SCHIZOPHRENIA SPECTRUM AND OTHER PSYCHOTIC DISORDERS

Schizophrenia

SZ

DSM-5-TR 295.90 | ICD-10-CM F20.9

Chronic psychotic disorder marked by positive, negative, and cognitive symptoms with functional decline lasting 6 months or more.

LIFETIME PREVALENCE	TYPICAL ONSET	SEX RATIO	COURSE
~0.3-0.7% worldwide	Men 18-25; women 25-35	~1.4:1 male:female	Chronic; ~5% die by suicide

CLINICAL PICTURE

- Positive symptoms dominate acute episodes: persecutory or referential delusions, auditory hallucinations that comment or command, and disorganized speech.
- Negative symptoms drive long-term disability: blunted affect, alogia, avolition, anhedonia, and asociality that persist between psychotic episodes.
- Cognitive deficits of 1-2 standard deviations in working memory, processing speed, and executive function predict vocational outcome better than delusions.
- A prodrome of social withdrawal, declining grades, odd beliefs, and attenuated perceptual disturbance typically precedes frank psychosis by 1-3 years.
- Insight is frequently absent; anosognosia rather than defiance underlies much nonadherence and shapes engagement, capacity, and treatment planning.
- Grossly disorganized or catatonic behavior, poor grooming, and inappropriate affect emerge in severe presentations and raise the risk of self-neglect.

DIAGNOSTIC CRITERIA AT A GLANCE

- Two or more of delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, or negative symptoms for much of one month.
- At least one of the required symptoms must be delusions, hallucinations, or disorganized speech, anchoring the diagnosis in positive psychotic phenomena.
- Continuous signs of disturbance persist at least 6 months, including prodromal or residual periods where only negative or attenuated symptoms appear.
- Functioning in work, relationships, or self-care falls markedly below the prior level, or fails to reach expected milestones in youth-onset cases.
- Schizoaffective disorder and mood disorders with psychosis are excluded, and the picture is not attributable to a substance or medical condition.

NEUROBIOLOGY & PHYSIOLOGY

- Mesolimbic dopamine hyperactivity generates positive symptoms, while mesocortical D1 hypofunction in dorsolateral prefrontal cortex tracks negative and cognitive deficits.
- NMDA receptor hypofunction on parvalbumin interneurons disrupts gamma oscillations, a model supported by ketamine and phencyclidine psychotomimetic effects.
- Heritability approaches 80%; risk is highly polygenic with the strongest signal at the MHC locus, implicating complement C4-mediated synaptic pruning.
- Imaging shows lateral ventricular enlargement, reduced hippocampal and superior temporal gray matter, and accelerated cortical thinning after onset.
- Obstetric complications, winter birth, urban rearing, migration, and adolescent cannabis use interact with polygenic load in a neurodevelopmental model.
- Life expectancy is shortened 15-20 years, driven by cardiovascular disease, smoking, and antipsychotic-related metabolic syndrome more than by suicide.

PSYCHOLOGICAL MECHANISMS

- Aberrant salience attribution assigns motivational significance to neutral stimuli, and delusions form as explanatory frameworks that resolve that dysphoric ambiguity.
- Jumping-to-conclusions reasoning and an externalizing attributional bias sustain persecutory beliefs and are direct targets of cognitive therapy for psychosis.
- Source-monitoring failure misattributes inner speech to external agents, producing the phenomenology of voices experienced as originating outside the head.
- Social cognition deficits in theory of mind and emotion recognition predict community functioning independent of positive symptom severity.
- High expressed emotion in the family, meaning criticism, hostility, and emotional overinvolvement, roughly doubles relapse risk over 9-12 months.

DIFFERENTIAL & COMORBIDITY

- Distinguish from schizoaffective disorder, where mood episodes occupy most of the illness, and from bipolar or depressive disorders with psychotic features.
- Substance-induced psychosis from methamphetamine, cannabis, or synthetic cannabinoids resolves within days to weeks of abstinence; obtain urine toxicology.
- Rule out autoimmune encephalitis, temporal lobe epilepsy, neurosyphilis, HIV, Huntington disease, and steroid or anticholinergic effects in atypical onset.
- Tobacco use disorder affects 60-80% and substance use disorder roughly 50%; depression, obsessive-compulsive symptoms, and social anxiety worsen outcome.
- Lifetime suicide risk is roughly 5%, highest early in the illness with preserved insight; command hallucinations and violence risk require direct assessment.

Treatment EVIDENCE-BASED MANAGEMENT

PHARMACOLOGIC

- Second-generation antipsychotics are first line: **risperidone 2-6 mg/day**, **aripiprazole 10-30 mg/day**, or olanzapine 10-20 mg/day for 2-6 weeks before judging response.
- **Clozapine 300-450 mg/day** is the only agent proven in treatment resistance after two adequate trials; monitor ANC for agranulocytosis and screen for myocarditis.
- Long-acting injectables such as **paliperidone palmitate** or **aripiprazole monohydrate** cut relapse and rehospitalization and are reasonable after a first episode.
- Monitor weight, waist circumference, fasting glucose, and lipids at baseline, 3 months, then annually; **olanzapine** carries the heaviest metabolic burden.
- Watch for akathisia, parkinsonism, hyperprolactinemia, and QTc prolongation; **valbenazine** or deutetrabenazine treat established tardive dyskinesia.

PSYCHOTHERAPY

- **CBT for psychosis** over 16-24 sessions produces small to moderate reductions in positive symptom distress and is recommended when symptoms persist on medication.
- **Family psychoeducation** lasting 9 months or longer lowers relapse rates by roughly 20 percentage points by reducing expressed emotion and improving crisis planning.
- **Cognitive remediation** paired with a real work or school placement improves processing speed and functional outcome far more than isolated drill practice.
- **Social skills training** in structured, role-played modules improves conversational and self-care performance, though transfer to community settings is modest.
- **Coordinated specialty care** in first-episode psychosis integrates therapy, medication, employment support, and family work with better 2-year outcomes than usual care.

ADJUNCT & SUPPORTIVE

- **Supported employment** using the individual placement and support model places 55-60% into competitive jobs versus about 20% with prevocational training.
- **ECT** augments clozapine in refractory psychosis and is first-line for catatonia, typically delivered as 8-12 bilateral treatments over several weeks.
- Assertive community treatment, clubhouse programs, and supported housing reduce hospital days among high utilizers with poor outpatient engagement.
- Track severity with the **PANSS** or the briefer **BPRS**, and screen for abnormal movements with the **AIMS** every 6 to 12 months on any antipsychotic.
- Smoking cessation with **varenicline**, metformin for antipsychotic weight gain, and annual metabolic labs directly address the excess mortality gap.

CLINICAL PEARLS

- Duration of untreated psychosis is the strongest modifiable predictor of long-term outcome.
- Two failed antipsychotic trials means clozapine, not a third me-too agent.
- Negative symptoms, not delusions, decide whether the patient ever works again.

References

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NOTE

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