The Clozapine & LAI Virtual Forum is a peer-to-peer, interactive dialogue between psychiatrists, nurse practitioners, and other prescribing clinicians. It is informal, no registration required — just join our Zoom call and share your challenges and questions on the month's trending topic around either clozapine or LAIs.

**TODAY’S TOPIC:**
Appropriate Use of Weight Loss Medication with Clozapine with a Focus on GLP-1 Agonists
MODERATORS

Donna Rolin, PhD, APRN
SMI Adviser Nursing Expert; University of Texas, Austin
Dr. Donna Rolin is Clinical Associate Professor and the Director of the Psychiatric Mental Health Nurse Practitioner program at the University of Texas with 23 years of experience in psychiatric nursing, including inpatient, community, forensic, and older adult settings.

Robert Cotes, MD
SMI Adviser Physician Expert; Emory University
Dr. Robert Cotes, MD, is an Associate Professor at Emory University School of Medicine in the Department of Psychiatry and Behavioral Sciences. He has interest in clozapine, characterizing persistent symptoms of schizophrenia, understanding cardiometabolic side effects of antipsychotic medications, and first episode psychosis.

Robert Laitman, MD
Clozapine Expert
Dr. Robert Laitman is an internist who specializes in the use of clozapine in an optimal fashion for individuals with schizophrenia or other psychotic spectrum disorders. He serves on the Board of Directors for the Schizophrenia and Related Disorders Alliance of America and is also a board member of the Westchester chapter of the National Alliance of Mental Illness. Dr. Laitman and his wife started Team Daniel, a 501 c-3 non-profit, to advocate for and support people living with mental illness.
Discussion Questions for Virtual Forum: Appropriate Use of Weight Loss Medication with Clozapine with a Focus on GLP-1 Agonists

• Do any insurances cover GLP-1 meds for clozapine or other SGAs?
• What medications or alternatives can I prescribe to promote weight loss to patients on clozapine?
• What screening panel blood tests must be used on a standard basis besides WBC to identify and address metabolic effects early and monitor continuously if Clozapine is working well overall?
Appropriate Use of Weight Loss Medication with Clozapine with a Focus on GLP-1 Agonists
All-Cause Mortality Versus BMI for Each Sex in the Range 15–50 kg/m² (excluding the first 5 years of follow-up)

Relative risks at ages 35–89 years, adjusted for age at risk, smoking, and study, were multiplied by a common factor (ie, floated) to make the weighted average match the PSC mortality rate at ages 35–79 years.

Floated mortality rates shown above each square and numbers of deaths below.

Area of square is inversely proportional to the variance of the log risk.

Boundaries of BMI groups are indicated by tick marks.

95% CI’s for floated rates reflect uncertainty in the log risk for each single rate.

Dotted vertical line indicates 25 kg/m² (boundary between upper and lower BMI ranges in this report).

Less Weight Gain

<table>
<thead>
<tr>
<th></th>
<th>Olanzapine Historical Data (N = 442) after 2.0 years</th>
<th>Clozapine Historical Data (N = 669) after 1.7 years</th>
<th>Team Daniel on Clozapine (N = 120) with average treatment of 6 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of Patients with More Than 7% Increase in Body Weight</td>
<td>46%</td>
<td>35%</td>
<td>22%</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Below/Normal Weight (N = 38)</th>
<th>Overweight/Obese (N = 59)</th>
<th>Severely Obese (N = 23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.2</td>
<td>-13</td>
<td>-34</td>
</tr>
</tbody>
</table>
TEAM DANIEL OPTIMIZED REGIMEN (N=120)

CLOZAPINE (98%)
LAXATIVE for CONSTIPATION (80%)
LAMOTRIGINE for SEIZURE PREVENTION (79%)
DOCUSATE for STOOL SOFTENER (76%)
METFORMIN / B12 for WEIGHT CONTROL (75%)
CYP1A2 INHIBITOR: FLUVOXAMINE (64%)
FAMOTIDINE for ALERTNESS & WEIGHT (63%)
BETA BLOCKER for HEART RATE (60%)
DONEPEZIL for COGNITION (49%)
BUPROPION for FOCUS, TOBACCO & WEIGHT (49%)
ODANSETRON for NAUSEA (38%)
IPRATROPIUM or ATROPINE sublingual (36%)
SGLT2 INHIBITOR for WEIGHT (36%)
GLP-1 AGONIST for WEIGHT (34%)
VARENICLINE + NRT (28%)
OTHER ANTIDEPRESSANT (28%)
PROTON PUMP INHIBITOR (26%)
LITHIUM / AMILORIDE (23%)
STATIN / COQ10 (23%)
DESMOPRESSIN (22%)
MODAFINIL (20%)
TOPIRAMATE (15%)

Average Number of Prescriptions: 11
## Optimizing the Regimen

<table>
<thead>
<tr>
<th>Drug</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorazepam Or Alprazolam</td>
<td>14%</td>
</tr>
<tr>
<td>Klonopin</td>
<td>14%</td>
</tr>
<tr>
<td>Linzess Or Trulance</td>
<td>13%</td>
</tr>
<tr>
<td>Synthroid</td>
<td>11%</td>
</tr>
<tr>
<td>Wakix (Pitolisant) Investigational</td>
<td>10%</td>
</tr>
<tr>
<td>Memantine</td>
<td>8%</td>
</tr>
<tr>
<td>Other Antipsychotic</td>
<td>7%</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>6%</td>
</tr>
<tr>
<td>Benztropine</td>
<td>5%</td>
</tr>
<tr>
<td>Naltrexone</td>
<td>5%</td>
</tr>
<tr>
<td>Depakote</td>
<td>4%</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>4%</td>
</tr>
<tr>
<td>Glycopyrrolate</td>
<td>3%</td>
</tr>
<tr>
<td>Fludrocortisone</td>
<td>3%</td>
</tr>
<tr>
<td>Buspirone</td>
<td>2%</td>
</tr>
<tr>
<td>Amantadine</td>
<td>2%</td>
</tr>
</tbody>
</table>
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

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)

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**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

**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

**SNACK**
- Unsalted nuts or fruit
  - Blueberries, strawberries, blackberries, apples, plums or pears.
In healthy individuals…

1. ingestion of food results in
2. release of gastrointestinal peptides (GLP-1 and GIP) as well as
3. pancreatic beta cell hormones (insulin and amylin). GLP-1 and amylin, in particular, have inhibitory effects on
4. gastric emptying,
5. glucagon release, and
6. appetite.
7. Following the absorption of food, GLP-1 and GIP promote insulin secretion, otherwise known as the incretin effect. In diabetes, these steps are disrupted.
# The Role of GLP-1 and GIP in Glucose Homeostasis

<table>
<thead>
<tr>
<th></th>
<th>GLP-1</th>
<th>GIP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Site of synthesis</strong></td>
<td>Small intestinal L cells</td>
<td>Small intestinal K cells</td>
</tr>
<tr>
<td><strong>Glucose-dependent stimulation of insulin secretion</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Reduction of gastric emptying</strong></td>
<td>Yes</td>
<td>No effect</td>
</tr>
<tr>
<td><strong>Reduction of inappropriate glucagon secretion</strong></td>
<td>During euglycemia or hypoglycemia: No effect</td>
<td>During euglycemia or hypoglycemia: Stimulates glucagon During hyperglycemia: No effect</td>
</tr>
<tr>
<td><strong>Weight loss</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Female Patient

Added Trulicity
Added Trulicity

Male Patient
Team Daniel on GLP-1 Agonist BMI Class Distribution Progress

**Before GLP-1 Agonist**

<table>
<thead>
<tr>
<th>GLP-1 Agonist Candidates at Intake (N = 40)</th>
<th>GLP-1 Agonist Candidates Feb 2021 (N = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity class III</td>
<td>5</td>
</tr>
<tr>
<td>Obesity class II</td>
<td>11</td>
</tr>
<tr>
<td>Obesity class I</td>
<td>13</td>
</tr>
<tr>
<td>Pre-obesity</td>
<td>9</td>
</tr>
<tr>
<td>Normal</td>
<td>2</td>
</tr>
</tbody>
</table>

**GLP-1 Agonist Added**

<table>
<thead>
<tr>
<th>Team Daniel on GLP-1 Agonist Feb 2022 (N = 40)</th>
<th>Team Daniel on GLP-1 Agonist Current (N = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity class III</td>
<td>2</td>
</tr>
<tr>
<td>Obesity class II</td>
<td>4</td>
</tr>
<tr>
<td>Obesity class I</td>
<td>17</td>
</tr>
<tr>
<td>Pre-obesity</td>
<td>15</td>
</tr>
<tr>
<td>Normal</td>
<td>2</td>
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</tbody>
</table>

| Normal                                       | 5                                             |

**Intake** 73% Obese  
**Year 1** 55% Obese  
**Year 2** 58% Obese  
**Current** 40% Obese
### Team Daniel Clozapine Regimen Initiation Summary

<table>
<thead>
<tr>
<th>Month</th>
<th>Week</th>
<th>Clozapine (mg)</th>
<th>Initial PRN’s</th>
<th>Colace (Constipation)</th>
<th>Metformin ER (Weight Control)</th>
<th>Lamotrigine ER (Seizure Prophylaxis)</th>
<th>Other Antipsychotics</th>
<th>Substance Use</th>
<th>Smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MONTH 1</strong></td>
<td></td>
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<tr>
<td></td>
<td>Week 1</td>
<td>12.5 PM</td>
<td>Zofran (nausea) 4 - 8 mg, up to 2X daily</td>
<td></td>
<td></td>
<td>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.</td>
<td>Acute psychosis: temporarily consider Zyprexa, Abilify or risperidone; to be discontinued after a therapeutic clozapine level is reached.</td>
<td>No changes first 2-4 weeks; keep on level. Discuss dangers of marijuana/THC. Consider 50 mg naltrexone (PM) for SUD.</td>
<td>Smoking decreases serum levels on average 50%</td>
</tr>
<tr>
<td></td>
<td>Week 2</td>
<td>25 PM</td>
<td>1% Atropine drops sublingual (Salivation)</td>
<td>1 - 3 drops at bedtime Up to 3 drops 3X daily</td>
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<td></td>
<td>Week 3</td>
<td>50 PM (Start TDM)</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
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<td></td>
<td>Week 4</td>
<td>75 PM</td>
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<td></td>
<td>Week 5</td>
<td>100 PM*</td>
<td>Famotidine H2 blocker (acid reflux) 20 mg 2X daily and/or omeprazole* once daily</td>
<td>Customize bowel regimen per patient symptoms: Colace up to 400 mg - Senna-S Dulcolax - Miralax - Laxine # needed (no fiber supplements)</td>
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<td></td>
<td>Week 6</td>
<td>125 PM*</td>
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<td></td>
<td>Week 7</td>
<td>150 PM*</td>
<td>Betablocker i.e. propranolol (tachycardia) 10 mg up to 3X per day</td>
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<td>Week 8</td>
<td>175 PM*</td>
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<td><strong>MONTH 2</strong></td>
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<td></td>
<td>Week 9</td>
<td>Increase 25 mg weekly or every two weeks per symptoms and Therapeutic Drug Monitoring (TDM).</td>
<td>Consider PRN clozapine 12.5 - 25 mg for daytime psychosis/anxiety Desmopressin (nocturnal enuresis/urinary urgency) 0.1 mg at bedtime to start</td>
<td>Use Bristol Stool chart and communicate often - patients may not be forthcoming.</td>
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<td></td>
<td>Week 10</td>
<td></td>
<td>Some patients need to go higher for adequate symptom control.</td>
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<tr>
<td></td>
<td>Week 11</td>
<td></td>
<td>Therapeutic range begins when clozapine serum level reaches 350-500 ng/mL.</td>
<td>Consider combining clozapine with other psychotropics to achieve therapeutic serum levels.</td>
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<td></td>
<td>Week 12</td>
<td></td>
<td></td>
<td>Consider splitting dose for strong positive symptoms with 2:1 ratio bedtime to morning dose.</td>
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<tr>
<td><strong>MONTH 3</strong></td>
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<td>Week 13</td>
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<td>Week 14</td>
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<td>Week 15</td>
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<td>Week 16</td>
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</tbody>
</table>

**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, H1C, ANC, HSCR lipids panel and where financially feasible EEG/Brain MRI.

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**Dr. Robert Laitman mobile: 914-629-5130**
# Team Daniel Clozapine Regimen Maintenance Summary

**TABLE 2**

<table>
<thead>
<tr>
<th>Suboptimal Clozapine Results (Most Resistant Schizophrenia)</th>
<th>Fluvoxamine</th>
<th>Depression &amp; Alertness</th>
<th>Cognition Improvement</th>
<th>Metabolic Syndrome Weight Control</th>
<th>Hypersalivation &amp; Pneumonia Prevention</th>
<th>Lithium Carbonate ER</th>
<th>Neutropenia &amp; Clozapine Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TDMS OF CLOZAPINE SERUM LEVELS:</strong> 75% of patients START responding at 400 ng/mL; the threshold for bipolar is lower.</td>
<td></td>
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</tr>
<tr>
<td>Up to 1000 ng/mL should be pursued for efficacy. With adjunct fluvoxamine, levels up to 1500 ng/mL or higher may be considered.</td>
<td></td>
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</tr>
<tr>
<td>Median Team Daniel patient serum levels are 450 ng/mL at 1 year of treatment. Statistics represent clozapine levels only, not the sum of clozapine &amp; norclozapine.</td>
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</tr>
</tbody>
</table>

**POSITIVE SYMPTOMS:** Split clozapine dosage 2-3x daily, largest dose before bed. Ineffective doses for the elderly may be doubled to achieve therapeutic effects.

**PREVIOUS ANTIPSYCHOTICS:** slowly taper & discontinue as clozapine is titrated to therapeutic levels. 

**ELECTROCONVULSIVE THERAPY (ECT):** Most effective for depression. Consider for audio & visual hallucinations.

**TMS:** for negative symptoms.

**ANTIPSYCHOTIC AUGMENTATION:** 1st choice - Aripiprazole for low weight gain & low sedation profile. 2nd choice - Risperidone. There is no compelling evidence that antipsychotic augmentation provides greater efficacy. Concomitant antipsychotic use can impede clozapine's efficacy & increase adverse side effects.

**MINOCYCLINE ANTIBIOTIC:** 100 mg 2x daily.

**AVOID:** smoking (decreases clozapine serum levels), marihuana & CBD (increases psychosis risk), herbal supplements (unknown medication interactions).

**FLUOXAMINE:**

- **Depression & Alertness:**
  - Serotonin-selective reuptake inhibitor (SSRI) - increases clozapine levels but without increasing norclozapine metabolite.
  - Goal: achieve therapeutic clozapine serum levels for adequate symptom control with lower dosage & fewer side effects. Can dramatically improve sialorrhea.
  - **CAUTION:** Medication Interaction: Seizure risk increases as clozapine serum levels increase. Fluvoxamine can double or triple seizure risk.
  - **SIDE EFFECTS:**
    - Seizure risk: Monitor for signs of seizures. If seizures occur, hold fluvoxamine and monitor patient closely.
    - Nausea, vomiting, diarrhea:
      - If severe, consider monitoring for electrolyte imbalances.
      - If necessary, adjust fluvoxamine dosage or consider alternative treatment options.

**CLOZAPINE: Dosing: 50 mg**

- **DEPRESSION & ALERTNESS:**
  - Antidepressant: Can improve mood, reduce negative symptoms, & increase alertness.
  - Use with caution in patients with a history of depression or bipolar disorder.

**CLOZAPINE INTERACTIONS:**

- **Angiography:**
  - Can increase clozapine levels, leading to adverse effects. Monitor for signs of toxicity & adjust dosing accordingly.

**CLOZAPINE INHIBITORS:**

- **GABA (Gamma-Aminobutyric Acid) Receptor Agonists:**
  - Can increase clozapine levels, leading to adverse effects. Monitor for signs of toxicity & adjust dosing accordingly.

**CLOZAPINE ADVERSE EFFECTS:**

- **Sialorrhea:**
  - Monitor for signs of sialorrhea & adjust dosing accordingly.
  - Consider using saliva-collecting devices or oral care products.

**CLOZAPINE MANAGEMENT:**

- **Blood Work:**
  - Monitor blood work regularly to ensure dosing is appropriate & to avoid adverse effects.
  - Consider tapering dosage if needed.

**CLOZAPINE Dosing:**

- **Initial Dosing:**
  - Start with a lower dose & titrate upward based on response & adverse effects.

**CLOZAPINE TACHYCARDIA:**

- **Uselevexine:**
  - Consider using levovexine to manage tachycardia & other side effects.

**CLOZAPINE TOXICITY:**

- **Neutropenia:**
  - Monitor for signs of neutropenia & adjust dosing accordingly.

**CLOZAPINE DRUG DRUG INTERACTIONS:**

- **Risperidone:**
  - Consider using risperidone as an alternative medication due to potential interactions with clozapine.

**CLOZAPINE MONITORING:**

- **Blood Work:**
  - Monitor blood work regularly to ensure dosing is appropriate & to avoid adverse effects.
  - Consider tapering dosage if needed.

**CLOZAPINE ADVERSE EFFECTS:**

- **Sialorrhea:**
  - Monitor for signs of sialorrhea & adjust dosing accordingly.
  - Consider using saliva-collecting devices or oral care products.

**CLOZAPINE MANAGEMENT:**

- **Blood Work:**
  - Monitor blood work regularly to ensure dosing is appropriate & to avoid adverse effects.
  - Consider tapering dosage if needed.

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Dr. Robert Laitman 914-629-5130
Dr. Ann Mandel Laitman 914-841-2095

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*For full reference, please see the source document.*
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!*
Feedback
Please help us improve the Clozapine & LAI Virtual Forum by completing this survey: http://smiadviser.org/forumfeedback

Pre-submit Cases
www.smiadviser.org/vfcases

Upcoming Virtual Forum
LAI Topic TBA
October 5 @ 4-4:45pm ET

For additional questions and resources – join the Clozapine and LAI Centers of Excellence Exchange Community
- www.smiadviser.org/cloz_lai_signup