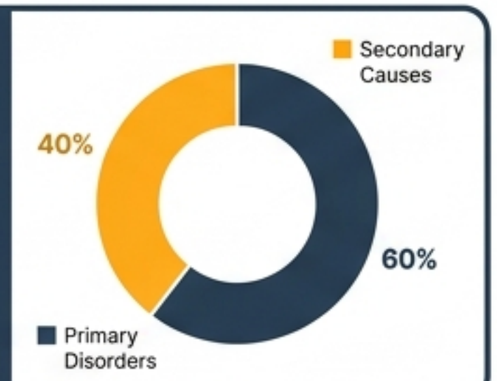
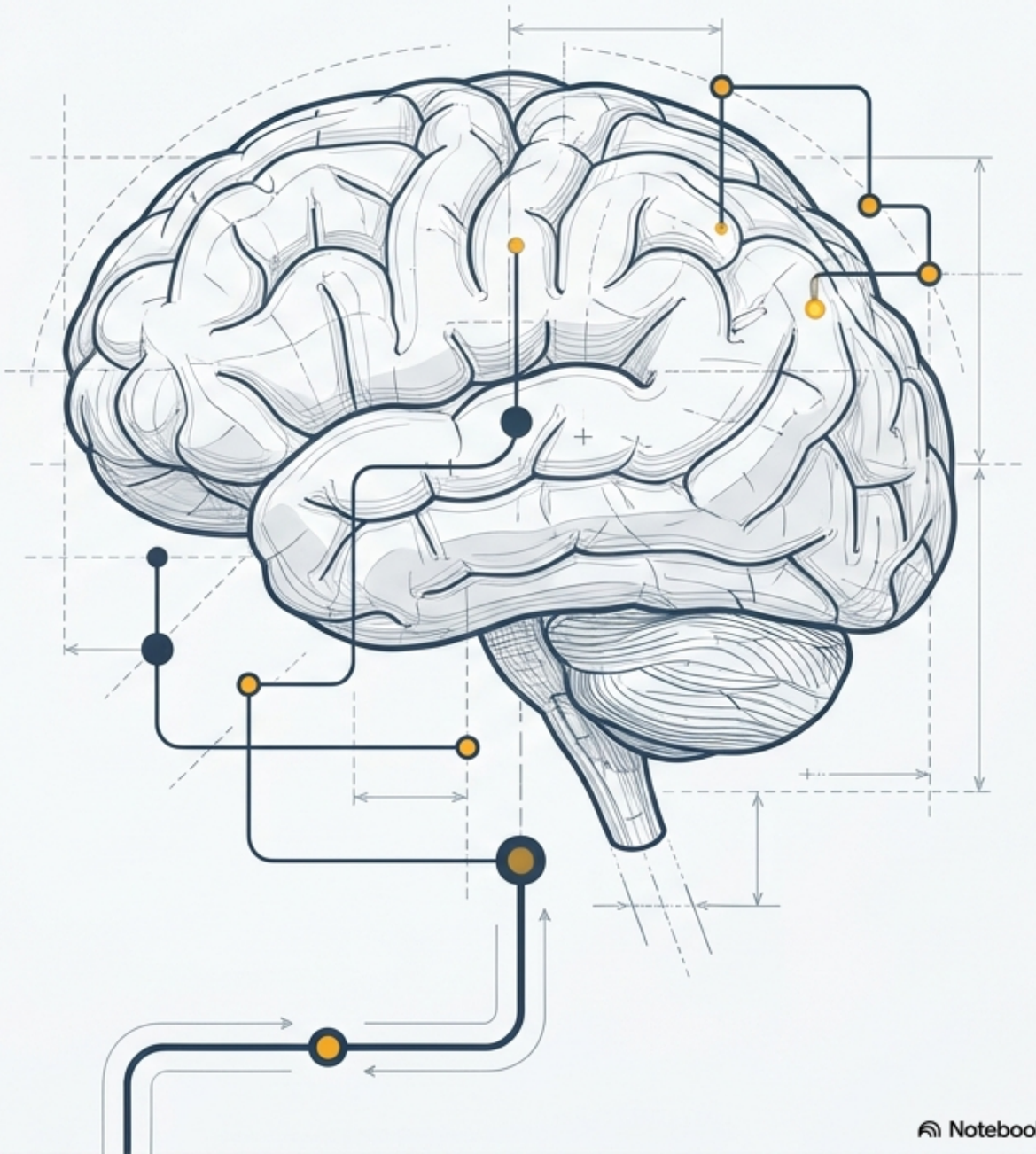
First-Break Psychosis Workup

A comprehensive diagnostic blueprint for first-episode psychosis (FEP)—from universal screening to atypical etiology investigation.

THE CLINICAL MISSION

Primary psychiatric disorders (Schizophrenia, Bipolar) account for ~60% of FEP. The workup exists to systematically identify and rule out the secondary, medically-driven causes hiding in the remaining 40%.





NotebookLM

The Urgency of Time: Duration of Untreated Psychosis (DUP)

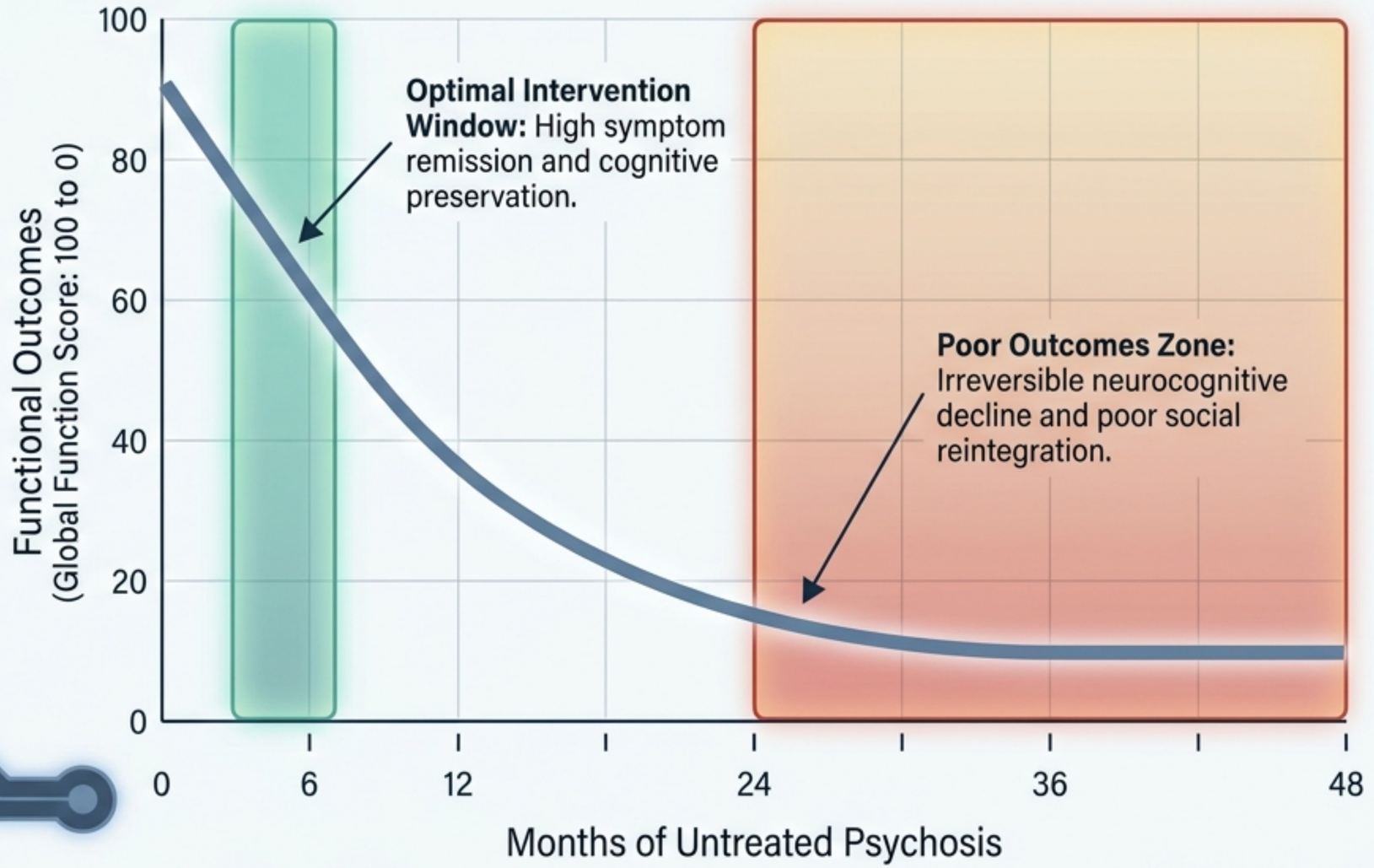
Defining the Event

The Threshold:

FEP is the inaugural presentation of frank psychosis (hallucinations, delusions, thought disorganization) meeting criteria for >1 week.

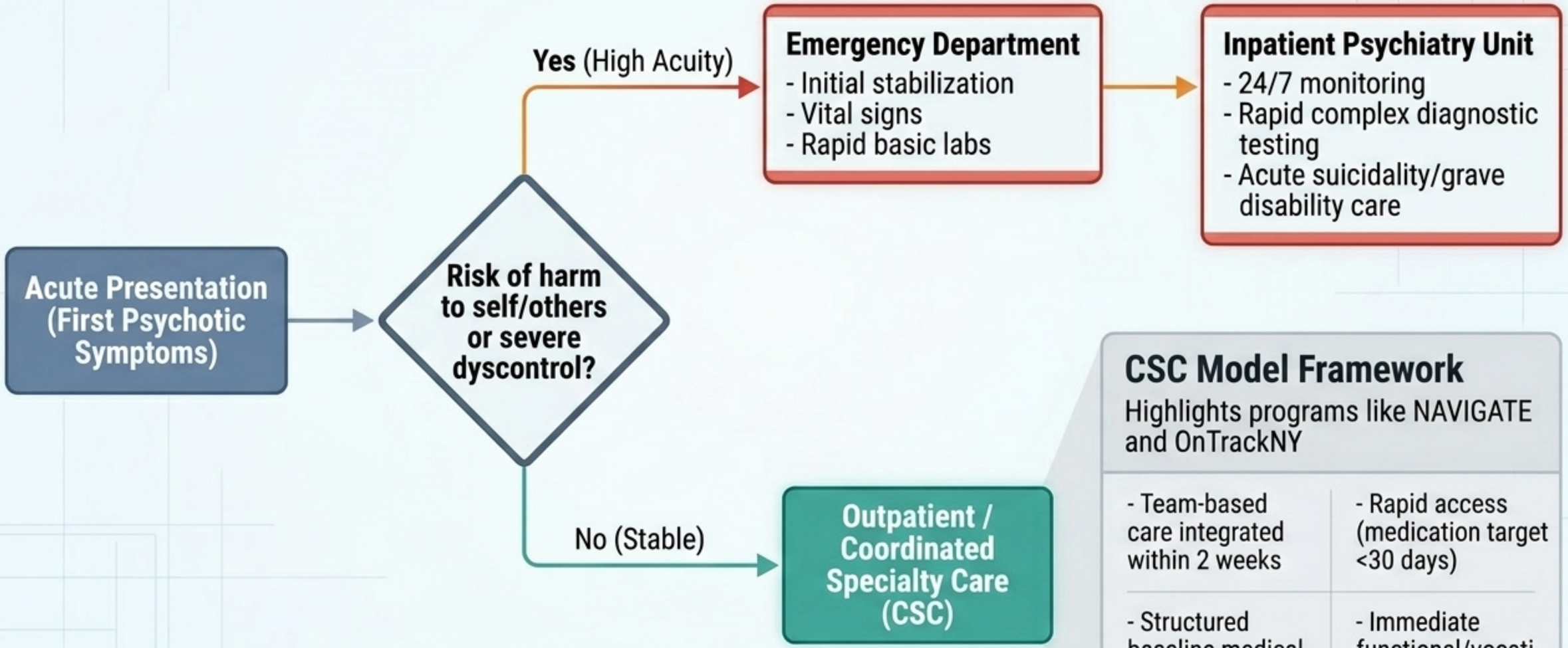
Demographics:

Median onset ages 15–35; males typically present 2–3 years earlier than females.



NotebookLM

Setting of Care and Initial Triage



NotebookLM

The Universal Filter: Essential Baseline Workup

Universal Labs

Test	Clinical Rationale
CBC	Infection (WBC), anemia, hematologic malignancy
CMP	Renal/hepatic baseline, hyponatremia, hyperglycemia
TSH	Thyroid disease (causes >2% of secondary psychosis)
UA/UDS	Substance-induced psychosis (~20-30% of FEP)
RPR/VDRL	Neurosyphilis screen
HIV	Late-stage HIV dementia/opportunistic infections
B12/Folate	Neuropsychiatric deficiency syndrome
ESR/CRP	Systemic inflammation (elevated in ~30% of FEP)

Clinical Exams

☑ Neurological

- ☑ - Cranial nerves
- ☑ - Motor tone/gait
- ☑ - Reflexes (Babinski)
- ☑ - Cerebellar signs

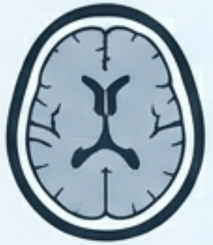
☑ Mental Status

- ☑ - Orientation
- ☑ - Cognition
- ☑ - Executive function
- ☑ - Thought process

Structural Imaging

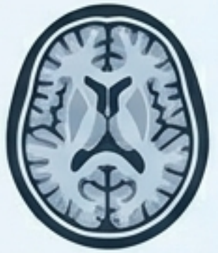
Head CT (Non-contrast)

Rapid screen. 95% sensitive for acute stroke, 85% for mass >1cm.



Brain MRI (3T Preferred)

Superior resolution for parenchymal abnormalities and demyelinating disease.



NotebookLM

Recognizing the Clinical Red Flags

Typical FEP onset is insidious and occurs between ages 15–35. The presence of any indicator below signals a likely secondary etiology and instantly pivots the patient to the Expanded Workup.

Age Extremes

Onset before age 15 or after age 40.

Acuity

Hyper-acute onset (hours to days).

Systemic Symptoms

Unexplained fever, rash, or vital sign instability.

Neurological

Focal neurological signs or previous head trauma.

Seizures

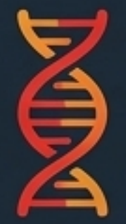
Any observed or suspected seizure activity.

Catatonia

Immobility, mutism, or waxy flexibility.

Cognitive Decline

Rapid deterioration in consciousness or memory.



Family History

Known family history of neurological or autoimmune disease.

NotebookLM

The Expanded Workup: Immunology & Metabolism

Immunological & Autoimmune Markers

ANA (Antinuclear Antibody)

Screens for SLE cerebritis. Positive in ~40% of SLE; can cause acute psychosis before rash appears. (Confirmatory: C3, C4, anti-dsDNA).

Anti-NMDA Receptor Antibody

Screens for Autoimmune Encephalitis. CSF testing is more sensitive than serum.

RULE: Psychosis + Movement Disorder + Seizures = Encephalitis until proven otherwise.

Rare Marker Panels

Anti-GABA B, anti-LGI1, anti-Caspr2 (Testing via specialized immunology labs).

Metabolic & Genetic Disorders

Ceruloplasmin & Serum Copper

Screens for Wilson's disease (presents ages 15-35). Low ceruloplasmin (<20 mg/dL) is highly specific. Look for psychosis + tremor/dystonia.

Heavy Metals

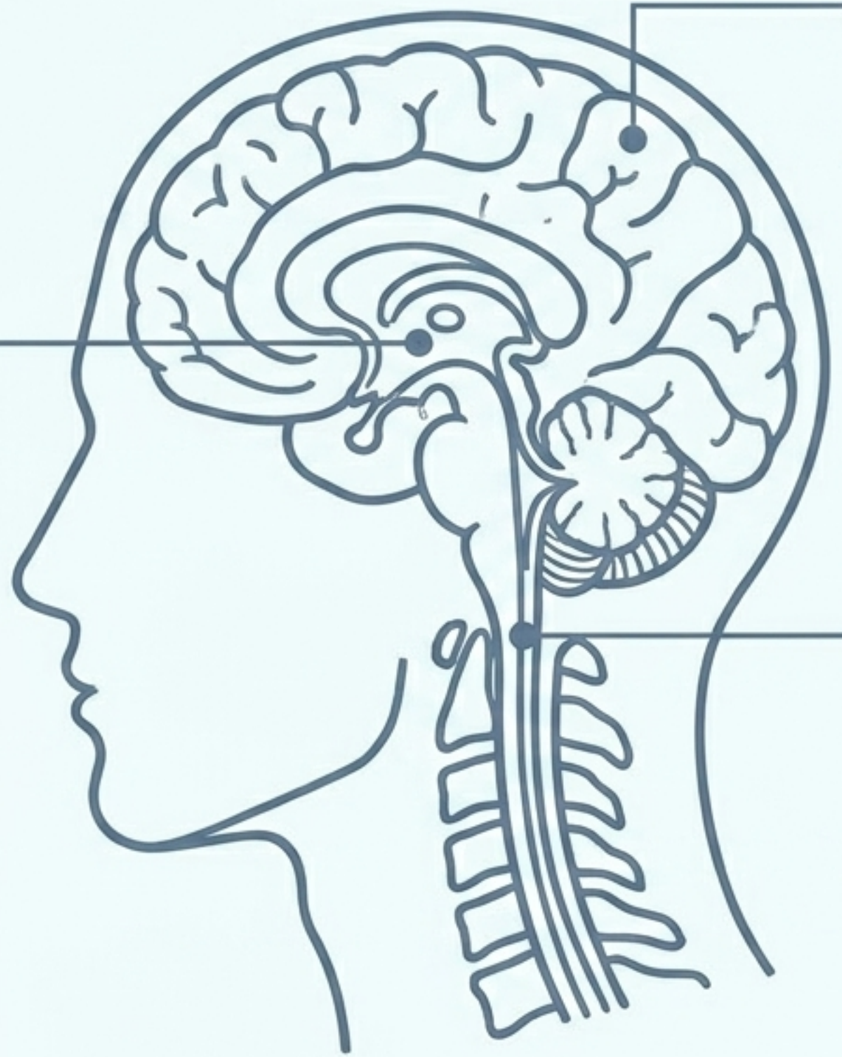
Lead (encephalopathy, ataxia) and Mercury (tremor, personality changes) via serum or 24-hour urine.

Homocysteine

Assesses one-carbon metabolism (MTHFR variants).

NotebookLM

The Expanded Workup: Neurophysiology & Advanced Imaging



EEG & Continuous Monitoring

Indicated for suspected seizures or catatonia. Crucial for ruling out nonconvulsive status epilepticus (50-70% sensitivity).

Advanced MRI Sequences

- **Contrast**: Inflammation / BBB disruption
- **DWI:** Acute stroke / encephalitis
- **FLAIR:** Demyelination
- **SWI:** Microhemorrhages

Lumbar Puncture (CSF Analysis)

Triggers on fever/stiff neck. Tests cell count, viral PCR, Anti-NMDA titers, Oligoclonal bands.

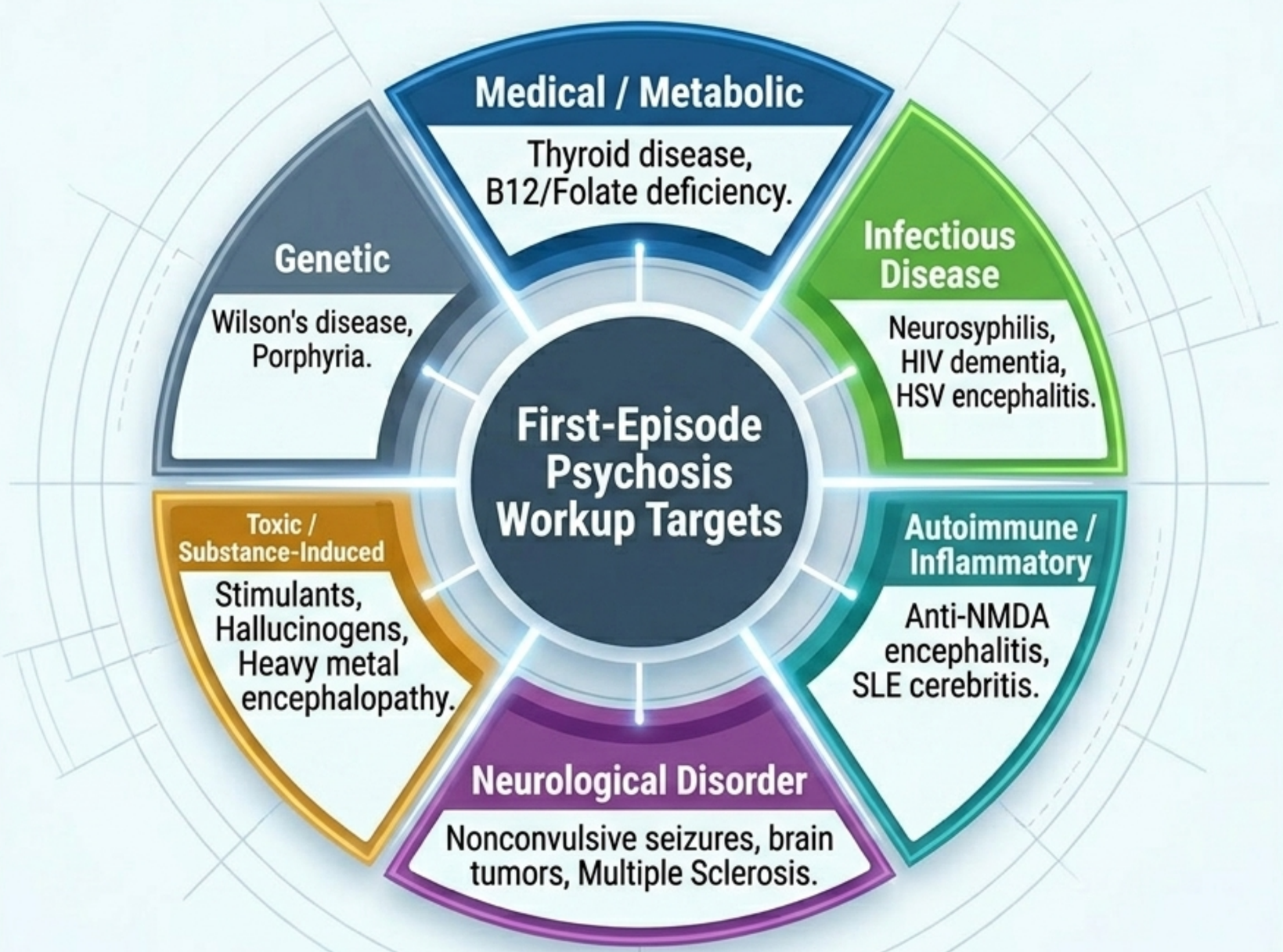
NotebookLM

Diagnostic Pathology Mapping Matrix

Diagnostic Test	Pathology Ruled In	Pathology Ruled Out / Prevalence
TSH / Free T4	Hyper/Hypothyroidism	Rules out thyroid-induced psychosis (~2-3% of FEP).
RPR / VDRL	Treponema pallidum	Negative effectively rules out neurosyphilis (0.5–2% prevalence).
Urine Drug Screen	Amphetamines, PCP, Cannabis	Negative does not exclude if use >48-72 hrs prior. Accounts for ~20-30% of FEP.
B12 / Folate	Subacute combined degeneration	~5–10% of psychiatric populations have deficiency.
Ceruloplasmin	Wilson's disease	Highly specific (<20 mg/dL). Rare (1:30,000) but highly treatable.
Anti-NMDA / Auto-antibodies	Autoimmune encephalitis	Positive in 1–3% of psychotic first episodes. CSF more specific than serum.
Head CT / MRI	Mass, hemorrhage, MS	Abnormalities found in 10–20% of FEP cases.

NotebookLM

The Differential Diagnosis Wheel



NotebookLM

Risk Stratification Profiles

Low Risk Profile (Standard Pathway)

- Age 18–35
- Insidious onset
- Family history of schizophrenia
- Normal basic labs and neurological exam

Clinical Action: Proceed with standard FEP care and antipsychotic initiation.

High Risk Profile (Expanded Pathway)

- Age extremes (<15 or >40)
- Acute presentation (hours/days)
- Fever, rash, or catatonia
- Rapid cognitive decline

Clinical Action: Prioritize expanded workup **BEFORE** antipsychotic initiation.

Specialist Consultation Triggers

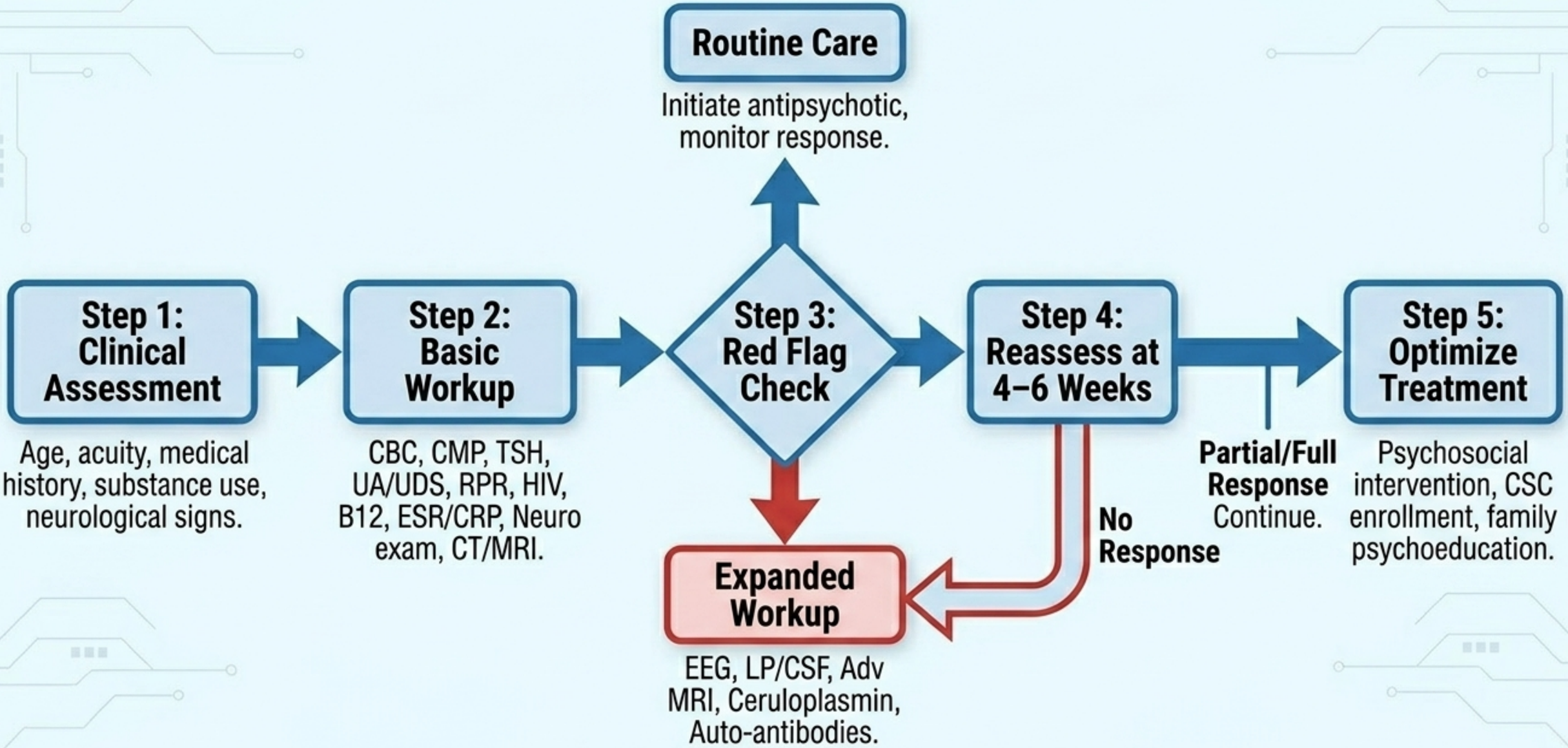
Neurology: Focal signs, seizures, movement disorders.

Rheumatology/Immunology: ANA positive, suspected autoimmune encephalitis.

Infectious Disease: RPR+, HIV+, CSF abnormalities.

NotebookLM

The Master Clinical Algorithm



NotebookLM

Outcomes & Monitoring Timeline

Week 0: Presentation

Initial assessment, basic/expanded, basic/expanded workup, safety evaluation.

Weeks 1–2: Early Response

Dosage optimization, side effect monitoring, family psychoeducation begins.

Weeks 3–6: Therapeutic Window

Peak therapeutic response emerges (target 20-30% symptom reduction).

Weeks 6–12: Consolidation

Continue monotherapy, repeat metabolic labs, begin cognitive remediation.

3–12 Months: Functional Recovery

Functional integration, return to work/school. Plan maintenance vs discontinuation.

NotebookLM

Core Clinical Pearls

DUP Dictates Destiny.

Every single month of delayed treatment actively worsens long-term functional and neurocognitive trajectories. Time is brain.

Never Skip the Basics.

UA, CBC, CMP, and TSH are non-negotiable. ~20-30% of FEP cases have concurrent substance use.

Beware the Encephalitis Triad.

Psychosis + Movement Disorder + Seizures = Autoimmune Encephalitis until proven otherwise.

The 4-6 Week Rule.

A total lack of response to an adequate antipsychotic dose over 4-6 weeks means the diagnosis is likely wrong. Re-evaluate the differential.

NotebookLM