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 – Empathize – Agree – Partner

- Engage the patient in every way possible, using AOT if necessary.
- Ensure the patient feels safe and accepted; we have few boundaries.

Achieving Goals - 2

- 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 also share 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 and Incretin mimetics. (GLP-1 receptor agonists)
- **High Triglycerides:** Statins, omega 3 and fibrates (fenofibrate).
- **Metabolic Syndrome and Diabetes:** Metformin, SGLT2 inhibitors, high-dose ranitidine or famotidine, plant-based diet, exercise and Incretin mimetics.
- **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 - 2

- **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, famotidine, memantine, modafinil, armodafinil, amantadine, and consider fluvoxamine.

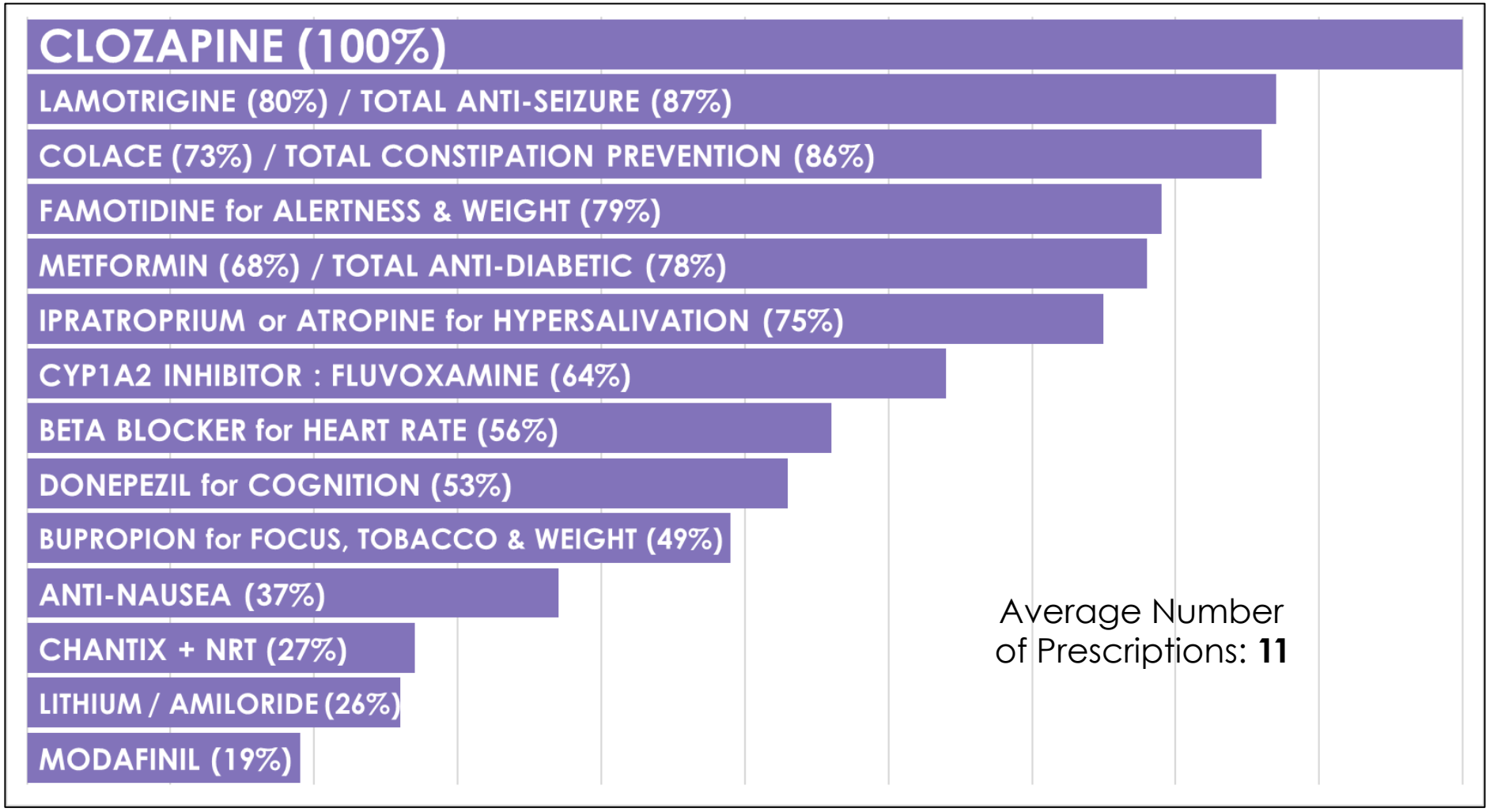
Presently investigating pitolisant (Wakix).

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

- **SMI is a team sport.**
- 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.
- 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).

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

Team Work

In July, 2021, Team Daniel ran the Long Island Jovia Marathon: Michael Orth, *Commissioner at WC, DCMH;* Dr. Rob Laitman, Jasper Bresolin, Malachy Friel.

The Diet

- **Eat 3 meals a day – Do NOT drink your calories**
- 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

Clozapine Initiation

Slow titration.

Get to therapeutic levels.

See the patient every week.

Shift majority of dose to bedtime dosing,
once positive symptoms are better

TEAM DANIEL©

Rev. 2/2/2022

TEAM DANIEL CLOZAPINE INITIATION SUMMARY

		Clozapine	Initial PRN's	Colace (Constipation)	Metformin ER (Weight Control)	Lamotrigine ER (Seizure Prophylaxis)	Other Anti-psychotics	Substance Use	Smoking
MONTH 1	Week 1	12.5 mg PM	Zofran (nausea) 4 - 8 mg, up to 2X daily 1% Atropine drops sublingual (salivation) 1 - 3 drops at bedtime Up to 3 drops 3x daily Famotidine -H2 blocker (acid reflux) 20 mg 2X daily and/or omeprazole** once daily Beta Blocker i.e. propranolol (tachycardia) 10 mg up to 3X per day Use 10-20 mg PRN for anxiety Consider PRN clozapine 12.5 - 25 mg for daytime psychosis/anxiety Desmopressin (nocturnal enuresis/urinary urgency) 0.1 mg at bedtime to start Klonopin 0.5 mg 2X daily for catatonia that has not responded to therapeutic clozapine serum levels. **PPI's decrease clozapine level		Start within first month of treatment to prevent metabolic syndrome and weight gain.	Prophylactic seizure prevention for patients with seizure history, mood disorder, or clozapine serum level over 500 ng/mL. This is especially critical to establish if a patient may need fluvoxamine in the future.	Acute psychosis: temporarily consider Zyprexa, Abilify or risperidone; to be discontinued after a therapeutic clozapine level is reached. Slowly down-taper and discontinue sleeping pills, stimulants, ADHD medications, and all other antipsychotics: clozapine is most effective as a mono-therapy antipsychotic. Smokers will require higher doses of clozapine and a longer transition from previous medications.	No changes first 2-4 weeks; keep it level. Discuss dangers of marijuana/THC. Consider 50 mg naltrexone (PM) for SUD. As clozapine becomes effective discuss life goals and how to transition from harmful substances. Consider drug counseling, DBT, possibly 12-step programs. DO NOT PUSH. Avoid short-acting benzodiazepines like Xanax. PRN Ativan or klonopin (low dose) for acute symptoms only during initial clozapine titration; discontinue after acute symptoms subside.	Smoking decreases serum levels on average 50% Discuss transition to vape or ideally NRT which is preferred. Consider Chantix or bupropion and other means of reducing dependence on nicotine. Continue to explain the value of non-smoked forms.
	Week 2	25 mg PM							
	Week 3	50 mg PM (Start TDM)		100 mg PM					
	Week 4	75 mg PM		Customize bowel regimen per patient symptoms: - Colace up to 400 mg - Senna-S - Dulcolax - Miralax - Linzess if needed (no fiber supplements) Use Bristol Stool chart and communicate often - patients may not be forthcoming.	500 mg PM				
MONTH 2	Week 5	100 mg PM*			500 mg PM	25 mg AM			
	Week 6	125 mg PM*			500 AM/500 PM	25 mg AM			
	Week 7	150 mg PM*			500 AM/500 PM	50 mg AM			
	Week 8	175 mg PM*			500 AM/1000 PM	50 mg AM			
MONTH 3	Week 9	Increase 25 mg weekly or every two weeks per symptoms and Therapeutic Drug Monitoring (TDM). Therapeutic range begins when clozapine serum level reaches 350-500 ng/mL. Some patients need to go higher for adequate symptom control. Consider splitting dose for strong positive symptoms with 2:1 ratio bedtime to morning dose.			500 AM/1000 PM	Continue increasing lamotrigine 50 mg every two weeks up to 200 mg. If lamotrigine is not tolerated consult Dr. Laitman for the next best option: - Gabapentin - Keppra - Trileptal (check for Asian ancestry) - Topamax Depakote is NOT recommended due to increased risks / side effects. **Watch carefully for Stevens-Johnson rash.**			
	Week 10				1000 AM/1000 PM				
	Week 11				Consider Farxiga/Xigduo and Trulicity (or similar) in patients with continuing weight or metabolic concerns. Metformin depletes B12 - add 1000 mcg daily.				
	Week 12								
MONTH 4	Week 13								
	Week 14								
	Week 15								
	Week 16								

Dr. Robert Laitman mobile: 914-629-5130

*** Note: Slow clozapine titration reduces incidence of myocarditis, seizure, cardiomyopathy and pneumonia. Start TDM at 50 mg to confirm patient adherence.**

Cautions:

- **Consult Dr. Laitman for instructions on how to handle medications in previous regimen that are anticholinergic or antihistaminergic, or that may lower blood pressure, increase clozapine levels or increase seizure risk.**
- **For mild neutropenia (ANC < 1500 ug/mL or ANC < 500 ug/mL for a BEN patient) start 450mg of lithium ER (PM dose). Increase as needed to 1.2 mmol/L serum level until resolved.**
- **Indigenous/Asian/Native American descent are slow metabolizers and on average need 1/3 the dosage of European descent. Slower titration with frequent TDM is recommended.**
- **Baseline tests prior to initiating clozapine: EKG, metabolic panel, A1C, ANC, HSCRP lipid panel and where financially feasible EEG/Brain MRI.**

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.**

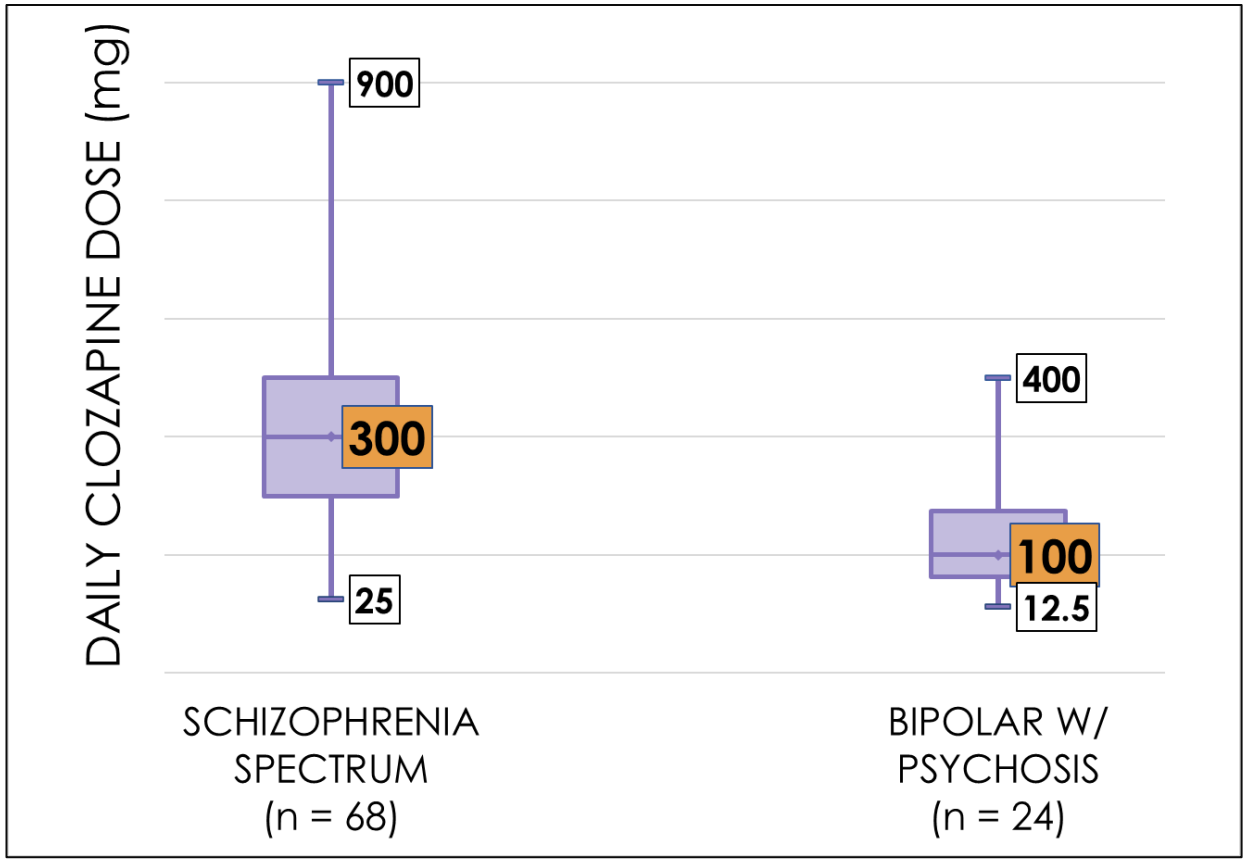
- **Expect a long cross-taper from the previous antipsychotic.**

Slow Titration Schedule

CLOZAPINE TITRATION SCHEDULE

Total Daily Dose (mg) Increases Per Week

No Standard Dose

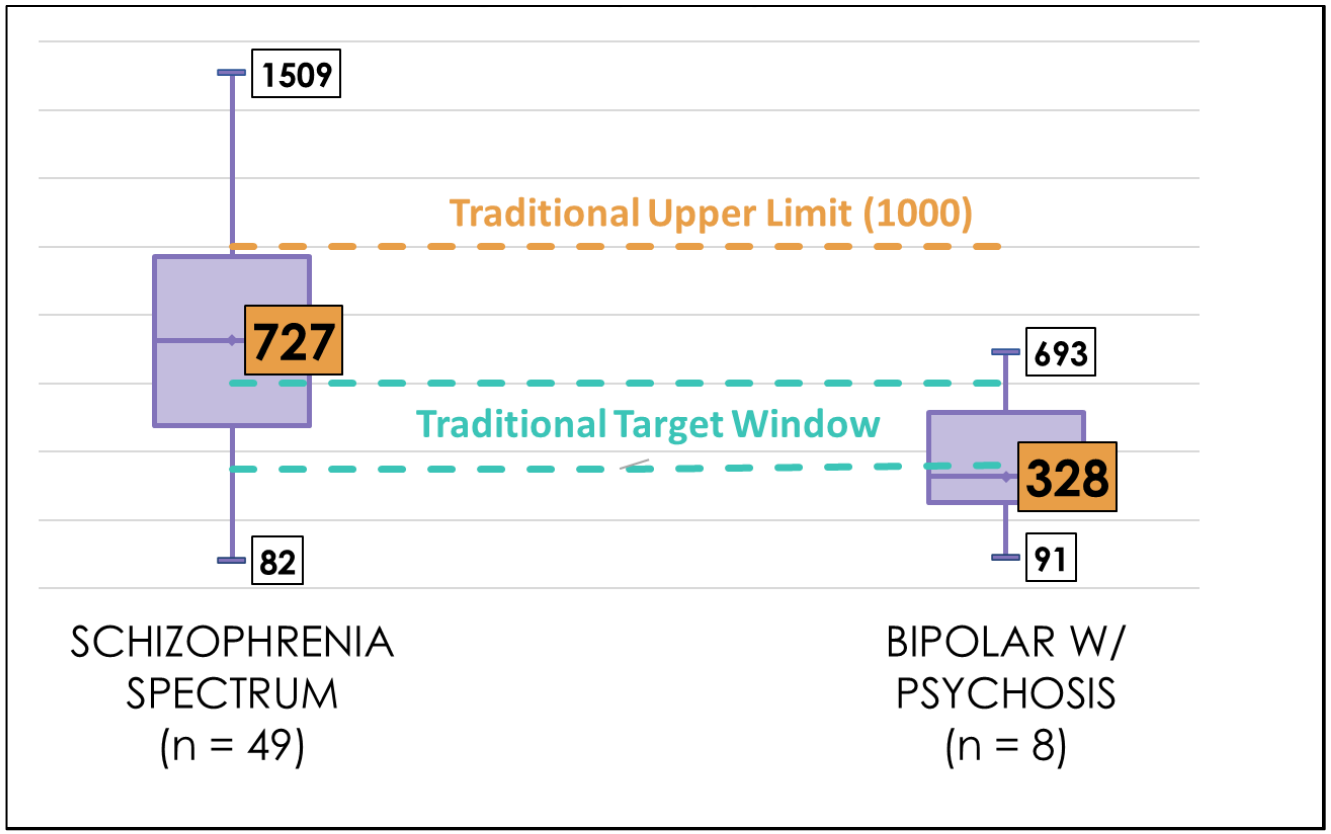


OPTIMIZED CLOZAPINE DAILY DOSE

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!**
  - Some quinolones increase levels (Ciprofloxacin)

- **Inflammation dramatically increases levels.**
  - With serious COVID, reduce dose by 50% until the fever resolves.

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 1.3 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:

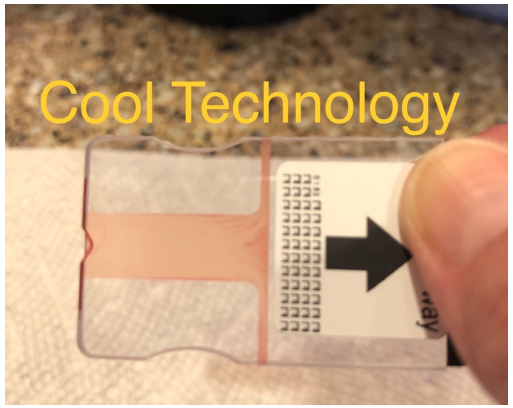
- Psychiatric MD or NP adept in medicine.
- Full time internist, or neurologist adept in clozapine.
- Psychologist or psychiatric social worker for P-CBT.
- Social workers for case management and housing and frequent legal interface.
- Peer specialist who is on clozapine.
- Work and social opportunities,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

The Clozapine Clinic - 2

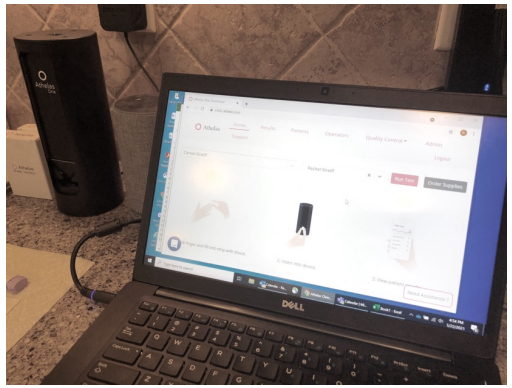
The General Model:

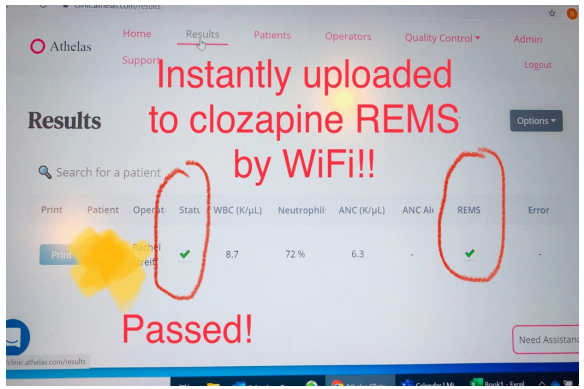
- Exercise training and nutrition support.
- Family support and education – the LEAP method.
- CBT-P, DBT, cognitive enhancement therapy and job training.
- Full supported therapeutic housing.
- Substance abuse intervention for cigarettes, drugs and alcohol.
- Pet therapy (dogs do matter).
- Full biopsychosocial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

The Clozapine Clinic



Finger Prick Testing
Real Photos from a Very Excited Patient!





Athelas

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 Else Does the Laitman Protocol?

SILVER HILL HOSPITAL

Inpatient, Transitional and IOP Program
New Canaan, CT

Viewpoint
Dual Recovery Center

Clozapine House Residential Program
Prescott, AZ

UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE

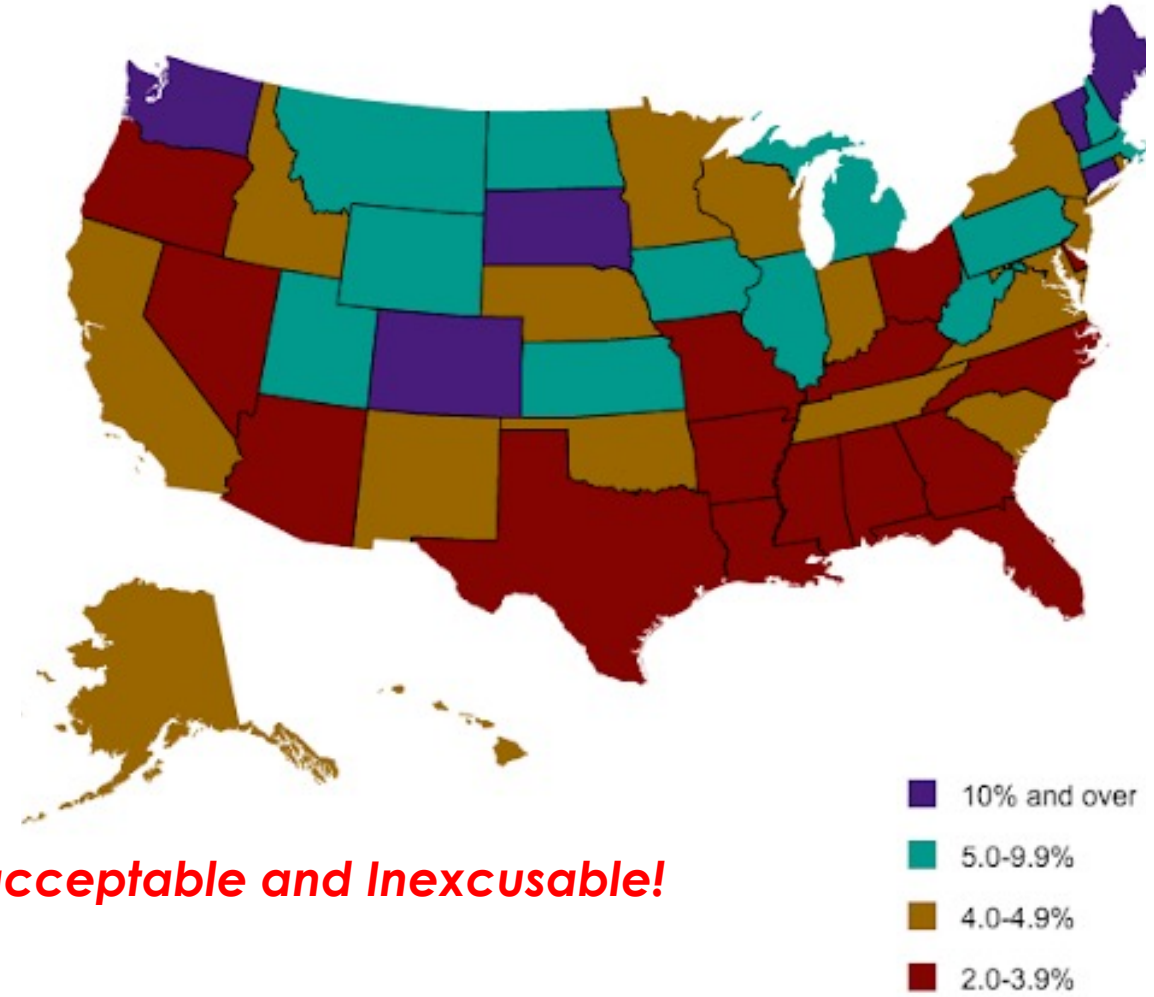
Inpatient Clozapine Program
Baltimore, MD

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%

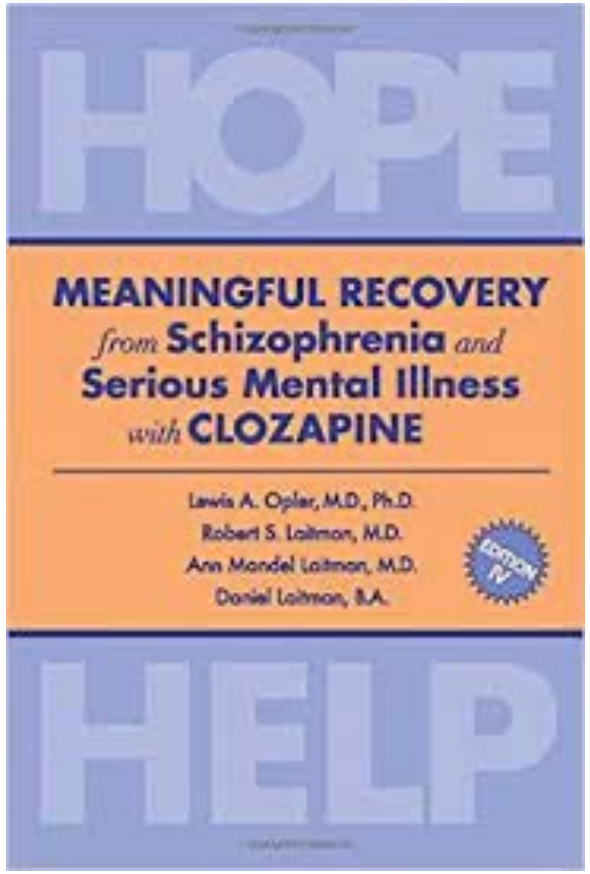


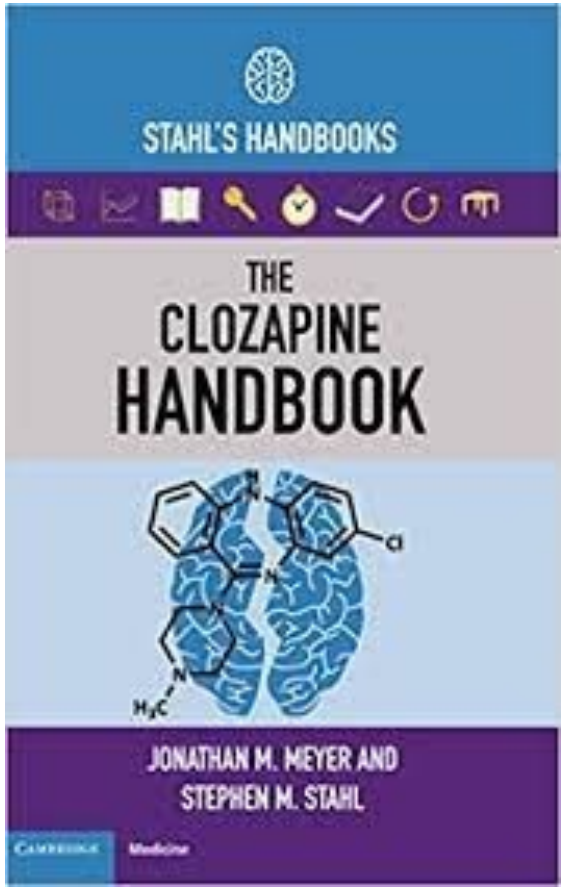
Unacceptable and Inexcusable!

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.
- Implement insurance reimbursement standards that challenge a provider using multiple antipsychotics without utilizing clozapine.
- Always be kind and competent!

Important References





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!

TEAM DANIEL
Running for Recovery
from Mental Illness