Achieving Goals

Critical first step: know the sufferer and hopefully engage family.

Often patients are in a lot of pain - no barriers - hugs help.

Be an active cheerleader and be a friend.

Use Xavier Amador's **LEAP** approach for patients with anosognosia (unawareness of Illness):
Listen – **E**mpathize – **A**gree – **P**artner

Engage the patient in every way possible, using AOT if necessary.

Ensure the patient feels safe and accepted; we have few boundaries.

Achieving Goals

Acknowledge the road to recovery will always have a few detours.

This helps everyone relax and know that even if they "screw up" you will never abandon them.

Always be available and make sure patient has information.

All patients and families get our cell phone #'s and e-mail.

Compassion and Availability really goes a long way.

Everyone leaves our office with the treatment note. We share also with the family.

Optimism is essential: Your belief combats learned hopelessness.

Clozapine Routine Monitoring

Therapeutic Drug Monitoring (TDM) is critical!

Blood serum levels of clozapine and norclozapine to guide dosing.

Thorough physical with a body mass index (BMI) and orthostatic blood pressures.

Baseline echo, EKG, HSCRP, troponin (periodically follow up), serum BNPs in patients with tachycardia (elevated heart rate).

Baseline and follow CBC with absolute neutrophil counts, chem panels including renal and liver function test, lipids, thyroid function, Glyco-hgb, and urine toxicology, immune/infection workup.

Dual diagnosis: urine and serum tox screens and cotinine levels every visit.

Avoid Predictable Side Effects

Weight Gain: Add diet and Metformin early; consider SGLT2 inhibitors.

High Triglycerides: Statins, omega 3 and fibrates (fenofibrate).

Metabolic Syndrome and Diabetes: Metformin, SGLT2 inhibitors, high-dose ranitidine or famotidine, plant-based diet and exercise.

Sinus Tachycardia: Add Beta Blocker (Propranolol) or in those with pulmonary disease Metoprolol or atenolol (if anxiety is already well controlled).

Seizure Prevention: Lamotrigine, Gabapentin, Topiramate or Valproate (if violent).

Drooling: Add .06% Ipratropium Nasal Spray, or 0.1% atropine eye drops under the tongue. Consider Glycopyrrolate and botox. Elevate the head of the bed.

Avoid Predictable Side Effects

Constipation: Hydrate! Cathartics (Dulcolax and Senna), stool softeners (Colace), laxatives (MOM, lactulose, Miralax), Linaclotide (Linzess), and Acarbose.

- Remedy the problem: clozapine causes a slow transit time!

Neutropenia:

- Draw blood in the afternoon and exercise beforehand.
- Consider adding lithium and granulocyte colony stimulating factor (CSF).
- Recognize Benign Ethnic Neutropenia (BEN) and confirm with genetic testing.

Nighttime Urination: Behavior changes, DDAVP or Myrbetriq.

Hypotension: Florinef (fludrocortisone), midodrine in severe cases.

Nausea and Vomiting: Early use of ondansetron (Zofran).

Enhancing Clozapine

Cognitive enhancement: donepezil, bupropion, memantine, modafinil, armodafinil, amantadine, and consider fluvoxamine.

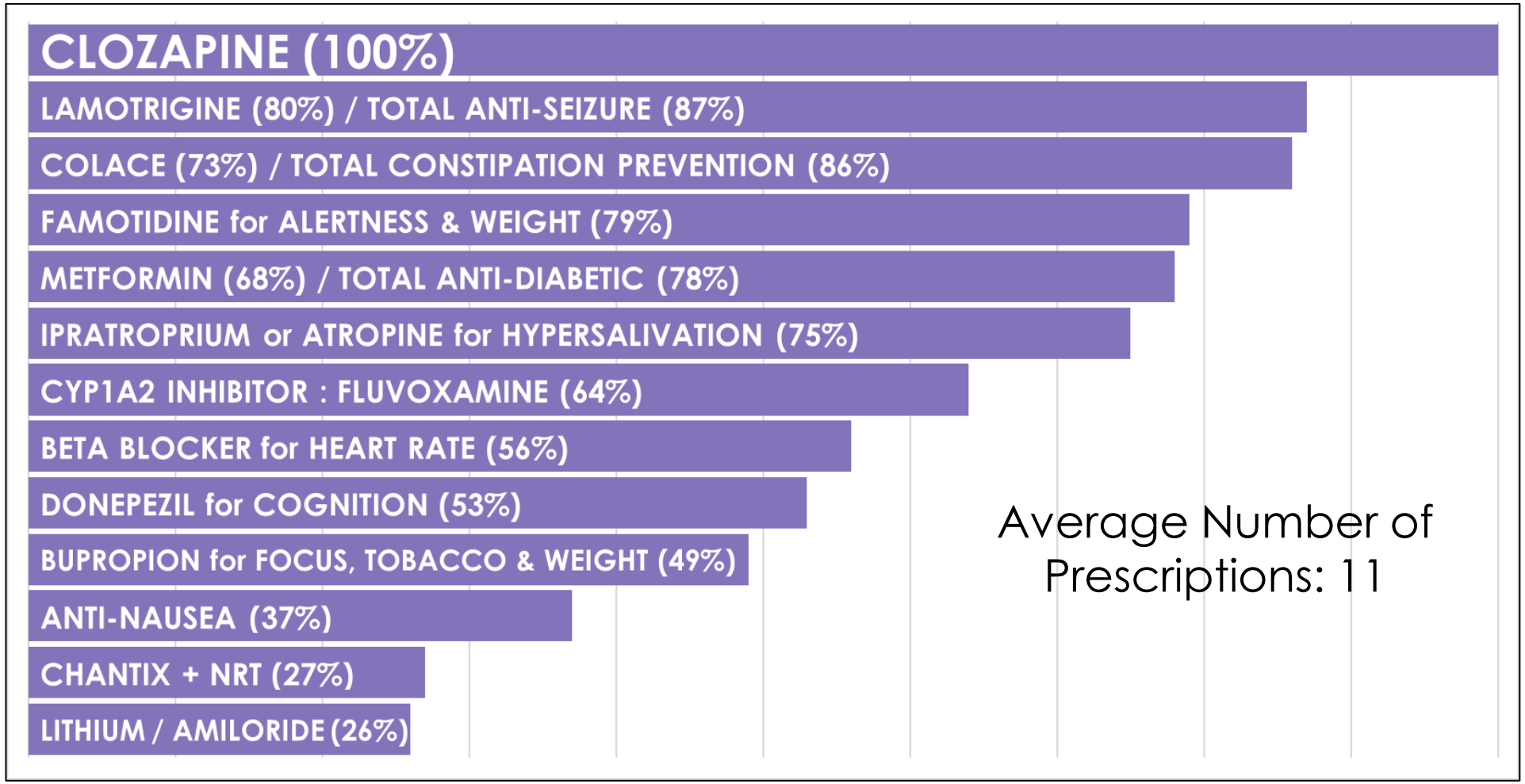
- Presently investigating pitolisant (Wakix).

Concomitant mood disorder and OCD: SSRI (i.e. escitalopram)and cognitive behavioral therapy(CBT), carefully consider fluvoxamine or buproprion.

Support: Socialization skills, educational, vocational, psychosis-informed CBT, dialectical behavioral therapy (DBT), family therapy, speech therapy and cognitive enhancement programs.

Treat co-occurring addictions

TEAM DANIEL OPITMIZED REGIMEN (N=95)



Optimizing the Regimen

Other Common Medications:

- Proton Pump Inhibitor for acid reflux (18%)
- Adjunctive Abilify™ (16%)
- Desmopressin for nocturnal enuresis (16%)
- Statin with CoQ10 for elevated lipids (16%)
- Linzess™ for recalcitrant constipation (14%)
- Glycopyrrolate for over-salivation (9%)
- Fludrocortisone for orthostatic hypotension (4%)
- Supplements: CoQ10, B12, Vitamin D3, Fish Oil, melatonin, caffeine

Medications NOT Used by TEAM DANIEL Patients

- Stimulants / ADHD medications
- Depakote
- Cogentin
- Multiple antipsychotics
- Benzodiazepines

Exercise and Engagement

Every Saturday morning, we have our willing patients and families come to our house for a run and seasonally swim.

The House is magic in fostering acceptance, engagement, and trust. It has taken the therapeutic relationship to another level.

Normalization, socialization, and befriending in a non-medical environment value cannot be overestimated.

SMI is a team sport.

With COVID we keep everyone engaged via two zoom sessions:

- A family/caregiver zoom led by physicians (Dr. Laitman and Dr. Mandel).
- A zoom for patients led by Daniel Laitman (TEAM DANIEL'S inspiration).

The Diet: Drink

NEVER drink your calories
NO soda NO juice NO alcohol

Drink 3 liters of water or coffee daily
2-4 cups coffee to suppress appetite

Milk: Almond or Skim

Sweeteners: Stevia or Splenda

The Diet: Eat

Eat 3 meals a day

Avoid all simple processed carbohydrates:

- NO cookies, candy, chips, dips, cakes, ice cream, donuts
- Minimize bread, pasta (whole grain only)and rice (small portion brown rice only)

BREAKFAST

High fiber cereal *or*
Eggs, (Veg omelet) *or*
Oatmeal with raisins

Coffee *or* tea

Milks: Almond *or* Skim
Sweeteners: Stevia, Splenda

LUNCH

Non tropical fruit
Blueberries, strawberries, blackberries, apples, plums or pears.
Greek yogurt *100-160cal*

SNACK

Unsalted nuts *or* fruit
Blueberries, strawberries, blackberries, apples, plums or pears.

DINNER

Garden salad *with only vegetables & a light low salt dressing spritzed on.*

Vegetable *like broccoli, brussel sprouts, string beans, spinach, or cauliflower.*

Protein *6-8 ounce of fish, poultry, pork, tofu, setain. or a legume : lentils, chick peas etc.*

Non tropical fruit

Exercise Benefits Meta-Analysis

In 29 studies, 1,109 patients statistically significant improvement in:

- Total symptom severity
- Positive symptoms
- Negative symptoms
- General psychopathology
- Quality of life
- Global functioning
- Depressive symptoms

Clozapine Initiation

Slow titration

Get to therapeutic levels

See the patient every week

Shift majority of dose to bedtime dosing

Benefits of Ultra-Slow Titration

Identify lowest effective dose:

Team Daniel's lower quartile (bottom 25%) for daily clozapine dose:

- Schizophrenia spectrum patients: 25mg to 200mg
- Bipolar patients: 12.5.g to 62.5mg

Minimize and proactively treat predictable early side effects:

Sedation
Constipation
Weight gain
Orthostasis (dizziness & low blood pressure)
Tachycardia (rapid heart rate)
Sialorrhea (over-salivation)

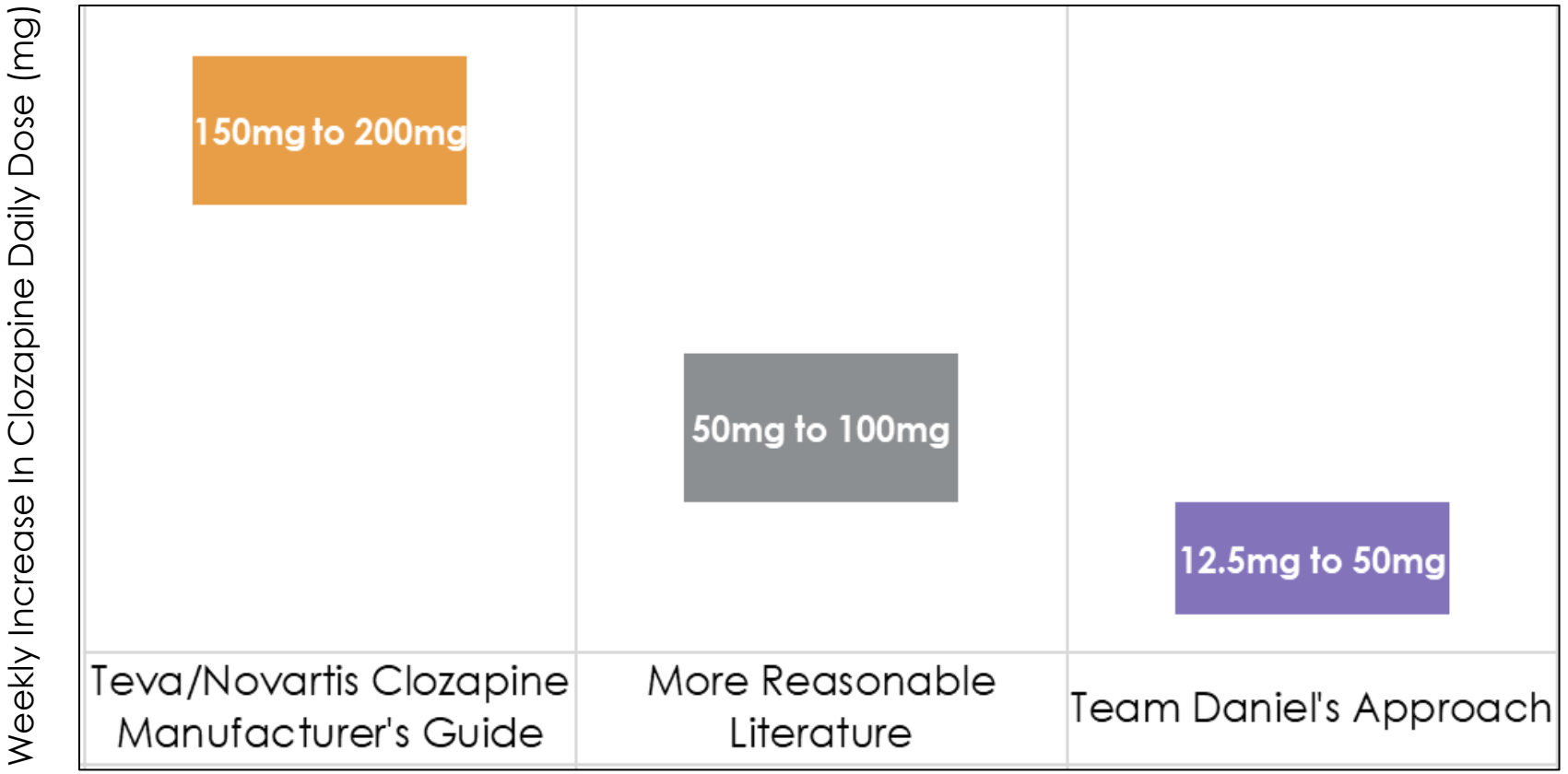
Reduced risk of cardiomyopathy and myocarditis.

Significantly more likely to have success and compliance.

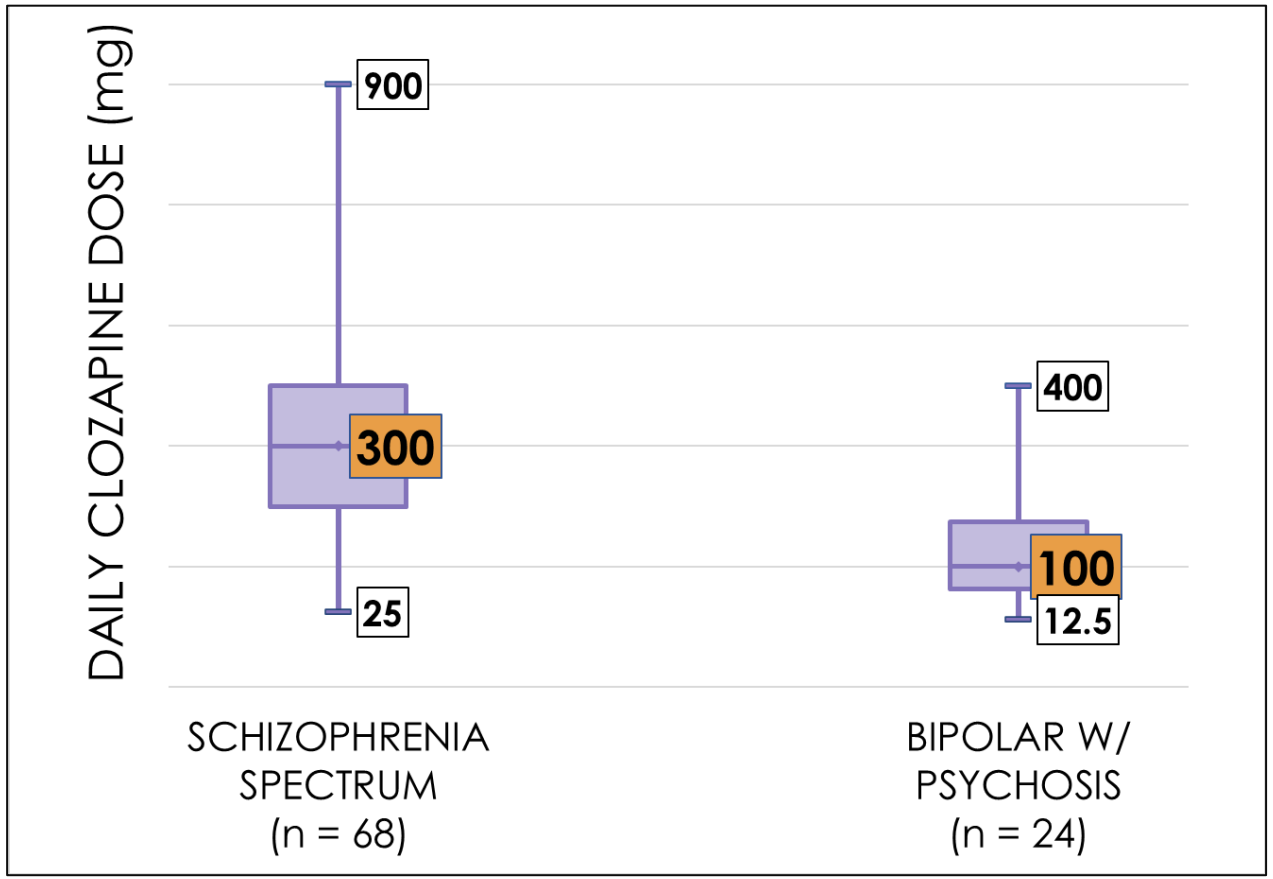
Expect a long cross-taper from the previous antipsychotic.

CLOZAPINE TITRATION SCHEDULE

Total Daily Dose (mg) Increases Per Week



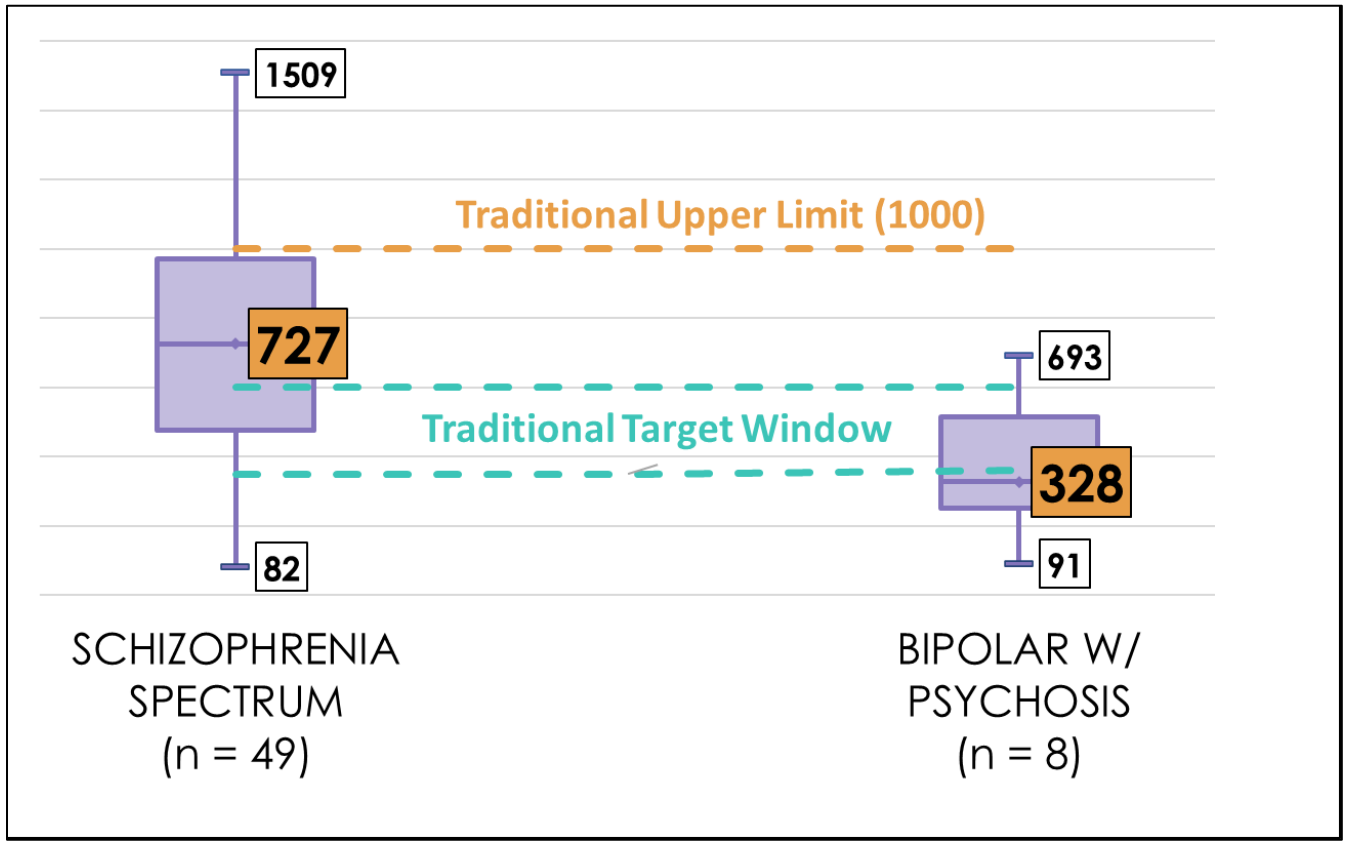
No Standard Dose



OPTIMIZED CLOZAPINE DAILY DOSE
Total mg per day (N=91)

Dosage Varies Widely:
Use therapeutic drug monitoring (TDM) to target the dose.

Pushing Traditional Boundaries



TEAM DANIEL CLOZAPINE SERUM LEVEL
ng/mL (N=57)

All TEAM DANIEL patients are on anti-seizure medications except at very low levels.

Many patients (64%) are on fluvoxamine to increase clozapine and reduce norclozapine.

Clozapine Metabolism via CYP1A2

"CYP1A2" refers to an enzyme in the body that breaks down clozapine.

Cigarettes: dramatically lowers clozapine

- Stopping dramatically raises levels
- Hydrocarbons & coal tars stimulate metabolism
- Nicotine has no affect

Caffeine: increases the levels - Keep it steady!

Be aware of drug interactions!

- Quinolones increase levels

Inflammation dramatically increases levels.

Clozapine & Fluvoxamine with TDM

Clozapine metabolizes into clozapine and norclozapine with CYP1A2.

Fluvoxamine: Blocks the CYP1A2 enzyme to increase ratio of clozapine/norclozapine for better efficacy and less side effects.

- Baseline ratio of clozapine/norclozapine: about 1.5 After adding fluvoxamine: 2.6

Benefits: Improve sedation, sleep time, weight, sialorrhea (over-salivation), positive and negative symptoms.

Risks: Higher levels of clozapine can cause seizures. ALL patients on the fluvoxamine-clozapine combo are maintained on Lamotrigine or other seizure prophylaxis.

CAUTION: Fluvoxamine must be added VERY slowly with TDM at each increase!

The Clozapine Clinic

The General Model:

- Psychiatric MD or NP adept in medicine.
- Full time internist, or neurologist adept in clozapine.
- Psychologist or psychiatric social worker for P-CBT.
- Social workers for case management and housing and frequent legal interface.
- Peer specialist who is on clozapine.
- Work and social opportunities, befriending, normalizing: **create a community!**

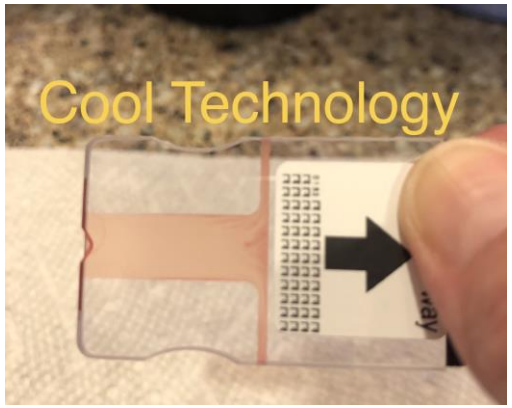
The Clozapine Clinic

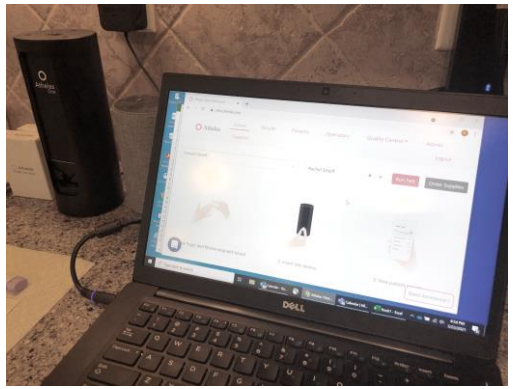
The General Model:

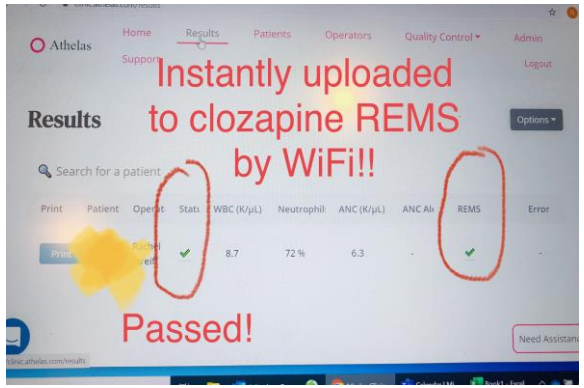
- Exercise training and nutrition support.
- Family support and education – the LEAP method.
- CBT-P, DBT, cognitive enhancement therapy and job training.
- Full supported therapeutic housing.
- Substance abuse intervention for cigarettes, drugs and alcohol.
- Pet therapy (dogs do matter).
- Full biopsychosocial model: **The Goal is Meaningful Recovery.**

A Game Changer

Finger Prick Testing - Real Photos from a Very Excited Patient!







Athelas

TEAM DANIEL©

TEAM DANIEL Families Are Saying…

"We were told to grieve, and that our child would never return to their former self - those doctors were wrong."

"Other than sleeping more hours than the average person, our child is recovered, perhaps even better than before the illness."

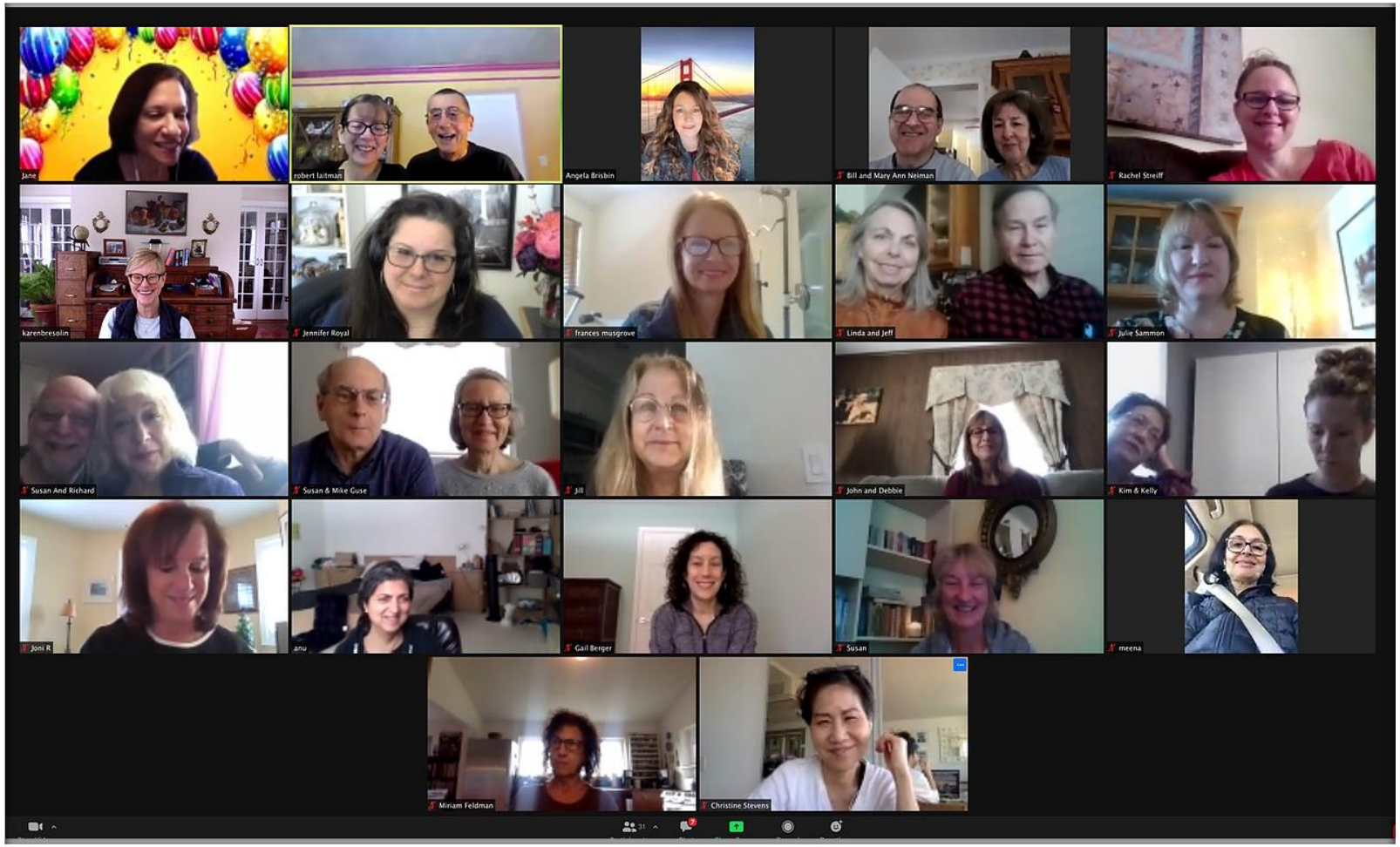
"Clozapine quieted my mind instead of deadening it."

"Kids on clozapine look normal and act normal."

"Clozapine turned the light back on in their eyes…"

"The Awakening Phenomenon" has been well-documented in observational studies of clozapine in patients with schizophrenia. Dr. Stephen Stahl called it "***the restoration of lost souls to near normal existence***"

Zoom with TEAM DANIEL



Who does Clozapine like TEAM DANIEL?

Inpatient, Transitional and IOP Program
New Canaan, CT

Clozapine House Residential Program
Prescott, AZ

Inpatient Clozapine Program
Baltimore, MD

Harsh Realities

Cerebral: A serious brain disease.

Common: 1.1% schizophrenia/2.2% severe bipolar of population.

Cognitive: Impairment is a central problem.

Costly: 2% of GNP, nearly $340 Billion in direct and indirect costs.

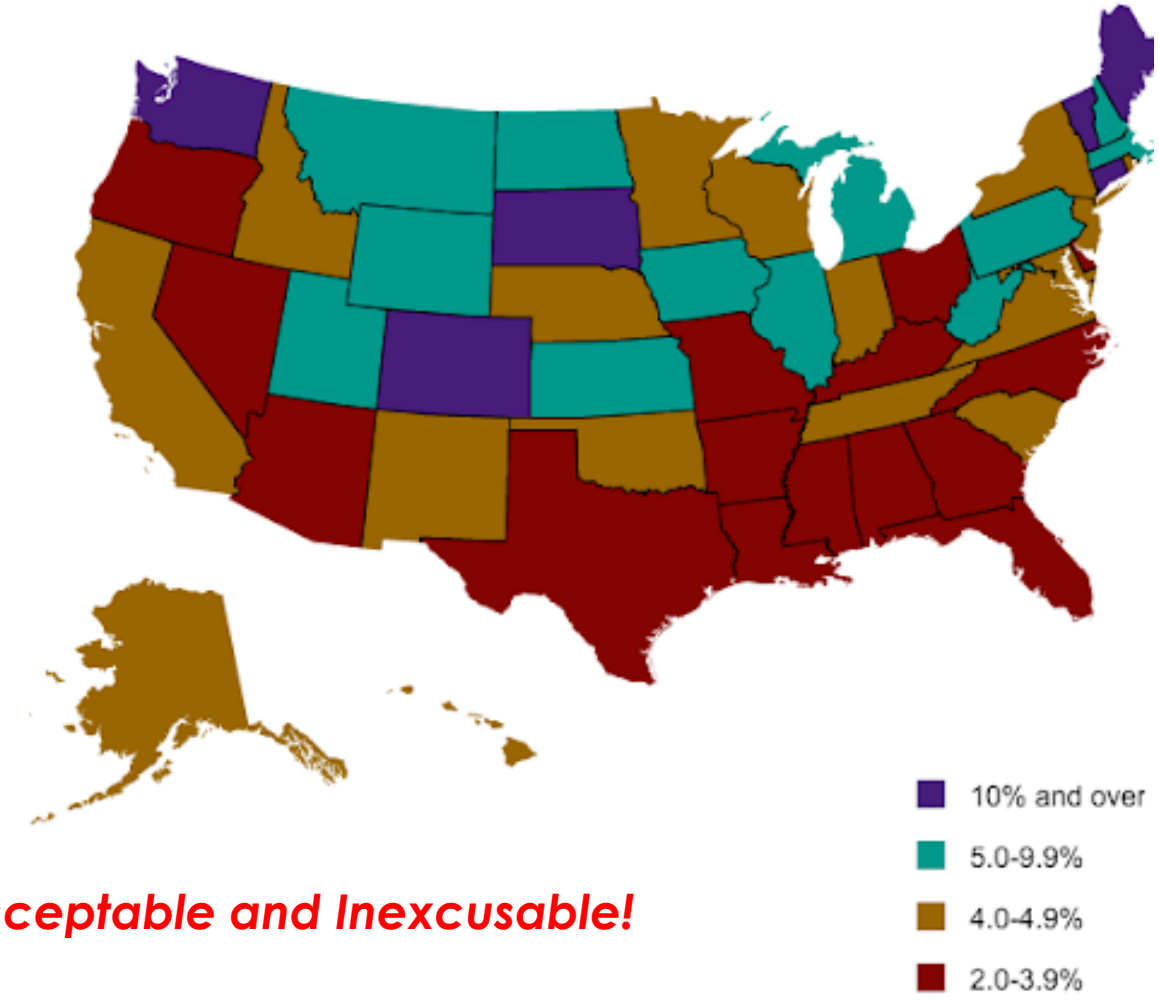
Chronic: Lifelong morbidity and increased mortality.

Crippling: One of 10 leading causes of disability in world (WHO).

Circuitry Disorder: Neuro-circuitry due to a combination of genetic and environmental factors.

Utilization Rates of Clozapine for Schizophrenia

Australia	35%
China	30%
England	23%
Sweden	22%
Germany	20%
India	13%
Korea	13%
Hong Kong	11%
Denmark	10%
Malaysia	4%
U.S.	4%



Unacceptable and Inexcusable!

Data compiled by the Treatment Advocacy Center

Work To Do

New laws: Improve AOT and HIPAA regulations.

Minimize the duration of untreated psychosis by utilizing the safest and most effective anti-psychotic at the inception of illness: clozapine.

Implement a rational clozapine REMS frequency - 95% of the risk is in the first 18 weeks, and after 1 year the risk is the same as other antipsychotics.

Use point-of-use finger-prick blood monitoring (Athelas).

Change the reimbursement structure for clozapine management to reflect the considerable amount of time and work appropriate management requires.

Develop a long-acting injectable clozapine.

Work To Do

Stop the learned helplessness and hopelessness:

- Educate the psychiatric community about what is possible with appropriate treatment (optimal clozapine) with robust **Meaningful Recovery** as the norm.

Do not accept devastating side effects; optimize the clozapine regimen and treat the whole person, including tobacco use, substance use disorders and physical fitness.

Establish slow titrations as the standard clozapine initiation.

Mandatory reading for all psychiatric providers:

- **The Clozapine Handbook** by Meyer and Stahl,
- **Meaningful Recovery from Schizophrenia and Serious Mental Illness with Clozapine** by Opler and the Laitman's.

Promote early intervention and awareness: the prodrome is high risk.

Work To Do

Reclassify Schizophrenia: psychotic disorders are neurobiological syndromes with heterogenous genetics that manifests as a neurodevelopmental condition, and when not appropriately treated a neurodegenerative disease.

Increase access to treatment:

- Promote universal healthcare.
- Integrated treatment with appropriate wrap-around services.
- Expand the number of providers by utilizing internists, psychiatric nurse practitioners, psychiatric pharmacists, and psychologists trained to prescribe.

Implement insurance reimbursement standards that challenge a provider using multiple antipsychotics without utilizing clozapine.

Demonstrate that using clozapine is cost-effective and financially feasible.

Always be kind and competent!

The System

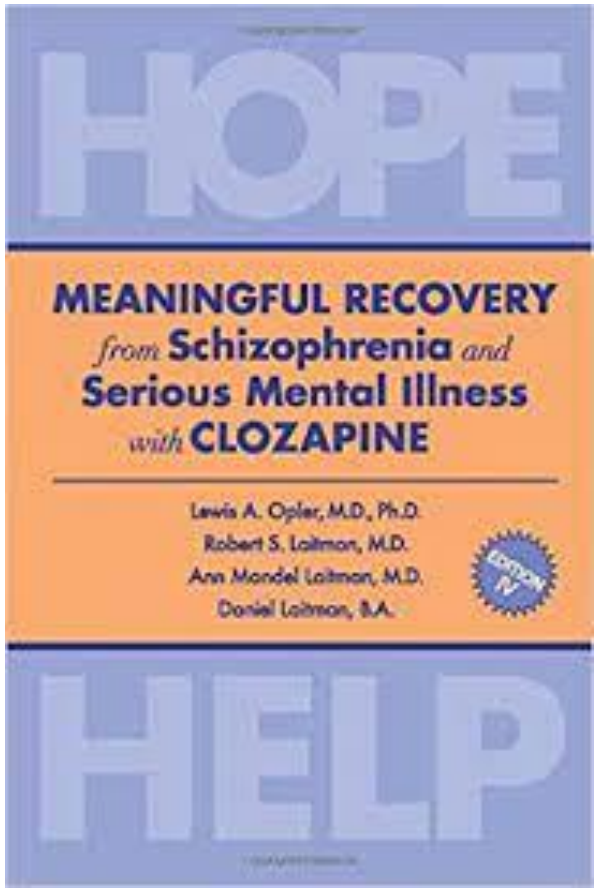
It is broken and fragmented.

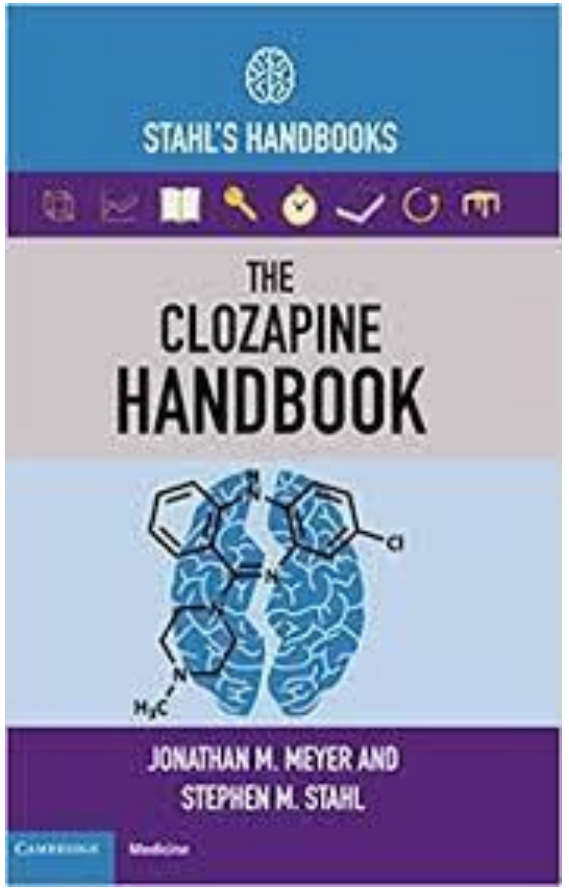
People are suffering.

We can do better.

We just need the will.

Important Literature





Connect with TEAM DANIEL

Website: Teamdanielrunningforrecovery.org

Email: Robert S. Laitman: rslaitman@aol.com

Cell: 914-629-5130 Personal Cell Phone

Facebook: Team Daniel and the Clozapine Community

Where there is help there is hope!