
SUD Treatment
Psychotherapy
Psychiatry
Medicine

LEARNING OBJECTIVES

1. Identify two functional benefits of newer treatments (like M1/M4 agonists) compared to traditional medications and identify three patient profiles who may benefit from a referral to discuss these options with their psychiatrist.

- **Focus:** Shifting the paradigm from D_2 blockade to muscarinic modulation.
- **Functional Benefits vs. Traditional Antipsychotics:**
- **EPS Avoidance:** No direct D_2 antagonism in the nigrostriatal pathway; avoids akathisia and tardive dyskinesia.
- **Metabolic Neutrality:** Minimal impact on weight, lipid profiles, or glycemic control compared to SGAs.
- **Ideal Referral Profiles:**
- **Metabolic High-Risk:** Patients with BMI >30 or existing Type 2 Diabetes.
- **Movement Disorder Sensitive:** History of severe EPS or pre-existing TD.
- **Cognitive Focus:** Patients prioritizing improvement in executive function and alogia.

2. List two comorbid conditions for a screening process for behavioral health clients.

- **Focus:** Enhancing outcomes through "Whole-Person" assessment.
- **Substance Use Disorders (SUD):**
- **The Challenge:** High prevalence of alcohol and stimulant use in SMI populations.
- **Clinical Impact:** SUD can mimic psychotic exacerbation and decrease treatment efficacy.
- **Cardiovascular & Metabolic Disease:**
- **The Challenge:** SMI patients face a 15–20-year reduction in life expectancy.
- **Clinical Impact:** Mandatory baseline and longitudinal screening for hypertension and dyslipidemia to mitigate CV mortality.

3. Identify two types of clients who could benefit from moving from oral medications to long-acting injections.

- **Focus:** Moving from "last resort" to "early intervention" tools.
- **First-Episode Psychosis (FEP):**
- Early use of LAIs protects against the "kindling effect" of repeated relapses.
- Stabilizes the neurobiological trajectory from the outset.
- **The "Partially Adherent" Patient:**
- Addresses the gap in patients who miss sporadic doses but don't meet criteria for complete refusal.
- Reduces "micro-relapses" that lead to cumulative functional decline and frequent ER utilization.

4. List two metabolic changes that can be identified using metabolic screening tools.

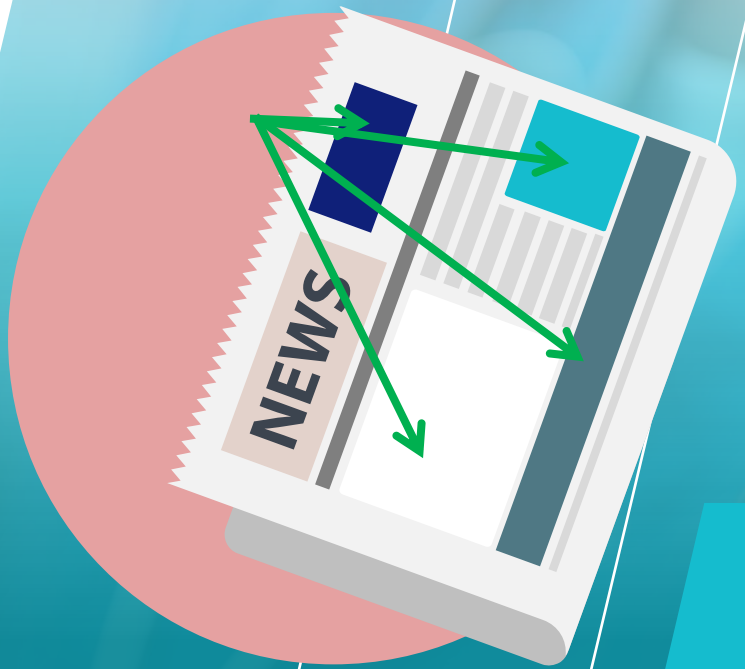
- **Focus:** Biomarkers for early intervention in treatment-induced side effects.
- **Insulin Resistance & Hyperglycemia:**
- **Metric:** Longitudinal tracking of Glycated Hemoglobin (HbA1c) and fasting plasma glucose.
- **Significance:** Early detection allows for medication adjustment before the onset of overt diabetes.
- **Atherogenic Dyslipidemia:**
- **Metric:** Tracking Triglyceride-to-HDL ratios.
- **Significance:** Identifies shifts toward a pro-inflammatory metabolic state common with certain second-generation antipsychotics.

5. Explain how the clinical team can use behavioral data — like medication adherence, social interaction frequency, routine changes, or signs of agitation or withdrawal—to determine effective next steps for patients thought to have treatment-resistant schizophrenia.

Focus: Differentiating pseudo-resistance from true treatment resistance.

- **Behavioral Data as Diagnostic Input:**
  - **Adherence Tracking:** Pharmacy refills and routine consistency to rule out non-adherence.
  - **Functional Metrics:** Decline in social interaction or increased agitation despite "therapeutic" dosing.
  - **Substance Use Disorder:** Screening tools such as The American Society of Addiction Medicine (ASAM) criteria.
- **Clinical Next Steps:**
  - **If Pseudo-resistance (Non-adherence):** Transition to **LAI** to ensure delivery.
  - **If True Resistance:** Initiate **Clozapine** titration or investigate novel **M1/M4 agonist** adjuncts.

What's on today's Agenda?



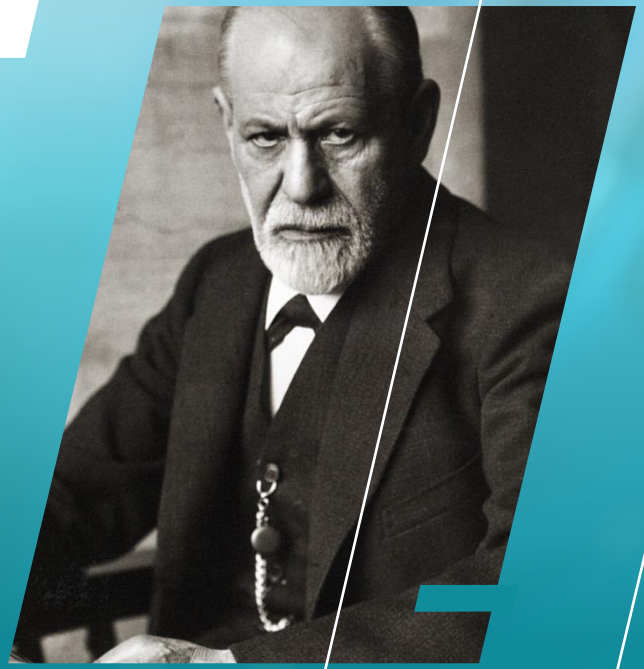
01 Frontiers in Neuroleptic Therapy and Mental Health Care

02 Precision in Mood & Crisis Intervention

03 The Metabolic-Psychiatry Interface

04 Systems-Level Practice Optimization

Implicit Bias: A Variable in Clinical Objectivity (2026)



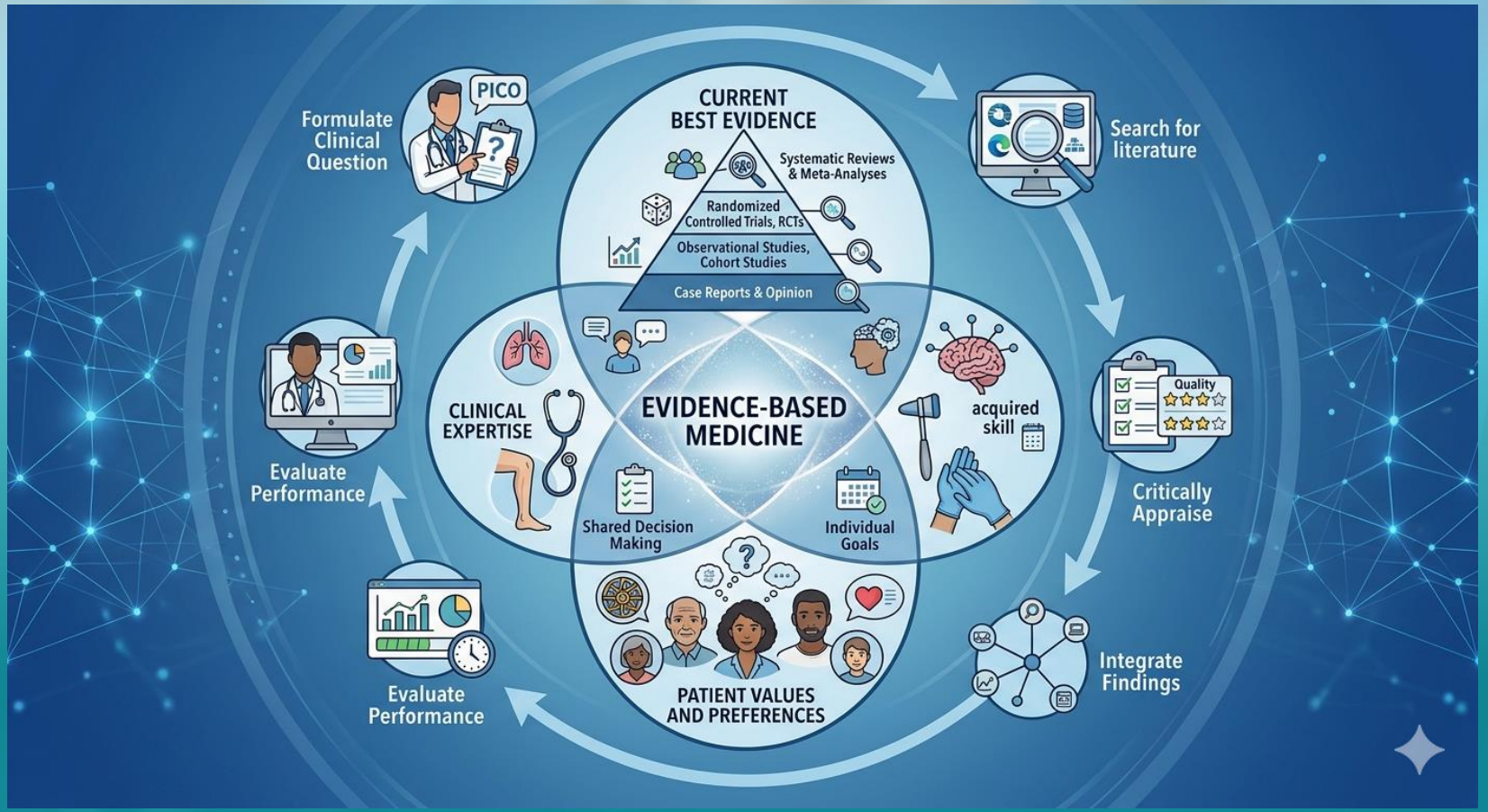
Implicit Bias

Definition: The automatic, non-conscious cognitive shortcuts (heuristics) that influence clinical perception and decision-making, often operating in direct opposition to a provider's stated professional values.

Consequence:

- Gatekeeping Revolutionary Medications
- Diagnostic Anchoring
- Impact on Precision Medicine
- Federal Quality & Compliance

Evidenced-Based Medicine



The Golden Hour: Rapid-Acting Strategies for Depression and Acute Suicidal Crises

The Golden Hour: Rapid-Acting Strategies for Depression and Acute Suicidal Crises

Distinct Diagnosis

Rapid Glutamatergic Agents

Emergency Stabilization

Psychedelics: Really??

Esketamine (Spravato) in Acute Suicidal Crisis

Onset: Rapid symptomatic relief within 4–24 hours; designed to bridge the "efficacy gap" of traditional monoaminergic antidepressants.

Pharmacodynamics: Functions as a non-competitive NMDA receptor antagonist.

Dosing (MDSI): 84 mg intranasally **twice weekly for 4 weeks** ; administered in conjunction with a new or optimized oral antidepressant.

Safety/REMS: Mandatory **2-hour post-dose observation** due to risks of sedation, dissociation, and transient hypertensive spikes.

Psilocybin — Serotonergic Reset & Sustained Remission

Clinical Status: Not currently FDA-approved for acute suicidality; typically an exclusion criterion (C-SSRS ≥ 4) in current Phase III MDD/TRD trials.

Mechanism: Targets the **5-HT2A receptor** to induce rapid neuroplasticity; pilot data suggests reductions in "death-implicit association" and existential distress.

Durability vs. Speed: Unlike esketamine's transient effect, psilocybin shows **durability (3–6 months)** after 1–2 doses, but the acute "trip" (6–8 hours) may be destabilizing for a patient in active crisis.

SUMMARY


Esketamine (Spravato) in Acute Suicidal Crisis
Macro Device
Clinical Administration
2-Hour REMS Room
REMS Protocol Flowchart
Synaptogenesis
Dendritic spine
"Efficacy Gap" Timeline
Esketamine (hours)
Slow peak of traditional SSRIs
Hours
weeks
Time
Molecular Structure
Esketamine (S-enantiomer)
Stabilization Metaphor
Team Collaboration
Vital Monitoring
Psilocybin and Ketamine: Rapid-Acting Antidepressants
DMN Disruption
Set and Setting
Monitoring Dynamic
Receptor Binding
psilocin
5-HT2A serotonin receptor
Durability vs. Speed
Esketamine
Psilocybin
Effect
Hours
Long-term
Time
Neuroplasticity
Increased new a dose
Increased dendritic dendritic plasticity
Existential Distress
Breakthrough Designation
FDA
Breakthrough Therapy
Palliative Care
Renovation Metaphor

Clozapine: Unlocking the Gold Standard: Bringing Treatment-Resistant Therapy into the 21st Century

Antipsychotics: The Swiss Army Knife of Psychiatry

Beyond Psychosis: Navigating the Risks and Rewards of Off-Label SGA Expansion.

01 The Rise of “Off-Label” Dominance

02 Low Dose Quetiapine as the New “Sleep Aid”

03 Adjunct or Mono Therapy for Mood Disorders

04 The Metabolic “Trade Off”

05 The Risk of Tardive Dyskinesia

06 Economic and Societal Costs

07 Cardiovascular and Cerebrovascular Risks

08 Cognitive and Emotional “Blunting”

09 The Need for “Deprescribing” Protocols

Clozapine: Unlocking the Gold Standard: Bringing Treatment-Resistant Therapy into the 21st Century

Defining TRS and Ultra-TRS:

- Treatment-Resistant Schizophrenia (TRS) is a poor response to at least two antipsychotics. Ultra-TRS describes even greater resistance to treatment.

Clozapine and Improved Access:

- As the gold standard for TRS, clozapine's clinical utility was historically hindered by regulatory hurdles. The FDA's February 2025 elimination of REMS requirements removes mandatory enrollment and reporting, drastically improving availability for high-need patients.

Management for Partial Responders:

- Partial responders may benefit from augmentation strategies, psychosocial interventions, or innovative therapies for improved outcomes.

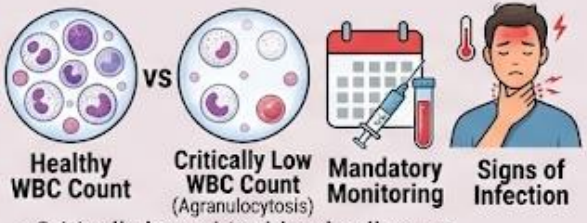
Monitoring Is Still Necessary and Required – But There Has Been a Game-Changer:

- Point-of-Care (POC) monitoring: the introduction of finger-prick technology for absolute neutrophil count (ANC) assessment, reducing the "blood draw barrier."

FDA BLACK BOX WARNINGS FOR CLOZAPINE (5+1 WARNINGS)

1) Severe Neutropenia

Risk of Agranulocytosis & Fatal Infection



- Critically low white blood cell count.
- Mandatory, regular absolute neutrophil count (ANC) monitoring.

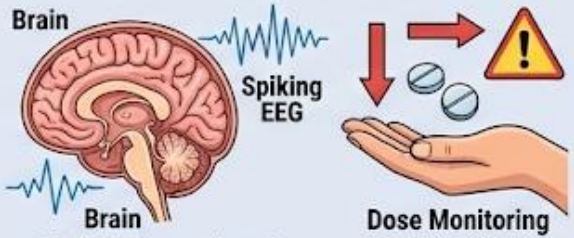
2) Orthostatic Hypotension, Bradycardia, & Syncope

Risk of Severe Low Blood Pressure & Fainting

- Severe low blood pressure, slowed heart rate, fainting. Risk highest during initial titration.

3) Seizures

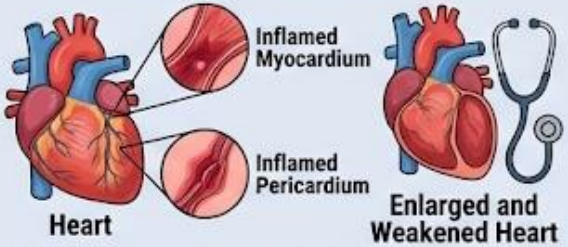
Dose-Related Seizure Risk



- Risk is dose-related.
- Patients must be monitored for seizure activity.

4) Myocarditis, Pericarditis, & Cardiomyopathy

Risk of Heart Muscle Inflammation



- Especially during first month.
- Signs: chest pain, rapid heart rate, fatigue.

5) Increased Mortality in Elderly Patients with Dementia-Related Psychosis

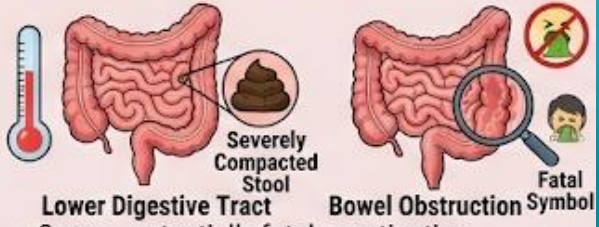
Class-Wide Warning for Antipsychotics

- Not approved for dementia.
- All antipsychotics carry this higher risk of death in this population.

6) Severe Constipation leading to Bowel Obstruction (July 2024 Update)

NEW UPDATE

Strengthened Warning: Potentially Fatal



- Severe, potentially fatal constipation.
- Can lead to bowel obstruction, fecal impaction, paralytic ileus. Monitor bowel function weekly.

KEY ADVERSE DRUG REACTIONS (ADRs) LINKED TO CLOZAPINE.

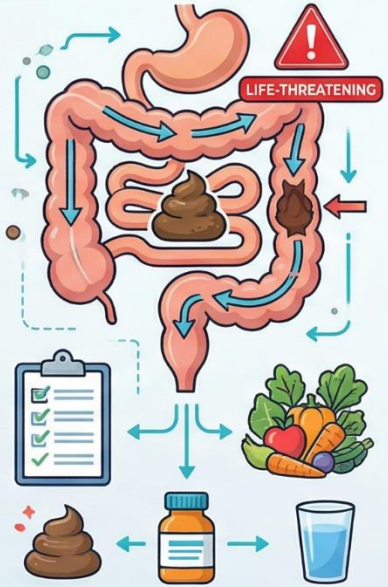
1 METABOLIC SYNDROME & WEIGHT GAIN

Monitor rapid increases in weight & waist circumference.

Screen for diabetes & dyslipidemia every 6-12 months.

Monitor metabolic parameters (lipids, glucose).

2 CONSTIPATION & GI HYPOMOTILITY



Constipation can be fatal.

Prophylactic laxatives & dietary measures often required.

3 SIALORRHEA, SEDATION, & TACHYCARDIA

SIALORRHEA (DROOLING)

Common drooling.
Monitor aspiration risk.

SEDATION (DROWSINESS)

Assess sedation level.

TACHYCARDIA (RAPID HEART RATE)

Routinely assess & manage.

4 OTHER KEY ADRs

Gastroesophageal Reflux (Heartburn/Acid Reflux)

Nocturnal Enuresis (Bedwetting)

Low BP reading

Orthostatic Hypotension

Sleep Apnea

Seizures

Sexual Dysfunction

Monitor for reflux, enuresis, dizziness, sleep apnea, seizures, sexual issues.

Consensus on Monitoring Protocols

Initiation Phase: Weekly ANC Monitoring

First 18 weeks require weekly absolute neutrophil count checks

Transition to Monthly Monitoring

After 18 weeks, ANC monitored every 4 weeks until 2 years

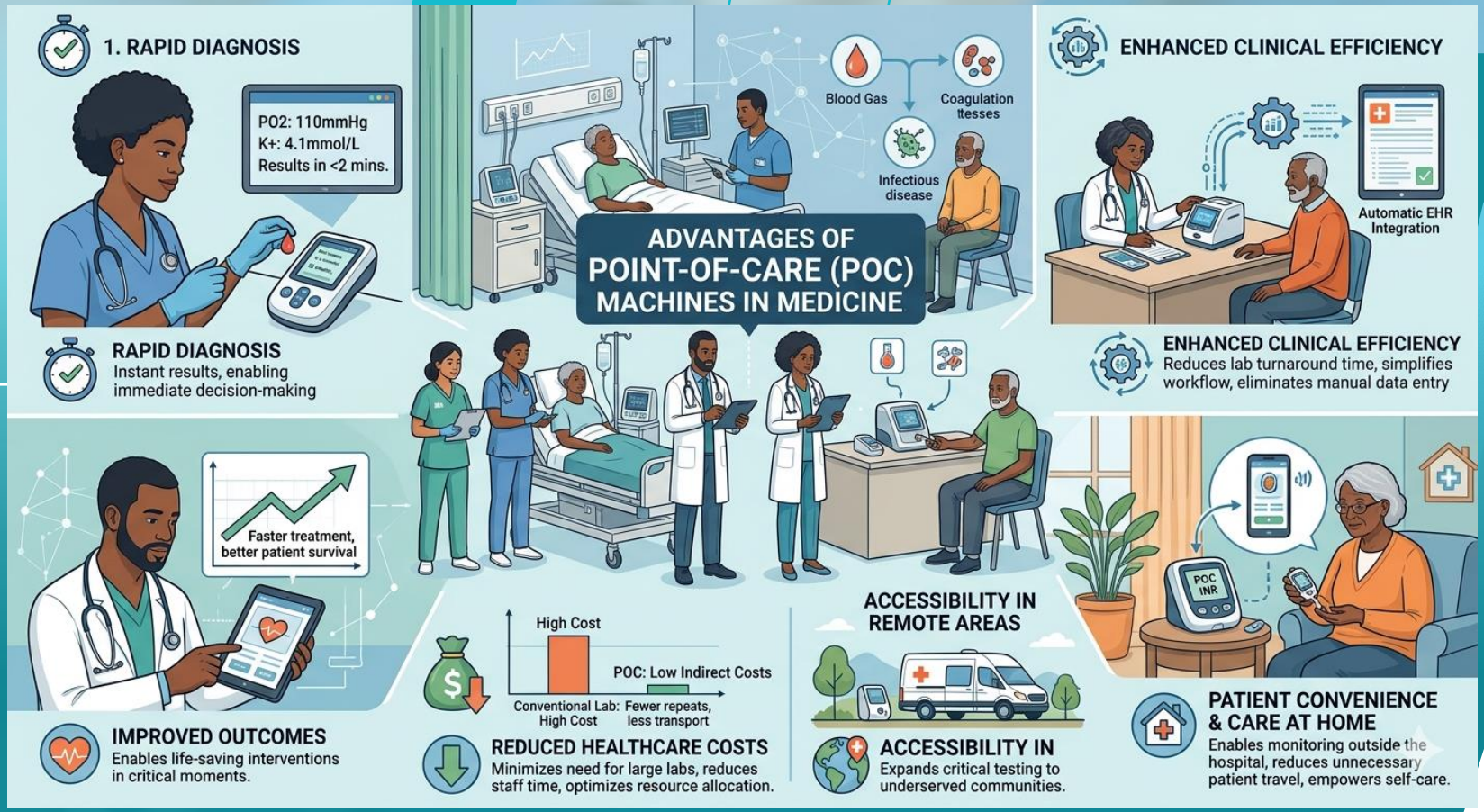
Discontinuation of Routine ANC Monitoring

Routine ANC monitoring can be stopped after 2 years if stable

Ongoing ADR Surveillance

Adverse drug reactions reviewed every 3 months after 2 years

POINT OF CARE (POC)




Athelas
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Beyond "Refer Out": Breaking the Silos of Physical and Mental Health

Collaborative Psychiatric and Medical Services

Infrastructure and Training Overview

Clinical Facilities Overview

Our largest psychiatric clinic features two functional medical exam rooms for comprehensive assessments.

Both clinics are involved in a metabolic syndrome initiative to provide specialized patient care.

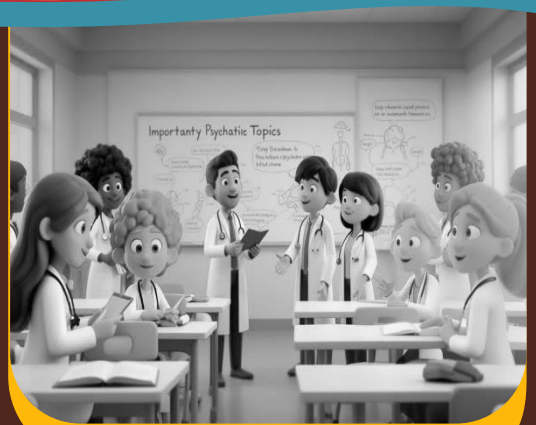
Collaborative Care Initiatives

Quarterly Collaborative Meetings

Regular meetings enhance communication and care coordination among various healthcare providers.

Integrated Educational Approach

Residents from psychiatry and family practice participate in joint educational sessions to promote collaboration.



Joint Projects with Public Health, Primary Care, and Psychiatry

- Vaccinations
- Infectious Disease
- PEP/PREP

Training for Psychiatric Providers

EKG Review Course

Providers gain crucial skills to interpret EKGs and recognize cardiac issues in patients.

Chest Pain Assessment Training

Training equips providers to swiftly identify and address chest pain symptoms in psychiatric patients.

Pregnancy Physiology Training

Education on pregnancy allows providers to cater to the specific needs of pregnant psychiatric patients.

Metabolic Syndrome Management

Providers learn to identify and manage metabolic syndrome to improve health outcomes in patients.

Training for Non-Psychiatric Providers

A. Providers learn to assess and treat pediatric eating disorders, enhancing their management skills.

B. Diagnosis and treatment of child and adolescent depressive and anxiety disorders for pediatricians.

C. Instruction in non-stimulant ADHD treatments provides alternative strategies for managing affected patients.

D. Providers are educated on non-benzodiazepine anxiety treatments, broadening their therapeutic approaches.

E. An evidence-based psychiatry guide is available, assisting non-psychiatrists in delivering quality care.

Under the Hood: Why the 2025 Update Changed the Engine of Hypertension Risk Assessment

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Blood Pressure Categories

American Heart Association.

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (top/upper number)		DIASTOLIC mm Hg (bottom/lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120–129	and	LESS THAN 80
STAGE 1 HYPERTENSION (High Blood Pressure)	130–139	or	80–89
STAGE 2 HYPERTENSION (High Blood Pressure)	140 OR HIGHER	or	90 OR HIGHER
SEVERE HYPERTENSION (If you don't have symptoms*, call your health care professional.)	HIGHER THAN 180	and/or	HIGHER THAN 120
HYPERTENSIVE EMERGENCY (If you have any of these symptoms*, call 911.)	HIGHER THAN 180	and/or	HIGHER THAN 120

*symptoms: chest pain, shortness of breath, back pain, numbness, weakness, change in vision or difficulty speaking

heart.org/bplevels

HYPERTENSION UPDATE

(Updates in diabetes and lipids)

Universal Blood Pressure Target

The new guidelines set a universal target of **less than 130/80** mmHg for essential hypertension management in all adults.

Prevention of Cognitive Decline

Keeping systolic blood pressure under 130 mmHg is Class 1A for reducing dementia and cognitive impairment risk, especially in psychiatric patients.

Advanced Risk Prediction

The PREVENT equation uses advanced models to help clinicians predict risk and guide timely medication for hypertension.

2025 AHA BLOOD PRESSURE GUIDELINES

1. When to Start Medication

The decision to start medication is now heavily driven by a patient's **overall cardiovascular risk**, calculated using the new **PREVENT™** tool (which replaced the older ASCVD risk calculator).

Stage 1 Hypertension (130–139 / 80–89 mmHg):

- **Start Meds Immediately if:** The patient has a 10-year CVD risk of **≥7.5%** (per PREVENT), or has established Cardiovascular Disease (CVD), Diabetes, or Chronic Kidney Disease (CKD).
- **Lifestyle First if:** The 10-year risk is **<7.5%**. Try lifestyle changes for 3–6 months. If BP remains ≥130/80, medication is then recommended.

Stage 2 Hypertension (≥140/90 mmHg):

- **Action:** Start medication immediately for all patients. Guidelines now recommend starting with **two medications** at once (ideally a single-pill combination) for faster control and better adherence.

BLOOD PRESSURE TARGETS

Population	Target BP (mmHg)	Key Reason / Clinical Note
General Adults	<130 / 80	Goal is to get as close to **<120/80** as possible.
Diabetes	<130 / 80	Intensive control is vital to prevent microvascular damage.
Chronic Kidney Disease (CKD)	<120 (Systolic)	New protocols (including KDIGO 2024/2026) favor a lower systolic target to slow progression.
Elderly (≥65 years)	<130 / 80	Lowering BP is now a Level 1A recommendation to prevent **dementia and cognitive decline.**
Pregnancy	<140 / 90	Targets are higher to maintain placental perfusion; therapy is adjusted if BP exceeds 140/90.

RACE AND HYPERTENSION

PSYCHIATRY AND HYPERTENSION

HTN & PSYCH MEDS

Medication Class	Example(s)	Incidence of BP Elevation	Clinical Characterization
SNRIs	Venlafaxine (Effexor)	3% to 13%	Highly dose-dependent; risk significantly increases above 300 mg/day.
Stimulants	Adderall, Ritalin	5% to 15%	Usually a modest mean increase (1–4 mmHg), but can be severe in a subset.
NRIs	Atomoxetine (Strattera)	6% to 12%	~10% of patients experience a "clinically important" rise (≥15–20 mmHg).
NDRIs	Bupropion (Wellbutrin)	~2%	Generally low risk; slightly higher incidence in SR/XL vs. placebo (~1% vs 2%).
MAOIs	Phenelzine (Nardil)	High (Potential)	Risk is primarily "Hypertensive Crisis" (acute) rather than chronic elevation.
Antipsychotics	Clozapine, Olanzapine	20% to 50%	Indirect risk; secondary to weight gain and metabolic syndrome development.
S-Ketamine	Esketamine (Spravato)	Very High (Transient)	Transient spikes (e.g., +20 mmHg) occur shortly after dosing in most patients.

The Evidence Blueprint: Using Global Algorithms to Solve Local Clinical Challenges

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INTEGRATE (Lancet Psychiatry, March 2025)

What Are the INTEGRATE Guidelines?

- An international consensus framework developed by experts from 30 United Nations regions, designed to standardize schizophrenia care using practical, algorithm-based decision support.

Why They Matter

- Balance clinical efficacy with patient-centered outcomes
- Built for real-world adaptability, not rigid sequencing
- Emphasize shared decision-making throughout treatment

Equity-Driven Development

- Included people with schizophrenia in guideline creation.
- Represented diverse populations across ethnicity, gender, and age

Clinical Recommendations -- Core Guiding Principles

- Prioritize metabolic health from treatment initiation
- Ensure early assessment and intervention for non-response
- Address SUD
- Tailor treatment to specific symptom domains
- Actively anticipate and mitigate side effects
- Initiate clozapine without delay for treatment-resistant schizophrenia

Clinical Takeaway

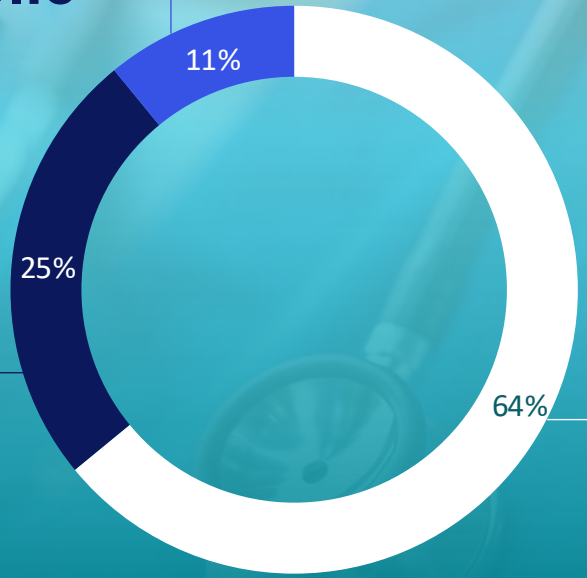
- A globally informed, locally adaptable blueprint that supports timely, equitable, and evidence-based schizophrenia care.

Beyond the Scale: A New Era of Pharmacological Shields Against Metabolic Drift

Beyond the Scale: A New Era of Pharmacological Shields Against Metabolic Drift

Beyond BMI

Prioritizing Urine Albumin-to-Creatinine Ratio (UACR) to detect early renal/metabolic stress.



Metabolic "Priming" Prevention

Initiating Metformin or GLP-1 RAs (e.g., semaglutide) concurrently with high-risk antipsychotics (Clozapine/Olanzapine).

Metabolic Age/Metabolic Syndrome Index

Using multi-factor assessments to communicate risk to patients effectively.

Rewiring the Highs and Lows: Neuroplasticity-Based Approaches to Long-Term Recovery in Bipolar Disorder

Rewiring the Highs and Lows: Neuroplasticity-Based Approaches to Long-Term Recovery in Bipolar Disorder

Monthly Injectable Treatments:

Long-acting injectables provide stable mood management for Bipolar I, reducing the need for daily medication.

Nutraceutical Adjuncts:

By 2026 standards, supplements such as Omega-3 fatty acids and NAC are recognized as evidence-based adjuncts in bipolar care.

FDA-Approved Pharmacotherapy for Bipolar Disorder

Medication	Acute Mania/Mixed	Bipolar Depression	Mainte-nance	DX	Therapy Mode
Aripiprazole	✓	—	✓	BPI	Mono & Adjunct
Asenapine	✓	—	—	BPI	Mono & Adjunct
Carbamazepine (ER)	✓	—	—	BPI	Monotherapy
Cariprazine	✓	✓	—	BPI	Monotherapy
Chlorpromazine	✓	—	—	BPI	Monotherapy
Divalproex Sodium	✓	—	—	BPI	Mono & Adjunct
Lamotrigine	—	—	✓	BPI	Monotherapy
Lithium	✓	—	✓	BPI	Monotherapy
Lumateperone	—	✓	—	BPI & BPII	Mono & Adjunct
Lurasidone	—	✓	—	BPI	Mono & Adjunct
Olanzapine	✓	—	✓	BPI	Mono & Adjunct
Olanzapine/Fluoxetine	—	✓	—	BPI	Monotherapy
Olanzapine/Samidorphan	✓	—	✓	BPI	Mono & Adjunct
Quetiapine (IR/XR)	✓	✓	✓	BPI (M/D/Mn) & BPII (D)	Mono (M/D), Adjunct (Mn)
Risperidone	✓	—	—	BPI	Mono & Adjunct
Risperidone (LAI)	—	—	✓	BPI	Mono & Adjunct
Ziprasidone	✓	—	✓	BPI	Mono (M), Adjunct (Mn)

Long-Acting Injectables (LAIs) for Bipolar I Disorder

Medication (Brand Name)	Active Ingredient	Injection Type & Site	Dosing Interval	Oral Lead-in Period
Abilify Asimtufii	Aripiprazole	IM (Gluteal)	Every 2 months	14 days
Abilify Maintena	Aripiprazole	IM (Gluteal or Deltoid)	Every 4 weeks	14 days
Uzedy	Risperidone	SC (Abdomen or Upper Arm)	Once monthly	Not required if already on oral risperidone
Risperdal Consta	Risperidone	IM (Gluteal or Deltoid)	Every 2 weeks	3 weeks
Rykindo	Risperidone	IM (Gluteal)	Every 2 weeks	Not required if already on oral risperidone

Precision Pro Re Nata: Using Data to Decipher the "Why" Behind the Dose

Precision Pro Re Nata: Using Data to Decipher the "Why" Behind the Dose

Arguments against PRN Antipsychotics

The prevailing body of recent clinical literature presents compelling arguments against the routine administration of PRN antipsychotics, primarily due to concerns regarding safety risks and the absence of substantiated efficacy.

- **Lack of High-Quality Evidence**
- **Risk of Polypharmacy and High Dosing**
- **Increased Adverse Effects**
- **Poor Clinical Outcomes**

Precision Pro Re Nata: Using Data to Decipher the "Why" Behind the Dose

Medication	Primary Sedative Mechanism	Sedation Incidence	Half-Life ($t_{1/2}$)	Peak Time (T_{max})	Dosing/Titration Strategy
Clozapine	Max H_1 & α_1 blockade	35–45%	~12–14h*	1.5–2.5h	Split dosing; heavy HS load; slow titration for α_1 safety.
Quetiapine (IR)	High H_1 affinity	25–35%	~6–7h	1–1.5h	BID/TID for psychosis; HS for sleep (though off-label).
Olanzapine	High H_1, M_1, & α_1	20–30%	~30h	6h	Once daily at HS; long $t_{1/2}$ minimizes "peak-trough" fluctuations.
Asenapine (SL)	High H_1 & α_1	15–20%	~24h	0.5–1.5h	BID (sublingual); caution patient on rapid post-dose sedation.
Iloperidone	Extreme α_1 blockade	~15%	18–33h**	2–4h	BID titration required to mitigate orthostatic hypotension.

SUBLINGUAL ANTIPSYCHOTICS

Asenapine (Saphris)

Perhaps the best-known, it is available only as a sublingual tablet because it is poorly absorbed when swallowed.

Clozapine (Fazaclo)

Available as an Orally Disintegrating Tablet (ODT). While this formulation is intended for dissolution on the tongue followed by ingestion, numerous clinicians administer it sublingually to expedite absorption.

Olanzapine (Zyprexa Zydis)

Similar to clozapine, this ODT formulation is frequently used for rapid stabilization.

Risperidone (Risperdal M-Tab)

Risperidone (Risperdal M-Tab): An ODT version often used for patients who may "cheek" or refuse to swallow standard pills.

Xanomeline and Trospium Chloride (Cobenfy): Novel Antipsychotic Approach

Xanomeline and Trospium Chloride (Cobenfy): Novel Antipsychotic Approach

Non-Dopaminergic Mechanism of Action

Reduced Side Effects

Cobenfy for Schizophrenia: Ideal Patient Profiles

Understanding the Suitable Patient Categories and Clinical Benefits

Overview of Patient Profiles

A. Cobenfy benefits various patient categories effectively.

B. It aids those with treatment-emergent side effects.

C. Patients responding poorly to standard treatments find hope.

D. Addressing cognitive and negative symptoms enhances overall care.

E. It offers a solution for those with prolactin concerns.

Patient Categories I

Metabolic and Motor Side Effect Sensitivity

Patients sensitive to EPS, dyslipidemia, or weight gain find relief with Cobenfy, which shows no major metabolic difference from placebo, ensuring a safer profile.

Responding to D2 Antagonist Limits

Cobenfy's dual M1/M4 agonist action offers an alternative for patients with suboptimal responses to traditional D2 antagonists, allowing for effective treatment.

Patient Categories II

Addressing Negative and Cognitive Symptoms

Cobenfy shows potential in addressing negative and cognitive symptoms of schizophrenia, providing a comprehensive treatment without emotional blunting associated with dopamine blockade.

Managing Prolactin Levels

This treatment helps manage prolactin levels effectively, minimizing risks for patients who are sensitive to prolactin elevation, which can complicate their treatment.

Minimizing sexual side effects

Cobenfy provides a compelling option for patients wanting minimal sexual side effects, as it mitigates the sexual dysfunction often associated with traditional antipsychotics. This allows patients to maintain a better quality of life while managing their schizophrenia effectively.

Pill Fatigue: The End of Clinical Inertia

- Rapid Long-Acting Injectables
- Novel Delivery Methods
- Weekly/Twice Yearly Medication Formulations
- Neuromodulation -- Electroconvulsive Therapy (ECT) & Transcranial Magnetic Stimulation (TMS)

Metric	ECT	TMS
Efficacy (Response)	70% – 90%	50% – 60%
Speed of Action	Very Rapid (1–2 weeks)	Gradual (4–6 weeks)
Systemic Impact	Requires GA and Oxygenation	None
Cognitive Impact	Retrograde/Anterograde Amnesia risk	None (Often improves cognition)
Main Safety Risk	Cardiovascular stress, Status Epilepticus (rare)	Seizure ($<0.1\%$)

Neuromodulation

Neuromodulation

Metric	ECT	TMS
Efficacy (Response)	70% – 90%	50% – 60%
Speed of Action	Very Rapid (1–2 weeks)	Gradual (4–6 weeks)
Systemic Impact	Requires GA and Oxygenation	None
Cognitive Impact	Retrograde/Anterograde Amnesia risk	None (Often improves cognition)
Main Safety Risk	Cardiovascular stress, Status Epilepticus (rare)	Seizure ($<0.1\%$)

Feature	Electroconvulsive Therapy (ECT)	Transcranial Magnetic Stimulation (TMS)
Primary Indications	• Major Depressive Disorder (Unipolar/Bipolar) • Treatment-Resistant Depression (TRD) • Catatonia (Lethal or Non-lethal) • Acute Mania / Mixed Episodes • Schizoaffective Disorder / Refractory Schizophrenia • High Suicide Risk / Nutritional Refusal	• Treatment-Resistant Depression (MDD) • Anxious Depression (MDD with comorbid anxiety) • Obsessive-Compulsive Disorder (OCD) — Deep TMS (H-Coil) • Smoking Cessation — Deep TMS (H-Coil) • Migraine (Acute/Prophylactic) — sTMS
Absolute Contraindications	• None (per the APA, if the procedure is lifesaving), however, traditionally considered: • Increased Intracranial Pressure (ICP) / Space-occupying lesions • Recent Myocardial Infarction (within <3 months) — considered high-risk relative	• Non-removable ferromagnetic metal in or within 30cm of the head (e.g., aneurysm clips, coils, stents, cochlear implants, bullet fragments). • Deep Brain Stimulators (DBS). • Implanted Vagus Nerve Stimulators (VNS) or Pacemakers (distance dependent).
Relative Contraindications	• Unstable Aneurysm (Cerebral or Aortic) • Recent Stroke / Intracranial Hemorrhage • Pheochromocytoma • Severe Pulmonary Disease (COPD/Asthma) • High-risk for General Anesthesia (ASA Class 4/5) • Retinal Detachment	• History of Epilepsy or Seizure Disorder. • Medications that significantly lower the seizure threshold (e.g., high-dose Bupropion, Clozapine). • Substance withdrawal (Alcohol/Benzodiazepines). • Traumatic Brain Injury (TBI) with cortical damage.