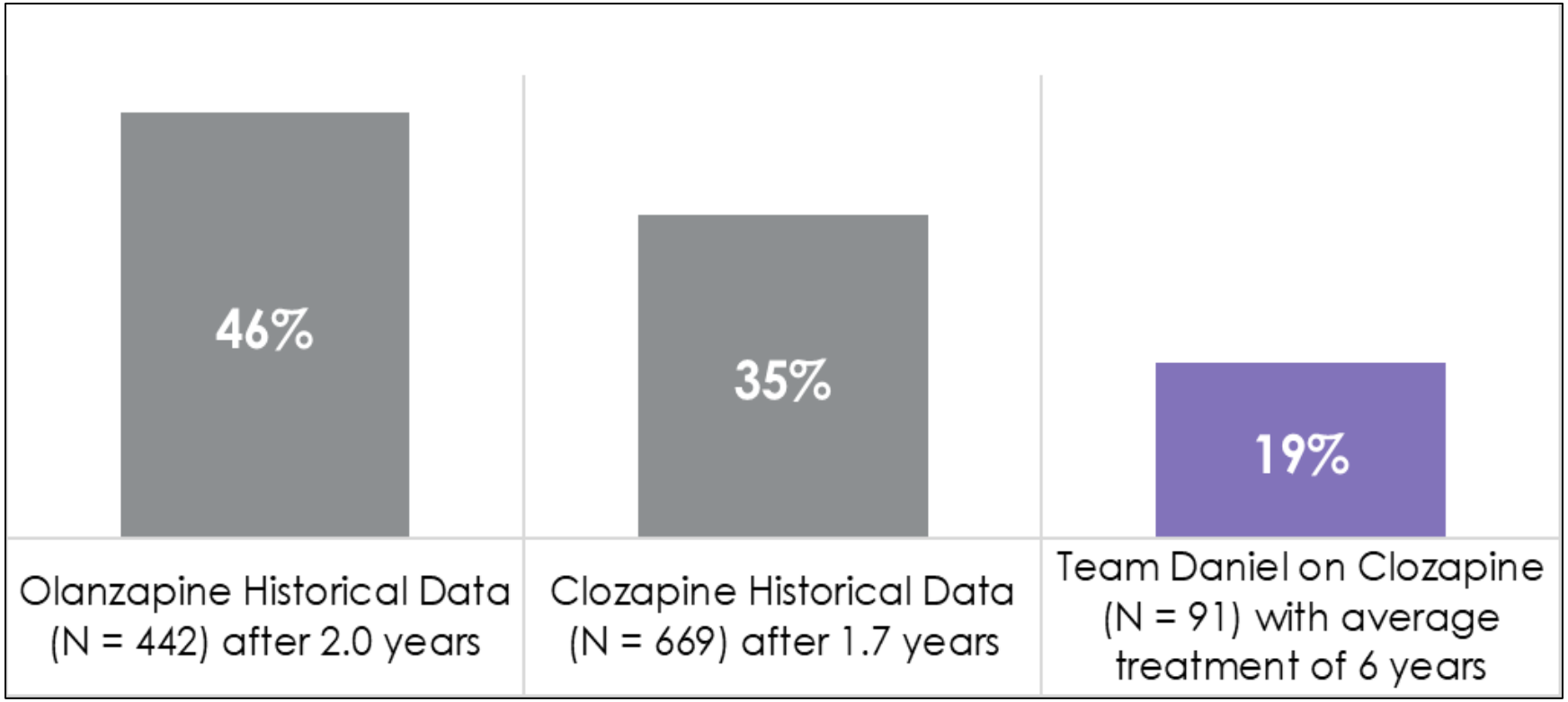
PATIENTS WITH ONE OR MORE HOSPITALIZATIONS

12 Hospitalizations:

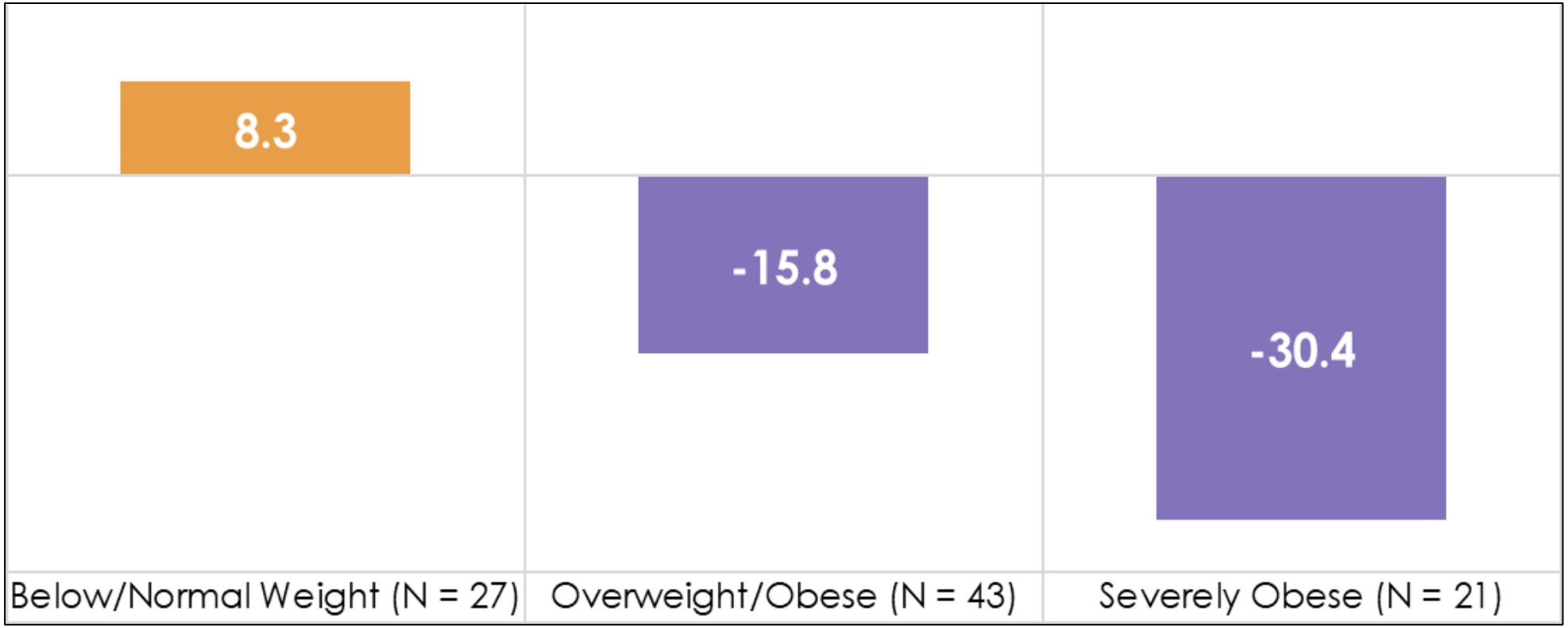
5 for Mental health
1 for Substance Use
4 for Adverse effect:
- **2** Seizures
- **1** Pneumonia
- **1** Lithium toxicity

2 for Medical reasons

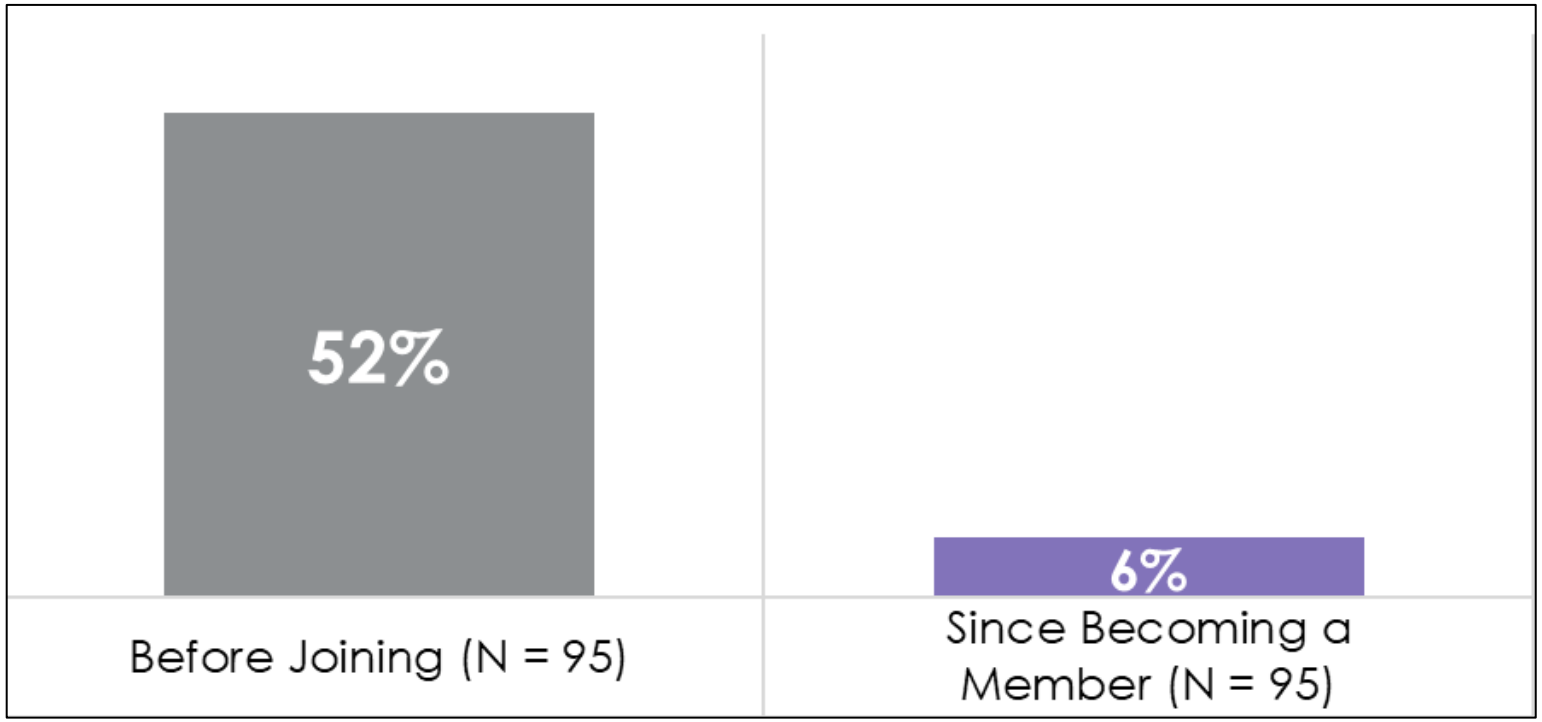
PROPORTION OF PATIENTS WITH MORE THAN 7% INCREASE IN BODY WEIGHT



TEAM DANIEL ON CLOZAPINE AVERAGE WEIGHT CHANGE (LB)



Recovery Rate Unprecedented



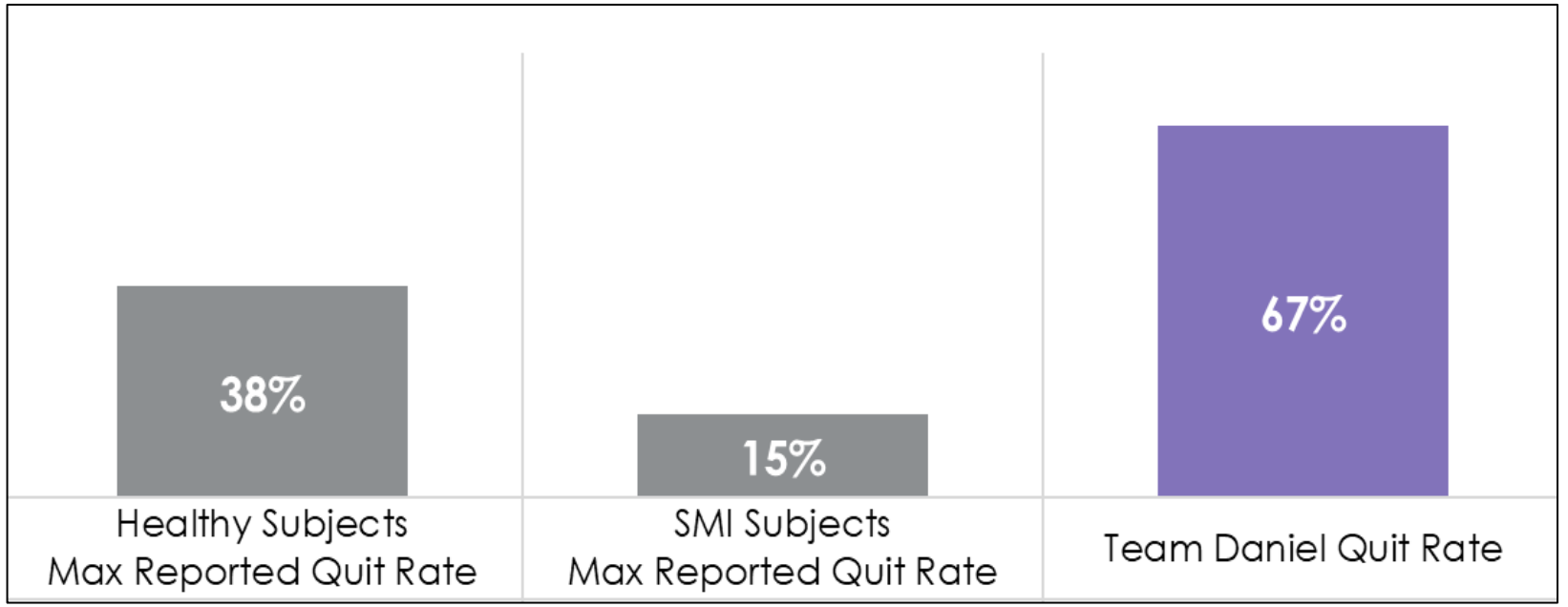
88% Recovery from Substance Use

86% Recovery from Cannabis Use

RATE OF SUBSTANCE USE DISORDER

Most Common: 90% Of Use Was Cannabis

Cessation Rate Beats The Odds



RATE OF TOBACCO CESSATION
(N=39 Team Daniel Smokers)

26 of 39 Smokers Quit

Most used combination therapy:
82% Chantix
49% NRT
64% Bupropion

TEAM DANIEL NOTABLE ADVERSE EVENTS (N=95)*

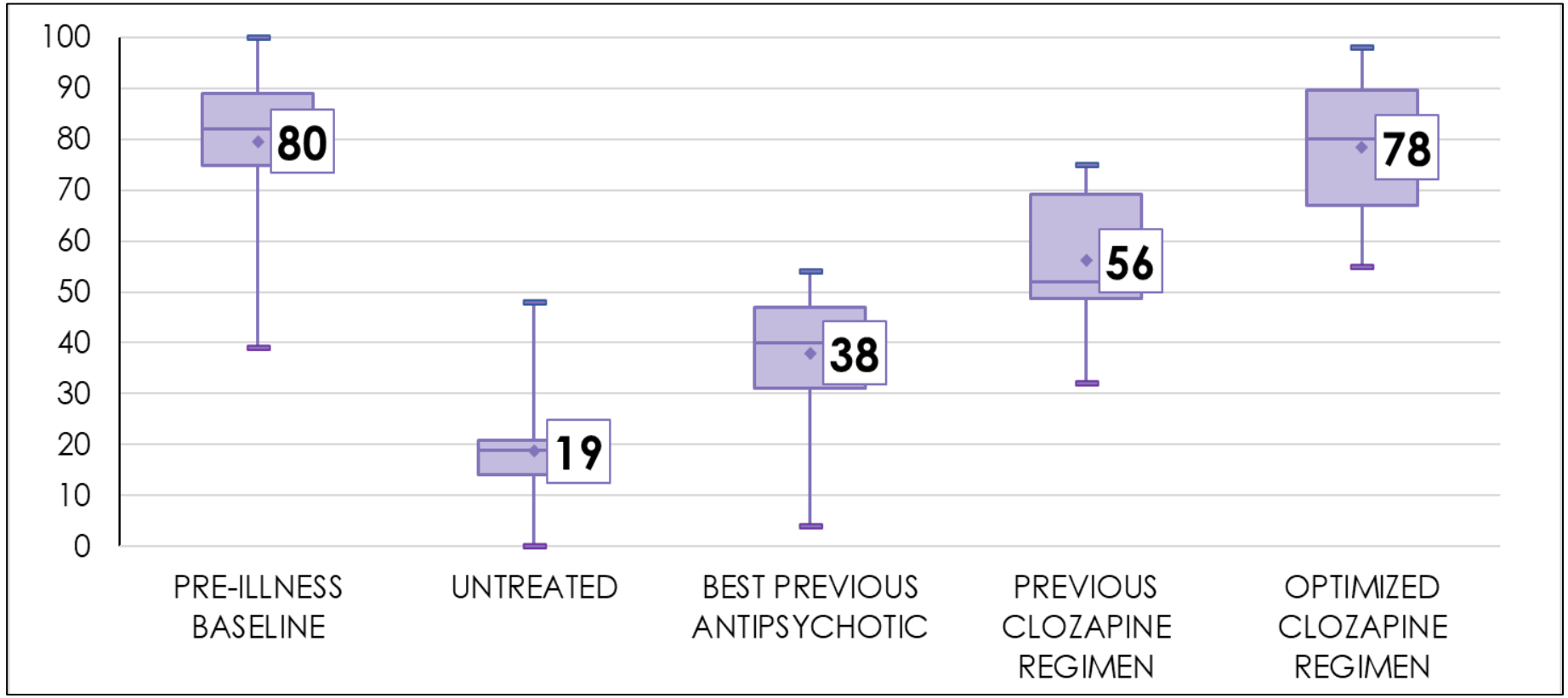
Pneumonia	**17**	**5** due to Covid-19 **2** patients hospitalized High rate of detection
Seizures	**5**	**2** patients of Asian descent **1** abruptly stopped smoking **2** patients hospitalized
Lithium Toxicity	**1**	Resolved with lowering lithium dose The patient was hospitalized
Cardiomyopathy	**1**	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
• 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

OTHER OBSTACLES AND CHALLENGES (N=95)

Neutropenia	**4**	**3** resolved after 1 instance **1** resolved with lithium
Substantial Weight Gain	**8**	**7** cases are tied to poor compliance with weight control medications **1** patient has recently lost over 20 lb
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



TEAM DANIEL Returns to Baseline Functioning & Well-being

GLOBAL ASSESMENT OF FUNCTIONING SCORES

Preliminary Data (N=14)