Psychology Research and Behavior Management

Dovepress

open access to scientific and medical research

Open Access Full Text Article

REVIEW

Identification of Psychosis Risk and Diagnosis of First-Episode Psychosis: Advice for Clinicians

Nancy B Lundin[1], Alexandra M Blouin[1], Henry R Cowan[1,2], Aubrey M Moe[1,3], Heather M Wastler[1], Nicholas JK Breitborde[1,3]

[1]Early Psychosis Intervention Center, Department of Psychiatry and Behavioral Health, The Ohio State University, Columbus, OH, USA; [2]Department of Psychology, Michigan State University, East Lansing, MI, USA; [3]Department of Psychology, The Ohio State University, Columbus, OH, USA

Correspondence: Nancy B Lundin, Early Psychosis Intervention Center, Department of Psychiatry and Behavioral Health, The Ohio State University, 1670 Upham Drive, Columbus, OH, 43210, USA, Tel +1 614 293 6361, Email Nancy.Lundin@osumc.edu

Abstract: Early detection of psychotic-spectrum disorders among adolescents and young adults is crucial, as the initial years after psychotic symptom onset encompass a critical period in which psychosocial and pharmacological interventions are most effective. Moreover, clinicians and researchers in recent decades have thoroughly characterized psychosis-risk syndromes, in which youth are experiencing early warning signs indicative of heightened risk for developing a psychotic disorder. These insights have created opportunities for intervention even earlier in the illness course, ideally culminating in the prevention or mitigation of psychosis onset. However, identification and diagnosis of early signs of psychosis can be complex, as clinical presentations are heterogeneous, and psychotic symptoms exist on a continuum. When a young person presents to a clinic, it may be unclear whether they are experiencing common, mild psychotic-like symptoms, early warning signs of psychosis, overt psychotic symptoms, or symptoms better accounted for by a non-psychotic disorder. Therefore, the purpose of this review is to provide a framework for clinicians, including those who treat non-psychotic disorders and those in primary care settings, for guiding identification and diagnosis of early psychosis within the presenting clinic or via referral to a specialty clinic. We first provide descriptions and examples of first-episode psychosis (FEP) and psychosis-risk syndromes, as well as assessment tools used to diagnose these conditions. Next, we provide guidance as to the differential diagnosis of conditions which have phenotypic overlap with psychotic disorders, while considering the possibility of co-occurring symptoms in which case transdiagnostic treatments are encouraged. Finally, we conclude with an overview of early detection screening and outreach campaigns, which should be further optimized to reduce the duration of untreated psychosis among youth.

Keywords: diagnostic assessment, early detection, recent-onset psychosis, clinical high risk for psychosis, psychosis continuum

Introduction

Psychotic-spectrum disorders such as schizophrenia have been recognized globally as among the most severe and debilitating health conditions that humans can experience.[1,2] Psychotic symptoms consist of positive symptoms such as hallucinations and delusions, negative symptoms such as diminished emotional expression and motivation, and disorganized symptoms such as incoherent speech and atypical behavior, and are often accompanied by disturbances in functioning, cognition, motor skills, and one's basic sense of self.[3–5] Symptom onset typically occurs from late adolescence to one's early twenties, an important developmental period referred to as emerging adulthood.[6] The onset of psychotic illness during emerging adulthood can lead to tremendous disruptions in key developmental milestones such as the formation and maintenance of meaningful interpersonal relationships, pursuit of educational and career aspirations, and exploration of personal identity and independence.[7]

Importantly, research has shown that these functional disruptions unfold rapidly within the first few years following onset of psychotic illness.[8–10] Moreover, longer duration of untreated psychosis (i.e., the delay between onset of psychotic symptoms and receipt of adequate mental health care) has been repeatedly shown to relate to poorer outcomes, including increased psychotic symptom severity, suicide risk, and criminal justice involvement, reduced quality of life, social functioning impairment, and lower likelihood of remission and treatment response.[11–15] Finally, the initial years following onset of psychotic symptoms may represent a critical period for intervention, during which pharmacological and psychosocial treatments elicit the greatest treatment

Received: 14 November 2023
Accepted: 7 March 2024
Published: 21 March 2024

response.[16] Therefore, intervention for youth early in the course of psychotic illness can be critical for improving chances of recovery.

Intervening among youth showing initial signs of psychosis is crucial, yet these signs can be difficult to identify and diagnose. This difficulty is in part due to the heterogeneity of clinical presentations of psychotic and related symptoms across individuals.[5,17] For example, one individual may struggle with persistent fears of being followed and blunted facial affect, whereas another may experience periods of hearing voices, speech disorganization, and intermittent depressive episodes. Added complexity of identifying early signs of psychosis comes with variability in symptom intensity and severity, as population-level genetic, neuropsychological, social, and environmental studies have consistently found that psychosis exists on a continuum.[18–20] An adolescent may present to the clinic reporting unusual perceptual experiences and odd beliefs, yet they may seem to be able to distinguish these experiences from reality, or perhaps these symptoms primarily occur when the person is exposed to reminders of a traumatic event. In such cases, it may not be readily apparent to the clinician whether the individual is exhibiting mild psychotic-like experiences common in the general population, early warning signs of psychosis, overt psychotic symptoms, or symptoms related to a non-psychotic illness.

At the lower end of the psychosis continuum, mild or transitory psychotic-like symptoms can include common experiences such as thinking that one's cell phone is ringing or vibrating when it is not.[18,19] Attenuated psychotic or clinical high-risk symptoms refer to more significant early warning signs of psychosis, such as hearing indistinct voices whispering a few times per week, with some distress or behavior change such as reducing social activities due to discomfort in groups of people.[21] Overt psychotic symptoms refer to symptoms meeting full clinical criteria for psychosis, such as hearing a clear voice making specific comments about one's behavior daily, with marked distress or behavior change such as not leaving the house due to intense discomfort interacting with others.[5] This psychosis continuum has been conceptualized as having a dimension of decreasing prevalence in the general population coinciding with a dimension of increasing severity.[18] Another key factor to consider is level of insight into the symptom, or the extent to which an individual can distinguish the symptom from reality, which decreases along the continuum from mild psychotic-like symptoms to overt psychotic symptoms.

Accurate assessment of where a person's symptoms fall on the psychosis continuum is important for both: 1) clarifying whether intervention is warranted; and 2) selecting the appropriate evidence-based interventions among available options. With regard to the former, for example, youth experiencing mild psychotic-like symptoms in some cases might not warrant clinical attention, whereas youth exhibiting distressing, attenuated psychotic symptoms may benefit from intervention (e.g., step-based care[22,23]), which could lower their risk of developing a psychotic disorder.[24] With regard to the latter, antipsychotic medications have demonstrated efficacy for many individuals with first-episode psychosis (FEP)[25–27] but are currently discouraged as front-line treatments for individuals with attenuated psychotic symptoms given limited evidence of efficacy for preventing conversion to psychosis and high side effect burden.[24,28,29]

Overall, the purpose of this article is to provide clinicians with a framework for determining whether a patient is experiencing symptoms of FEP or early warning signs which may indicate heightened risk for developing psychosis. We will begin by outlining the defining characteristics of FEP and psychosis-risk syndromes, as well as common assessment tools used to diagnose these conditions. Next, we will provide examples of differential diagnoses which have phenotypic overlap with psychotic illnesses but for which different treatments may be indicated. Finally, we will conclude with an overview of approaches toward outreach and screening for psychosis in the clinic and community.

Clinical Characteristics of First-Episode Psychosis

Defining First-Episode Psychosis

FEP is a term used to describe a recent onset of overt psychotic symptoms, particularly delusions and/or hallucinations that are at times indistinguishable from reality, or disorganized speech that is tangential or incoherent.[18] These symptoms occur frequently (e.g., averaging at least 1 hour per day, 4 days per week for 1 month[30]) and/or are seriously disorganizing or dangerous to oneself or others. The term "first-episode psychosis" often refers to the experience of psychotic symptoms with an onset within the past 2–5 years rather than exclusively referring to the individual's initial psychotic episode. A more accurate term may therefore be "recent-onset psychosis."[31] However, given the widespread usage of the term FEP in clinics and research literature, we use it here for consistency.

Symptoms of FEP tend to present in the late teenage to early adult years of life.[3,32] The etiology of psychotic-spectrum disorders is complex, with research suggesting these are neurodevelopmental disorders which emerge through gene-environment interactions.[33] Individuals with FEP may meet criteria for a variety of psychiatric disorders outlined in current diagnostic systems.[3,34] Schizophrenia is the prototypical psychotic-spectrum disorder, consisting of two or more symptoms of delusions, hallucinations, disorganized speech, disorganized or catatonic behavior, and negative symptoms, lasting at least six months and resulting in functional impairment. Individuals with FEP may also meet criteria for schizophreniform disorder (i.e., schizophrenia symptoms lasting less than six months with no requirement of functional decline), brief psychotic disorder (i.e., one or more positive or disorganized symptoms of psychosis lasting between one day and one month), schizoaffective disorder (i.e., concurrent symptoms of schizophrenia and a major depressive/manic episode, with psychotic symptoms persisting for at least two weeks without mood symptoms, and mood symptoms present for the majority of the illness), major depressive disorder or bipolar disorder with psychotic features (i.e., psychotic symptoms present primarily within mood episodes), delusional disorder (i.e., delusions as the primary psychotic symptom, with functioning intact aside from the impact of the delusions), or an unspecified psychotic-spectrum disorder, among others.

While discrete psychotic disorder diagnoses have clinical and practical utility (e.g., for assessing comorbid mood episodes, insurance billing), these disorders often share more overlap than differences with regard to neurobiology, cognitive function, and other illness features.[35] Specific diagnoses may be even less clear among individuals with FEP than those with longstanding psychotic illness, as consistent patterns of co-occurring symptoms can take years to emerge. Therefore, here we focus on the identification and diagnosis of FEP generally rather than specific psychotic disorders. Nevertheless, assessment over time of affective components of FEP (e.g., co-occurring depressive and/or manic episodes) and specific symptom profiles is warranted to inform pharmacological and psychological interventions. Additionally, clinicians should rule out psychosis due to physiological effects of drugs of abuse, medications, and medical conditions prior to intervention.

Overall, though the specific clinical presentation of FEP is diverse and individualized across youth, many symptoms will fall into one of several characteristic symptom clusters: positive, negative, and disorganization of thinking, speech, and/or behavior.

Positive Symptoms

Positive symptoms are perhaps the most defining feature of psychotic disorders and are characterized by alterations in perception and thinking that often lead to significant impact on behavior and functioning.[5] In the context of psychosis, "positive" denotes the addition of sensory and/or thought experiences that would not otherwise be present, namely hallucinations and delusions. Though positive symptoms are often highly distressing, they are the domain of psychotic symptoms most responsive to clinical intervention.[36]

Hallucinations within psychotic disorders describe sensory experiences that occur in the absence of external stimuli (i.e., another person in the same situation would not share the sensory experience) which are perceived as true stimuli. Hallucinations can occur in any sensory modality (i.e., visual, auditory, olfactory, gustatory, tactile), but most commonly occur in the auditory modality among individuals with first-episode[37] and longstanding[3] psychosis. Common types of auditory hallucinations among individuals with FEP include second-person voices making negative or derogatory comments and command hallucinations instructing the experiencer to take certain actions. Common types of visual hallucinations among individuals with psychotic disorders include seeing distressing images of animals, people, faces, objects, or events (e.g., a lit fire in front of them).[38]

Delusions are tenaciously held, false beliefs that are not responsive to contrary information[5] and are inconsistent with the individual's cultural norms.[39] The content and expression of delusional beliefs is highly individualized among people with psychotic disorders. The most common delusional themes among individuals with FEP[37] and longstanding[5] psychosis are persecution (i.e., false belief of being targeted or followed by a malicious person or entity, such as belief of being monitored by hidden cameras) and reference (i.e., false belief that there are messages or significant meaning in otherwise unremarkable aspects of the surrounding environment, such as belief of receiving special messages through the television). Other common delusional themes include grandiosity, thought insertion and withdrawal, guilt, mind reading, somatic, nihilistic, erotomaniac, and loss of control, among others.[3]

Negative Symptoms

Negative symptoms of psychosis are characterized by an attenuation or absence of various normative emotional, behavioral, and experiential processes.[40,41] Negative symptoms can include reductions in motivation and interest, decreased social drive

and social behavior, diminished emotional experience and/or expression, and a reduced ability to experience pleasure.[42] Negative symptoms can be pervasive during the course of FEP;[43] they are often treatment-resistant, tending to persist even when other aspects of illness are well-managed.[44] Individuals with prominent negative symptoms during FEP tend to have poorer clinical outcomes over time.[45] At the same time, negative symptoms can fluctuate early in the course of illness,[46] with evidence that many individuals with prominent negative symptoms at the onset of FEP experience a significant reduction in these symptoms in the first year of treatment.[47]

Disorganized Symptoms

Many individuals with psychosis experience symptoms of disorganization impacting thinking, speech, and/or behavior.[5] Disorganized speech and disrupted communication are common among individuals with psychosis and can manifest in a variety of ways, ranging from mild difficulties with tangential speech to moderate or severe impairments that interfere with one's ability to communicate even basic meaning to others.[5,48] Disorganized behavior also exists on a continuum of severity and can include odd or inappropriate displays of affect, wearing clothing that is grossly mismatched to the weather or situation, and changes in movements and overall motoric activity.[5] Though current diagnostic systems consider disorganized symptoms as a distinct symptom domain,[3] these symptoms also overlap with the negative and positive symptom domains.[49,50]

Associated Clinical Features and Comorbidity

Though the positive, negative, and disorganized symptom clusters are highly representative of psychotic disorders, additional signs and symptoms are also common among individuals with FEP. In particular, individuals with FEP have prominent cognitive impairments across domains (e.g., attention, memory, processing speed)[51] by the time of illness onset.[52] Though cognitive impairment is robustly linked to functional outcomes in more longstanding psychotic disorders,[53] the associations between cognitive impairment and functioning among individuals with FEP are less clear.[54,55] Many individuals with FEP also experience diminished insight or awareness of illness,[56] which has been associated with longer inpatient psychiatric hospitalizations.[57]

Individuals with FEP have high rates of psychiatric comorbidity in the early course of illness,[58] including mood disorders, anxiety, and substance use disorders.[59,60] Many comorbid conditions and cognitive impairment predate the onset of psychosis and may represent underlying risk factors for FEP.[61] Individuals with FEP also have elevated rates of physical health comorbidities, including elevated rates of cardiometabolic conditions (i.e., elevated blood pressure and blood lipid levels).[62] Longitudinal cohort studies suggest that, overall, individuals with FEP have an 11-fold increase in all-cause mortality in the 10 years following illness onset.[63] Finally, individuals with FEP are at elevated risk for suicide and self-harm,[64] particularly in the first three months following the initial diagnosis of a psychotic disorder.[65] An estimated 5–10% of individuals with schizophrenia die by suicide,[66] and suicide is the leading cause of death among individuals with a psychotic disorder in the first five years following initial diagnosis.[67]

Clinical Characteristics of Psychosis Risk

Defining Clinical High Risk for Psychosis

Psychotic disorders are often preceded by a phase in which psychotic-like experiences become progressively more severe while daily functioning deteriorates, culminating in a full psychotic episode.[68] "Clinical high risk for psychosis" (CHR-P) is a term that has been created to identify and provide preventative care to youth who are exhibiting these early warning signs prior to onset of a full psychotic episode. In addition to CHR-P, other commonly used terms for this state are "at-risk mental state" and "ultra-high risk for psychosis."[24,69] While previously referred to as the psychosis "prodrome", usage of this term is decreasing as the majority of individuals who exhibit early warning signs of psychosis do not go on to develop a psychotic disorder.[70] The CHR-P syndrome is also transdiagnostic and dimensional in the sense that it confers shared risk for all psychotic disorders, rather than specific risk for specific psychotic disorders (e.g., schizophrenia).[71]

Three subtypes of psychosis-risk syndromes are often recognized.[21,30,69] The most common CHR-P syndrome subtype is attenuated positive symptom syndrome (APSS), comprising around 85% of cases.[72] APSS is identified by the presence of persistent attenuated positive psychotic symptoms, occurring at least once per week for a month or more. A second CHR-P subtype is brief intermittent psychotic syndrome (BIPS), comprising around 10% of cases.[72] BIPS is

identified by the presence of overt psychotic symptoms which occur intermittently and spontaneously resolve after a short span of time (i.e., lasting for at least several minutes, once per month, but occurring less than one hour per day, four days per week). A third CHR-P subtype is genetic risk and functional decline (GRD), comprising around 5% of cases.[72] GRD is identified by genetic risk (i.e., a psychotic disorder in a first-degree relative or the individual meeting criteria for schizotypal personality disorder) plus significant decline in functioning (i.e., a greater than 30% drop in Global Assessment of Functioning [GAF][73] scores within one year).

Finally, psychosis risk has also been conceptualized through the lens of "basic symptoms."[74] Basic symptoms are subtle, subjectively observed alterations in thinking, speech, perception, motor function, stress tolerance, affect, drive, and self-experience, which are posited to be early manifestations of the neurobiological processes underlying psychosis. These symptoms can fluctuate over time and might not be observable by others. While they can precede a psychotic episode[75] (and can even precede attenuated psychotic or CHR-P symptoms), basic symptoms may also be present during an acute psychotic episode as well as residual states of illness.[74]

Attenuated Positive Psychotic Symptoms

Most cases of individuals at CHR-P are identified via the presence of attenuated positive psychotic symptoms.[21,76] Onset of these symptoms may occur following a stressful event (e.g., parents' divorce, peer conflict, death of a loved one, other traumatic event) or following no apparent stressors. For some individuals, attenuated positive symptoms are experienced as longstanding since childhood but may become more frequent and impairing over time, and for others, they emerge for the first time in adolescence or young adulthood. Domains of attenuated positive symptoms are subthreshold delusional beliefs, subthreshold hallucinatory experiences, and subthreshold disorganized thought and speech. For example, an individual at CHR-P may begin to experience distressing thoughts that they are living in a simulation (i.e., unusual thought content), thoughts that others are laughing at them or playing tricks on them (i.e., suspiciousness), ideas that they have special talents like the ability to predict the future (i.e., grandiosity), hearing footsteps or doors slamming when no one is present (i.e., perceptual abnormalities), and/or difficulties connecting their thoughts and conversing clearly with others (i.e., disorganized communication). See Table 1 for further examples and comparisons with symptoms at other stages in the psychosis continuum.

Most people in the general population have had one or more of the mild experiences described in Table 1 in their lifetime, consistent with fully dimensional models of a psychosis continuum in the general population.[20] To meet criteria for the APSS CHR-P syndrome, attenuated positive symptoms must be frequent (e.g., occurring at least once a week), perceived as significant or cause some level of distress, and may interfere with one's daily functioning (e.g., an individual refrains from showering at night due to worries about someone breaking into their apartment), among other criteria.[21] Unlike overt psychotic symptoms (Table 1), attenuated psychotic symptoms include some capacity to distinguish symptoms from reality (in APSS subtype) or include full delusional conviction that is brief and intermittent (BIPS subtype). Of note, it is possible for individuals with psychotic-spectrum disorders to experience attenuated symptoms after already experiencing overt psychotic symptoms, in which case these would be classified as residual psychotic symptoms.

Associated Clinical Features and Comorbidity

Individuals at CHR-P may also exhibit attenuated psychotic symptoms in domains other than positive symptoms, such as negative (e.g., avolition, anhedonia, blunted affect), disorganized (e.g., odd behavior or appearance), and general (e.g., sleep and mood disturbance) symptoms.[21,30] However, attenuated positive symptoms are primarily used in the diagnosis of psychosis-risk syndromes.

Youth at CHR-P also typically experience mild-to-moderate cognitive impairment across many cognitive domains compared their typically developing peers,[77] which often persists even among individuals whose attenuated psychotic symptoms remit over time.[78] Additionally, youth meeting CHR-P criteria tend to retrospectively report poorer premorbid functioning (i.e., functioning up to one year prior to baseline assessments) in social and academic domains in proportion to the severity of their attenuated negative symptoms.[79] Premorbid social functioning may be particularly relevant, as rapid declines in social functioning are known to increase risk for psychotic disorders within the clinical high-risk syndrome.[80] Individuals at CHR-P are also at elevated risk for suicide,[81,82] with one meta-analysis indicating that 66% of individuals reported suicidal ideation and 18% reported suicide attempts, although there were high levels of heterogeneity across studies.[83]

Table 1 Example Experiences Spanning the Psychosis Continuum

Symptom Domain	Normative or Mild Psychotic-Like Symptoms	Attenuated Psychotic Symptoms or Early Warning Signs	Clinical or Overt Psychotic Symptoms
Unusual thought content or delusional beliefs	Infrequently noticing coincidences (e.g., repeated words in various news headlines), but easily brushing this off as a common experience that happens to many people	Noticing coincidences on a weekly basis and starting to think these are meaningful and may be conveying important messages to the individual	Being certain that internet webpages and headlines in the news are communicating directly and specifically to the individual
Suspiciousness or persecutory delusions	Brief occasional worry about a stranger breaking into one's home at night	Suspecting that strangers at the grocery store might have malicious intent toward the individual, leading them to shop less often	Strongly believing that the government has a plot against the individual, leading them to move to a new apartment every few months
Grandiosity or grandiose delusions	Personal thoughts or occasional boasting about one's talents or knowledge	Wondering if one may have special gifts that others do not have such as the ability to predict the future	Being fully convinced that one is internationally famous without logical evidence
Perceptual abnormalities or hallucinations: Auditory domain	Thinking one hears their name being called in a crowd without a clear source but determining that this was just a mistaken perception	Hearing frequent whispering or indistinct murmurs that cause uneasiness	Hearing clear, loud female voices criticizing one's behavior and personality traits which is upsetting and disruptive of one's daily functioning
Perceptual abnormalities or hallucinations: Visual domain	Thinking one sees their pet cat in a dimly lit room but quickly realizing they were misperceiving a box on the floor	Seeing shadows or outlines of vague figures or animals which are unsettling but disappear soon after the person looks at them	Seeing clear, disfigured human or animal figures for sustained periods frequently, resulting in severe distress
Difficulties organizing thoughts and speech or thought disorder	Occasionally responding to questions with speech that is excessively wordy	Regularly rambling and getting off track in conversations but eventually returning to the point when others redirect them	Speaking in a way that is tangential, difficult to follow, illogical, and/or contains made-up words

Notes: Above are examples of symptoms that a clinician may consider to be: 1) mild, non-distressing, not warranting clinical attention; 2) attenuated positive psychotic symptoms potentially indicating that one is at clinical high risk for psychosis (i.e., at-risk mental state; ultra high-risk for psychosis); and 3) overt psychotic symptoms potentially indicating that one is experiencing FEP or a persistent psychotic disorder. Note that thorough clinical assessment and relevant training and certifications are needed to diagnose these symptoms and corresponding syndromes.

Most individuals meeting CHR-P also meet criteria for at least one other psychiatric disorder (roughly 80%), most commonly mood (45%), anxiety (35%), trauma-related (30%), and personality (25%) disorders (especially schizotypal personality disorder).[84] Some comorbid disorders remit over time; at follow-up durations longer than 2 years, prevalence of comorbid disorders decreases to around 45–50%. This suggests that individuals are more likely to be identified as being at CHR-P at times when comorbid psychopathology is particularly pronounced.

Likelihood of Developing a Psychotic Disorder

When individuals at CHR-P develop a psychotic disorder, they are said to have "converted" or "transitioned" to psychosis. Overall, only a minority of clinical high-risk cases convert to psychosis within typical follow-up periods. At one year since presentation to the clinic, approximately 15% of individuals at CHR-P have converted to a psychotic disorder; at two years, roughly 20% have converted; and at four years the conversion rate plateaus between 25% and 30%.[70] Rates of conversion to psychosis differ between the three subtypes, with conversion being more likely in the BIPS group and less likely in the GRD group.[72] Conversion is more likely among individuals with more severe functional impairment (especially recent declines in social functioning),[85] more severe attenuated positive psychotic symptoms, and among those who are male, unemployed, and/or have trauma histories.[86]

Personalized risk calculators have been developed to estimate individuals' risk of conversion.[85] Conversion rates have decreased somewhat over time, potentially due to a combination of earlier treatment[87] and case identification strategies based on broad outreach among clinicians and in the general population.[88,89] In general, help-seeking individuals appear to be at higher risk of conversion to psychosis than individuals identified by screening or outreach in the general population.[90] However, individuals who do not convert to psychosis do not necessarily experience symptomatic or functional remission; around half experience persistent or worsening symptoms (roughly 60%)[78] and functional impairment (roughly 40–45%),[91] despite not developing clinical psychotic disorders.

Diagnostic Assessment Tools

In this section, we provide a brief overview of several assessment tools that clinicians and researchers use to diagnose psychosis-risk syndromes, FEP, and particular psychotic-spectrum disorders (see Table 2). Many of these tools require specialized training and formal certification prior to use in clinical and research settings. There are numerous additional scales beyond those described here which assess level of symptom severity across the psychosis continuum.[49,92,93]

Tools for Diagnosing Psychosis-Risk Syndromes

The Structured Interview for Psychosis-risk Syndromes (SIPS)[21,30] and the Comprehensive Assessment of At-Risk Mental States (CAARMS)[69] are semi-structured interviews designed to diagnose CHR-P syndromes (SIPS) or at-risk mental states

Table 2 Assessment Tools for Psychosis-Risk Syndromes, FEP, and Psychotic-Spectrum Disorders

Assessment Type	Instrument	Abbreviation	Description
Psychosis-risk and first-episode psychosis diagnosis	Structured Interview for Psychosis-risk Syndromes[21,30]	SIPS	Trained rater-administered semi-structured interviews to assess psychosis-risk symptoms and syndromes and first-episode psychosis
	Comprehensive Assessment of At-Risk Mental States[69]	CAARMS	
	Positive Symptoms and Diagnostic Criteria for the CAARMS Harmonized with the SIPS[94]	PSYCHS	
Basic symptom assessment	Bonn Scale for the Assessment of Basic Symptoms[95]	BSABS	Trained rater-administered semi-structured interviews to assess "basic symptoms" which can be associated with psychosis risk, active psychosis, and residual states of psychosis
	Schizophrenia Proneness Instrument[96,97]	SPI	
Psychotic-spectrum disorder diagnosis	Structured Clinical Interview for DSM-5 Disorders[98]	SCID-5	Trained rater-administered semi-structured interviews to assess diagnostic criteria for psychotic and other psychiatric disorders in adults (SCID-5; SADS) and youth (K-SADS)
	Schedule for Affective Disorders and Schizophrenia[99]	SADS	
	Kiddie Schedule for Affective Disorders and Schizophrenia for School-Aged Children[100]	K-SADS	
Psychosis-risk screening	Prodromal Questionnaire-Brief Version[101]	PQ-B	Example self-report screening questionnaires for psychosis risk (among others[102])
	PRIME Screen-Revised[103]	PS-R	
	Youth Psychosis At-Risk Questionnaire[104]	YPARQ	
	The Early Psychosis Screener[105]	EPS-26	

Notes: This is a summary of a subset of available assessment tools for evaluating and diagnosing psychosis risk and psychotic-spectrum disorders.

(CAARMS) and FEP among treatment-seeking individuals. In clinical practice, the clinical high-risk state and the at-risk mental state are quite similar, and a new measure has been developed to harmonize the two sets of criteria.[94,106] The Bonn Scale for the Assessment of Basic Symptoms (BSABS)[95] and the Schizophrenia Proneness Instrument (SPI)[96,97] are semi-structured interviews used to assess basic symptoms, which are also indicative of psychosis risk.[75]

The SIPS and the CAARMS both include assessment of attenuated positive, negative, disorganized, and general psychopathology symptoms, among other domains. Psychosis-risk syndromes defined using these tools include: 1) APSS in SIPS; attenuated psychosis in CAARMS; 2) brief (limited) intermittent psychosis syndrome (BIPS in SIPS; BLIPS in CAARMS); and 3) genetic risk and functional decline (GRD in SIPS; vulnerability group in CAARMS); see Clinical Characteristics of Psychosis Risk section for further detail. These diagnoses are not mutually exclusive (e.g., an individual may have APSS and GRD). Attenuated positive symptoms on these measures include unusual thought content, perceptual abnormalities, disorganized communication (SIPS and CAARMS), non-bizarre ideas (CAARMS), and suspiciousness and grandiosity (SIPS). Symptoms are each rated on a 0–6 scale considering levels of severity, distress, behavioral impact, and conviction (i.e., insight, or ability to distinguish the symptom from reality). Ratings of 0–2 are considered to be within the range of typical functioning, ratings of 3–5 are within the clinical high-risk range, and a rating of 6 indicates overt psychosis. In the SIPS, psychosis-risk diagnoses are given only if attenuated positive symptoms are not better explained by another psychiatric disorder. In the CAARMS, diagnosable psychosis-risk syndromes require that symptoms be present in the past year.

The BSABS[95] and the SPI[96,97] assess basic symptoms in domains such as alterations in energy, drive, stress tolerance, emotional reactivity, cognition, attention, depersonalization, perception, motor function, self-experience, and central-vegetative function (e.g., sleep, appetite, libido, heart rate, thermoregulation). Psychosis-risk criteria using these tools primarily rely on cognitive and perceptual disturbances (e.g., thought interference, thought blockage, unstable ideas of reference, decreased ability to discriminate between fantasies and true memories, visual and acoustic perception disturbances). Basic symptom cognitive disturbances measured in conjunction with SIPS CHR-P criteria have more accurately predicted conversion to psychosis than either set of criteria in isolation,[107] suggesting clinical utility in combining psychosis-risk assessments.

Of note, inclusion of psychosis-risk syndromes in psychiatric diagnostic classification systems has been debated.[108] "Attenuated psychosis syndrome" currently resides in the "Conditions for Further Study" section of the DSM-V and as a specifier of other specified psychotic disorders rather than being represented as a formal diagnostic category. Opponents of adding psychosis-risk syndromes as clinical diagnoses cite concerns of potential high false positive rates due to symptom ambiguity and low overall incidence of conversion to psychotic disorders, increases in unwarranted treatment (e.g., antipsychotic medication), and unnecessary stigma to diagnosed individuals.[108,109] In contrast, proponents argue that formalizing psychosis-risk syndromes as clinical diagnoses would promote early identification and intervention for help-seeking individuals, catalyze clinical trials to strengthen the evidence-base for relevant treatments, and potentially decrease unwarranted treatment by reducing rates of misdiagnosis.[110] Lastly, some evidence suggests that stigma may be more related to psychosis-risk symptoms than the diagnostic label itself.[111] Proponents for formalizing the diagnosis argue that stigma is unlikely to be greater for psychosis-risk diagnoses than the potentially inaccurate diagnoses that these individuals are already receiving, and regardless, increased access to care may outweigh any increases in stigma.[110]

Tools for Diagnosing First-Episode Psychosis and Psychotic-Spectrum Disorders

Psychosis-risk assessment tools (e.g., SIPS, CAARMS) are useful for assessing for the presence of FEP in addition to diagnosing clinical-high risk and at-risk mental state symptoms. These tools include ratings systems which offer a clear delineation between symptoms which fall within ranges of normative functioning, CHR-P, and overt psychosis indicative of FEP among youth. For example, if unusual thought patterns, perceptual abnormalities, and/or communication disturbances are rated as a 6 in severity on the SIPS, occur frequently for sustained periods, are not accounted for by another psychiatric illness, and began or worsened within the past 2–5 years, the individual might meet criteria for FEP.[30]

If an individual is determined to be experiencing overt psychotic symptoms, a clinician may assess whether their symptoms meet criteria for a specific psychotic-spectrum disorder diagnosis (e.g., schizophrenia, schizoaffective disorder, delusional disorder, etc.) using the Diagnostic and Statistical Manual for Mental Disorders (DSM-5)[3] or the International Classification of Diseases (ICD–11).[34] Common clinical interviews used to assess these diagnostic criteria

include the Structured Clinical Interview for DSM-5,[98] the Schedule for Affective Disorders and Schizophrenia[99] (and the K-SADS youth version[100]), and the Mini International Neuropsychiatric Interview,[112] among others.

Differential Diagnosis

There are many instances in which a young person presents to the clinic with psychotic-like symptoms (e.g., odd beliefs, perceptual abnormalities, unusual speech patterns), and it is not clear whether they are experiencing overt psychotic symptoms, clinical high-risk symptoms, or symptoms of another psychiatric illness altogether.[113] Moreover, comorbid psychiatric conditions are the norm rather than the exception for individuals with psychotic disorders, making differential diagnosis a challenging task for clinicians.[114] Differential diagnosis can have important clinical implications, influencing access to care and treatment selection. See Table 3 for case examples of client presenting concerns, preliminary clinical impressions, and potential referrals. Next, we provide examples and recommendations for differential diagnosis with a focus on three diagnostic categories that have significant phenotypic overlap with psychotic disorders: 1) autism spectrum disorder; 2) obsessive-compulsive disorder; and 3) post-traumatic stress disorder.

Autism Spectrum Disorder

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by social communication difficulties and restricted or repetitive patterns of behavior or interests.[3] Early conceptualizations of ASD and schizophrenia recognized their phenotypic overlap, with autism initially considered to be a symptom of schizophrenia.[115] While current diagnostic systems treat ASD and psychotic disorders as distinct,[3,34] their overlap and differentiation are still debated.[116] For example, social communication difficulties among individuals with ASD can be misperceived as negative symptoms of psychosis, disorganized thinking, and paranoia. Additionally, ASD symptoms of sensory sensitivities and idiosyncratic speech and thinking patterns can be misperceived as hallucinations and delusions. We offer the following recommendations to aid in the differential diagnosis of these disorders.

First, age of symptom onset and functional impairment typically begins in childhood for ASD and emerging adulthood for psychotic disorders.[3] Second, tangential, stereotyped, or unusual speech which returns to specific or restricted topics of interest and reflect an individual's baseline speech patterns may be more characteristic of ASD than psychotic disorders.[117] Third, as distinguishing characteristics of psychotic disorders are overt hallucinations and delusions, asking clarifying questions and eliciting specific examples is critical for differential diagnosis. For instance, an individual with ASD may endorse seeing or hearing things that others do not see due to hypersensitivity to sensory stimuli.[118] An individual with ASD may also endorse

Table 3 Case Examples of Patients Arriving to Clinic with Presenting Concerns, Preliminary Clinical Impressions, and Potential Referrals

Presenting Concerns	Preliminary Clinical Diagnostic Impression	Example Treatment Or Assessment Referral
Janelle is a Black adolescent with occasional feelings of being unsafe and mistrust toward others. She attributes these feelings to living in a high-crime neighborhood and experiences of discrimination. She says that these feelings make her initially wary of establishing close relationships but overall keep her safe and do not interfere with her life. She also has persistent fears of forgetting to lock her apartment door and turn off the stove, which she knows are excessive. These fears lead her to spend hours each day checking the door and the stove and have led her to miss class.	Janelle might be experiencing obsessive-compulsive disorder (OCD). Janelle's occasional feelings of being unsafe and mistrust toward others due to environmental factors and personal history of discrimination are currently more consistent with adaptive cultural paranoia than psychosis or psychosis risk.	Referral to evidence-based treatment for OCD (e.g., cognitive behavioral therapy [CBT] with exposure and response prevention). Continue monitoring worries about safety and mistrust for increases in distress, generalization to other areas without clear environmental explanation, and functional impairment. As clinically indicated, consider re-assessing for psychosis risk.

(*Continued*)

Table 3 (Continued).

Presenting Concerns	Preliminary Clinical Diagnostic Impression	Example Treatment Or Assessment Referral
Trevor is a White adolescent who occasionally sees a monster in his bedroom for 20-minute periods two times per month. During these periods, he fully believes the monster is real and hides in his closet out of fear. This occurs while he is fully awake and resolves without medication. Outside of these periods he knows the monster is not real.	Trevor may be exhibiting symptoms of a psychosis-risk syndrome (BIPS/BLIPS subtype). His clinical presentation is currently not consistent with a full-threshold psychotic disorder given that his psychotic symptoms are brief, spontaneously resolve, and are not seriously disorganizing or dangerous.	Referral for psychosis-risk assessment (e.g., SIPS, CAARMS), followed by referral to psychosis-risk specialty care clinic (e.g., step-based care or other appropriate services within the local community) as clinically indicated.
Rowan is a White child who endorses hearing voices and exhibits affective flattening. When prompted to elaborate, he explains that by "hearing voices", he is referring to his own internal thought monologue. He makes minimal eye contact with others, struggles to understand social interactions, has hypersensitivities to textures of food and clothing, and has difficulty deviating from his rigid daily schedules.	Rowan's clinical presentation might be more consistent with autism spectrum disorder than psychosis or psychosis risk. Rowan's endorsement of hearing voices may be better accounted for by idiosyncratic thought and interpretation of the assessment question rather than overt psychotic hallucinations.	Referral for autism spectrum disorder assessment (e.g., Autism Diagnostic Observation Schedule) and multicomponent autism treatment program tailored to the individual's needs. Continue monitoring for potential psychotic symptoms and consider re-assessing for psychosis risk as clinically indicated.
Alex is a Black young adult who quit his job last week due to becoming certain that his boss was plotting against him and poisoning his coffee at work. When asked for further information, Alex says that a voice that he has heard daily for hours at a time over the past two months which his co-workers do not hear told him about his boss's plans.	Alex might be experiencing first-episode psychosis (i.e., indicative of a psychotic disorder) given the frequency, severity, functional impact, and recent onset of his symptoms.	Referral to Coordinated Specialty Care for First-Episode Psychosis or other appropriate services within the local community.
Casey is a Korean American nonbinary young adult who endured a serious physical assault one year ago. Since the event, they have experienced flashbacks, persistent feelings of guilt, sleep troubles, detachment from others, an exaggerated startle response, hearing the voice of the attacker in their head, and they avoid thinking about the assault. Starting three months ago, they began hearing voices unrelated to the attacker in the absence of anyone else being in the room. They have also become fully convinced that the government is monitoring them via cameras outside of their house, which has led them to keep all the lights off and not leave home for days at a time.	Casey might be experiencing comorbid post-traumatic stress disorder (PTSD) and first-episode psychosis given their history of a traumatic assault and symptoms of both overt psychosis and PTSD which are not fully accounted for by one another.	Referral to evidence-based trauma-focused treatment (e.g., cognitive processing therapy, prolonged exposure), Coordinated Specialty Care for First-Episode Psychosis incorporating trauma-focused treatment, and/or other appropriate services within the local community. Initial treatment targets may depend on concerns that are considered primary, concerns that result in the most distress and/or impairment, and the patient's recovery goals.

(*Continued*)

Table 3 (Continued).

Presenting Concerns	Preliminary Clinical Diagnostic Impression	Example Treatment Or Assessment Referral
Madison is a White adolescent who endorses a special connection with God and feels as though she can personally communicate with God. When asked what others in her religious community think of this connection, she shares that her priest and other church members say that this is a common experience for them as well. She additionally reports month-long periods of sadness and low interest, difficulties falling asleep, low appetite, and thoughts of suicide that are distressing and interfere with her schoolwork.	Madison might be experiencing major depressive disorder. Madison's religious beliefs are currently more consistent with the cultural norms of her church community than indications of psychosis or psychosis risk.	Suicide risk assessment and collaborative safety planning as clinically indicated, followed by referral to evidence-based depression-focused treatment (e.g., CBT, interpersonal therapy). Continue monitoring for development of beliefs inconsistent with the norms of her church community, increases in distress, and functional impairment. As clinically indicated, consider re-assessing for psychosis risk.
Marcos is a Venezuelan American adult with a seven-year history of major depressive and manic episodes. Exclusively during manic episodes, he hears voices that others do not hear complimenting him on his behavior and appearance, and he holds strong false beliefs that he is a famous athlete and that strangers are in love with him.	Marcos might be experiencing bipolar disorder with mood-congruent psychotic features. The duration of Marcos' symptom presentation is more consistent with longstanding psychosis than first-episode psychosis.	Referral to evidence-based services for treatment of serious mental illness.
Charlie is a White adolescent transgender woman who is starting to wonder if spirits are communicating with her. She is seeing shapes of animals out of the corner of her eye multiple times per week and is experiencing time as moving unnaturally quickly. These experiences began within the past year. She finds them unsettling, but she is still able to distinguish them from reality.	Charlie may be exhibiting symptoms of a psychosis-risk syndrome (APSS/attenuated psychosis subtype, current progression). Her clinical presentation is currently not consistent with a full-threshold psychotic disorder given the presence of attenuated psychotic symptoms which are not seriously disorganizing or dangerous and lack full delusional conviction.	Referral for psychosis-risk assessment (e.g., SIPS, CAARMS), followed by referral to psychosis-risk specialty care clinic (e.g., step-based care or other appropriate services within the local community) as clinically indicated.

Notes: These are fictitious case examples that are not based on actual individuals. Thorough clinical assessment by qualified individuals and relevant trainings and certifications are warranted to make formal clinical diagnoses and treatment decisions.

hearing voices when no one is present for several reasons other than experiencing psychosis, such as: 1) concrete interpretation of the question (e.g., they hear voices on the radio); or 2) vivid imaginative experiences (e.g., difficulty distinguishing hearing their own thoughts in their head from an external voice).[119–121]

Importantly, there is not always a clear distinction between ASD and psychotic disorders even with rigorous clinical assessment,[116,117] as there is substantial comorbidity[122,123] and genetic overlap.[124] While some individuals with ASD also experience attenuated positive symptoms, rates of transitioning from clinical high-risk state to a psychotic disorder do not appear to be impacted by the presence of ASD.[125] Overall, if an individual is ultimately exhibiting comorbid ASD and psychotic illness, clinical services addressing the symptoms associated with distress and functional impairment from either or both conditions should be carefully considered.

Obsessive-Compulsive Disorder

Obsessive-compulsive disorder (OCD) is characterized by: 1) recurrent and persistent thoughts that cause significant distress and are perceived as intrusive or unwanted (i.e., obsessions); and 2) repetitive behaviors or mental acts (i.e., compulsions) that serve to reduce the distress associated with the obsession.[3] Symptoms of OCD and psychotic disorders have phenotypic overlap, such as obsessions and compulsions which may present similarly to delusional beliefs and corresponding avoidance behaviors. To

further complicate matters, the DSM-5 includes a "with delusional beliefs" OCD specifier, indicating full conviction of the obsessional belief(s). The DSM-5 provides few recommendations for differentiating between OCD and psychotic disorders, merely noting that obsessions and compulsions are not diagnostic criteria for psychotic disorders, and hallucinations are not diagnostic criteria for OCD. Thus, we offer the following additional recommendations to aid in their differential diagnosis.

First, the content of the belief might be useful in distinguishing between obsessions and delusions.[126] For instance, common themes in psychotic delusions include persecution, grandiosity, guilt, religion, thought insertion and withdrawal, thought broadcasting, mind reading, delusions of reference, and somatic delusions. In contrast, common themes for obsessions include contamination, violent or sexual thoughts, and "not just right experiences" (i.e., unsettling feeling that something is not as it should be). Second, the intrusive quality of obsessions and the experiencer's retained insight into their excessive nature may be useful for differentiating obsessions and delusions.[126] Finally, the repetitive, ritualistic, and often time-consuming nature of compulsions might be useful in differentiating between compulsions and psychosis-related avoidance behaviors. For instance, checking locks a specified number of times might be more characteristic of OCD, whereas using multiple locks, blocking windows and doorways, and using surveillance strategies (e.g., security systems) might be more characteristic of psychotic paranoia. However, it is important to note that OCD and psychotic disorders can be comorbid,[127] and clinicians should consider the possibility of co-occurring disorders.

Post-traumatic Stress Disorder

Post-traumatic stress disorder (PTSD) is a trauma-related disorder characterized by the experience of a traumatic event (exposure to an actual or threatened death, serious injury, or sexual violence) followed by at least one month of re-experiencing or intrusive symptoms, avoidance behaviors, negative alterations in mood or cognition, and increased arousal or reactivity.[3] Trauma history is strikingly high among individuals with psychotic disorders (~28 to 73%),[128] and severe symptoms of PTSD can overlap with the phenotypic expression of psychotic disorders.[129] For instance, hypervigilance may overlap with paranoia, flashbacks may overlap with hallucinations, and both disorders can lead to significant occupational and social impairment.[129] To aid in the differential diagnosis of PTSD and psychotic disorders, we offer the following recommendations.

First, hypervigilance and paranoia might be differentiated by inquiring about the patient's specific reasons for having such concerns. Trauma-specific mistrust may be more characteristic of PTSD (e.g., fear of future encounters with a specific male perpetrator, generalized fear of all men), whereas fears that are broader or unrelated to the trauma may be more characteristic of psychotic disorders (e.g., fear of all people, fear of the government). Second, the content of hallucinations in the context of PTSD is often trauma-specific and includes themes related to threat (e.g., hearing the perpetrators voice),[130] whereas hallucinations in psychotic disorders may have broader themes and are rarely solely trauma-specific. Thorough assessment of the nature and timeline of the trauma can also be helpful for differential diagnosis. For example, psychotic-like symptoms which occur primarily in response to trauma cues (e.g., situational triggers, anniversary of the trauma) may be more indicative of PTSD, whereas psychotic-like symptoms which occur without a particular cue or in response to stressors more broadly may be more indicative of a psychotic disorder. Importantly, studies have demonstrated that common assessment tools for PTSD (e.g., CAPS-5, PCL) are valid for use among individuals with psychotic disorders,[131,132] and researchers have also developed modified versions of these tools to assess for co-occurring PTSD among individuals with schizophrenia.[131]

Transdiagnostic Approaches

In addition to the recommendations above for aiding in differential diagnosis, we encourage clinicians to identify underlying themes (e.g., mistrust, avoidance, social difficulties) that might be useful treatment targets that can guide treatment selection among individuals with complex or comorbid presentations. For instance, avoidance behaviors may be addressed using behavioral techniques (e.g., exposures and reality testing) regardless of whether the patient is experiencing symptoms of OCD, overt psychosis, or attenuated psychosis. Additionally, transdiagnostic treatment approaches (e.g., The Unified Protocol)[133] are utilized for treating patients with various types of emotional disturbances, including those at CHR-P.[22] Finally, many evidence-based interventions designed for other diagnoses (e.g., Cognitive Processing Therapy for PTSD)[134] can be useful for addressing comorbidities among individuals with psychotic-spectrum disorders.

Screening and Outreach

Despite a rapid increase in specialized clinical services for individuals at CHR-P[22] and individuals with FEP,[135] the majority of individuals early in the course of a psychotic or putative psychotic disorder do not access such specialized treatment programs. Consequently, outreach and recruitment activities are critical components for identifying individuals early in the course of a psychotic disorder to ensure access to specialized care during the time their illnesses are most malleable.[136] Common strategies employed to date include use of screening measures and outreach campaigns.

Screening Measures

Identification and diagnosis of individuals at CHR-P and those with FEP typically requires completion of lengthy clinical assessments such as the SIPS[21,30] or the SCID-5.[98] Although these assessments are the gold standard for identifying individuals at risk for psychosis and those experiencing FEP, they require significant training and time to complete, making them of limited use to many clinicians.[137] Consequently, there has been increased interest in developing and validating brief, self-report assessments that can be administered in the general population to screen individuals prior to completing time-intensive clinical assessments.

Several questionnaires specifically developed to screen for attenuated or overt psychotic symptoms have shown promise in identifying individuals at CHR-P and individuals with FEP, including the Prodromal Questionnaire-Brief Version,[101] the PRIME Screen-Revised,[103] and the Youth Psychosis At-Risk Questionnaire,[104] among others[102,105,138] (Table 2). Validity and accuracy of these measures has also been examined across cultures.[139–141] Some common mental health assessments not designed to screen for psychosis (e.g., Child Behavior Checklist[142] and both the self-report and parent-report versions of the Behavior Assessment System for Children[143]) have also shown promise as screening measures to identify individuals who may be early in the course of a psychotic disorder.

However, several limitations hinder the use of such measures as universal screening tools, including the lack of normative, demographic-specific data to inform thresholds for identifying psychosis or psychosis risk,[144] the lack of symptom overlap across measures,[145] and many scales' exclusive focus on positive (or attenuated positive) symptoms of psychosis.[146] Additionally, the ability of such scales to accurately differentiate individuals at CHR-P from those already experiencing overt psychotic symptoms is often limited.[101] Finally, screening measures for psychosis and psychosis risk are in need of cross-cultural validation, as they may artificially inflate perceived rates of psychosis-related pathology among individuals from underrepresented and underserved backgrounds due to potential factors such as experiences of prejudice, crime, trauma, and variations in cultural norms.[147–150]

Outreach Campaigns

Many early psychosis intervention services have paired their clinical programming with an active outreach campaign designed to facilitate early identification and referrals to their program. To date, such campaigns are most well operationalized within the context of FEP programs, and their presence is often considered a marker of a high fidelity program.[151] Through such activities, FEP clinical services strive to facilitate the early identification and referral of individuals to their service as soon as possible following the onset of psychotic symptoms with the goal of reducing the duration of untreated psychosis—a key, modifiable risk factor for which longer duration of untreated psychosis is associated with a worse course of illness for individuals with a psychotic disorder.[14,152] Yet, despite the near ubiquity of outreach campaigns within FEP programs, available evidence questions their effectiveness in reducing duration of untreated psychosis among program participants.[153,154] These findings may be in part due to heterogeneity in how both duration of untreated psychosis and FEP were operationalized across studies.[154]

The presence of structured outreach activities designed to facilitate early care are less ubiquitous in programs for individuals at CHR-P than among FEP programs.[155] Although research on outreach campaigns for clinical high-risk programs is limited, available evidence suggests that a combined outreach program geared toward simultaneously increasing early access for individuals at CHR-P and individuals with FEP may increase eligible referrals to a CHR-P clinical service.[156] More research is needed on the design and delivery of effective community outreach campaigns to facilitate early identification and access to care for individuals at CHR-P. Lastly, expansion of early psychosis detection campaigns is particularly needed within underserved communities which often have limited access to mental health care, such as among individuals from under-represented racial and ethnic groups and those within criminal justice settings.[157–159]

Conclusion

Psychotic-spectrum disorders and psychosis-risk states are complex, heterogeneous, frequently comorbid with other conditions, and lie on a continuum of human experience. Growing evidence indicates that the early phase of psychotic illness is a critical period in which intervention has maximum benefit for individuals in their recovery. Therefore, this review aimed to provide clinicians with a framework for identifying and diagnosing psychotic symptoms, attenuated psychotic symptoms, and psychotic-like experiences to increase diagnostic clarity for help-seeking youth. Screening and outreach campaigns are particularly important across a variety of key settings (including schools, hospitals, criminal justice settings, and the general public) to promote early detection of psychosis and rapidly connect individuals to clinical care. Given that early signs and symptoms of psychosis often emerge alongside other forms of psychopathology (e.g., anxiety, mood disturbances, trauma-related illness), a transdiagnostic approach to identification and treatment is strongly encouraged. Such work will address issues related to high rates of psychiatric comorbidity and promote overall wellness among youth.

Acknowledgments

AMM received funding support from a Research Innovation Career Development Award (RICDA) from the Ohio State University College of Medicine and a Mentored Patient-Oriented Research Career Development Award from the National Institute of Mental Health (K23MH131967). HMW received funding support from a Young Investigator Grant from the American Foundation for Suicide Prevention (YIG-0-184-20). NJKB received funding support from the Substance Abuse and Mental Health Services Administration (SM086173-01) as well as through cost matching funds provided by the Alcohol, Drug and Mental Health Board of Franklin County, Ohio. The content of this work is solely the responsibility of the authors and does not necessarily represent the official views of any funding agencies.

Disclosure

HMW reports grants from Department of Defense (W81XWH-22-2-0072) and honorarium for serving as scientific reviewer for CDMRP; travel award from American Foundation for Suicide Prevention, outside the submitted work. NJKB participates in paid and unpaid consulting for Arizona Complete Health and Indiana University with regard to specialty care for individuals early in the course of a psychotic disorder. The remaining authors declared no conflicts of interest related to this work.

References

1. GBD 2019 Mental Disorders Collaborators. Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Psychiatry*. 2022;9(2):137–150. doi:10.1016/S2215-0366(21)00395-3
2. Salomon JA, Haagsma JA, Davis A, et al. Disability weights for the Global Burden of Disease 2013 study. *Lancet Glob Health*. 2015;3(11):e712–723. doi:10.1016/S2214-109X(15)00069-8
3. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-V*. 5th ed. American Psychiatric Association; 2013.
4. Lysaker PH, Lysaker JT. Narrative Structure in Psychosis: schizophrenia and Disruptions in the Dialogical Self. *Theory Psychol*. 2002;12(2):207–220. doi:10.1177/0959354302012002630
5. Tandon R, Nasrallah HA, Schizophrenia KMS. "just the facts" 4. Clinical features and conceptualization. *Schizophr Res*. 2009;110(1–3):1–23. doi:10.1016/j.schres.2009.03.005
6. Arnett JJ. Emerging adulthood. A theory of development from the late teens through the twenties. *Am Psychol*. 2000;55(5):469–480. doi:10.1037/0003-066X.55.5.469
7. Moe AM, Breitborde NJK. Psychosis in Emerging Adulthood: phenomenological, Diagnostic, and Clinical Considerations. *Evid Based Pract Child Adolesc Ment Health*. 2019;4(2):141–156. doi:10.1080/23794925.2018.1509032
8. Liberman RP, Kopelowicz A, Ventura J, Gutkind D. Operational criteria and factors related to recovery from schizophrenia. *Int Rev Psychiatry*. 2002;14(4):256–272. doi:10.1080/0954026021000016905
9. Lieberman JA, Perkins D, Belger A, et al. The early stages of schizophrenia: speculations on pathogenesis, pathophysiology, and therapeutic approaches. *Biol Psychiatry*. 2001;50(11):884–897. doi:10.1016/s0006-3223(01)01303-8
10. McGlashan TH. A selective review of recent North American long-term followup studies of schizophrenia. *Schizophr Bull*. 1988;14(4):515–542. doi:10.1093/schbul/14.4.515
11. Barrett EA, Sundet K, Faerden A, et al. Suicidality before and in the early phases of first episode psychosis. *Schizophr Res*. 2010;119(1–3):11–17. doi:10.1016/j.schres.2010.03.022
12. Kane JM, Robinson DG, Schooler NR, et al. Comprehensive Versus Usual Community Care for First-Episode Psychosis: 2-Year Outcomes From the NIMH RAISE Early Treatment Program. *Am J Psychiatry*. 2016;173(4):362–372. doi:10.1176/appi.ajp.2015.15050632
13. Marshall M, Lewis S, Lockwood A, Drake R, Jones P, Croudace T. Association between duration of untreated psychosis and outcome in cohorts of first-episode patients: a systematic review. *Arch Gen Psychiatry*. 2005;62(9):975–983. doi:10.1001/archpsyc.62.9.975

14. Penttilä M, Jääskeläinen E, Hirvonen N, Isohanni M, Miettunen J. Duration of untreated psychosis as predictor of long-term outcome in schizophrenia: systematic review and meta-analysis. *Br J Psychiatry*. 2014;205(2):88–94. doi:10.1192/bjp.bp.113.127753
15. Perkins DO, Gu H, Boteva K, Lieberman JA. Relationship between duration of untreated psychosis and outcome in first-episode schizophrenia: a critical review and meta-analysis. *Am J Psychiatry*. 2005;162(10):1785–1804. doi:10.1176/appi.ajp.162.10.1785
16. Birchwood M, Todd P, Jackson C. Early intervention in psychosis. The critical period hypothesis. *Br J Psychiatry Suppl*. 1998;172(S33):53–59. doi:10.1192/S0007125000297663
17. Kontis D, Theochari E, Giannoulis A, Louki F, Tsaltas E. T92. Possible Combinations Of DSM-IV and DSM-5 Criteria In Schizophrenia And Schizoaffective Disorder Versus Major Depressive And Manic Episodes. *Schizophr Bull*. 2020;46(Supplement_1):S266–S267. doi:10.1093/schbul/sbaa029.652
18. Compton MT, Broussard B. *The First Episode of Psychosis: A Guide for Young People and Their Families*. Revised and updated ed. Oxford University Press; 2021.
19. van Os J, Hanssen M, Bijl RV, Ravelli A. Strauss (1969) revisited: a psychosis continuum in the general population? *Schizophr Res*. 2000;45(1–2):11–20. doi:10.1016/s0920-9964(99)00224-8
20. van Os J, Reininghaus U. Psychosis as a transdiagnostic and extended phenotype in the general population. *World Psychiatry*. 2016;15(2):118–124. doi:10.1002/wps.20310
21. McGlashan TH, Walsh BC, Woods SW. *The Psychosis-Risk Syndrome: Handbook for Diagnosis and Follow-Up*. Oxford University Press; 2010.
22. Breitborde NJK, Guirgis H, Stearns W, et al. The Ohio State University Early Psychosis Intervention Center (EPICENTER) step-based care programme for individuals at clinical high risk for psychosis: study protocol for an observational study. *BMJ Open*. 2020;10(1):e034031. doi:10.1136/bmjopen-2019-034031
23. Hamilton SA, Wastler HM, Moe AM, et al. Symptomatic and functional outcomes among individuals at clinical high risk for psychosis participating in step-based care. *Psychiatric Serv*. 2023;2023:appi–ps.
24. McGorry PD, Nelson B, Amminger GP, et al. Intervention in individuals at ultra-high risk for psychosis: a review and future directions. *J Clin Psychiatry*. 2009;70(9):1206–1212. doi:10.4088/JCP.08r04472
25. Lieberman JA, Tollefson G, Tohen M, et al. Comparative efficacy and safety of atypical and conventional antipsychotic drugs in first-episode psychosis: a randomized, double-blind trial of olanzapine versus haloperidol. *Am J Psychiatry*. 2003;160(8):1396–1404. doi:10.1176/appi.ajp.160.8.1396
26. Perkins D, Lieberman J, Gu H, et al. Predictors of antipsychotic treatment response in patients with first-episode schizophrenia, schizoaffective and schizophreniform disorders. *Br J Psychiatry*. 2004;185(1):18–24. doi:10.1192/bjp.185.1.18
27. Zhang JP, Gallego JA, Robinson DG, Malhotra AK, Kane JM, Correll CU. Efficacy and safety of individual second-generation vs. first-generation antipsychotics in first-episode psychosis: a systematic review and meta-analysis. *Int J Neuropsychopharmacol*. 2013;16(6):1205–1218. doi:10.1017/S1461145712001277
28. Block JJ. Ethical concerns regarding olanzapine versus placebo in patients prodromally symptomatic for psychosis. *Am J Psychiatry*. 2006;163(10):1838; author reply 1838. doi:10.1176/ajp.2006.163.10.1838
29. McGlashan TH, Zipursky RB, Perkins D, et al. Randomized, double-blind trial of olanzapine versus placebo in patients prodromally symptomatic for psychosis. *Am J Psychiatry*. 2006;163(5):790–799. doi:10.1176/ajp.2006.163.5.790
30. McGlashan TH, Walsh BC, Woods SW. Structured Interview for Psychosis-risk Syndromes, Version 5.6.1; 2017.
31. Breitborde NJK, Srihari VH, Woods SW. Review of the operational definition for first-episode psychosis. *Early Interv Psychiatry*. 2009;3(4):259–265. doi:10.1111/j.1751-7893.2009.00148.x
32. Kessler RC, Amminger GP, Aguilar-Gaxiola S, Alonso J, Lee S, Ustün TB. Age of onset of mental disorders: a review of recent literature. *Curr Opin Psychiatry*. 2007;20(4):359–364. doi:10.1097/YCO.0b013e32816ebc8c
33. van Os J, Rutten BP, Poulton R. Gene-environment interactions in schizophrenia: review of epidemiological findings and future directions. *Schizophr Bull*. 2008;34(6):1066–1082. doi:10.1093/schbul/sbn117
34. World Health Organization. *International Statistical Classification of Diseases and Related Health Problems: ICD-11*. 11th ed. World Health Organization; 2019.
35. Clementz BA, Sweeney JA, Hamm JP, et al. Identification of Distinct Psychosis Biotypes Using Brain-Based Biomarkers. *Am J Psychiatry*. 2016;173(4):373–384. doi:10.1176/appi.ajp.2015.14091200
36. Tandon R. Antipsychotics in the treatment of schizophrenia: an overview. *J Clin Psychiatry*. 2011;72(Suppl 1):4–8. doi:10.4088/JCP.10075su1.01
37. Rajapakse T, Garcia-Rosales A, Weerawardene S, Cotton S, Fraser R. Themes of delusions and hallucinations in first-episode psychosis. *Early Interv Psychiatry*. 2011;5(3):254–258. doi:10.1111/j.1751-7893.2011.00281.x
38. Waters F, Collerton D, Ffytche DH, et al. Visual hallucinations in the psychosis spectrum and comparative information from neurodegenerative disorders and eye disease. *Schizophr Bull*. 2014;40 Suppl 4(Suppl 4):S233–245. doi:10.1093/schbul/sbu036
39. Jenkins JH. Diagnostic criteria for schizophrenia and related psychotic disorders: integration and suppression of cultural evidence in DSM-IV. *Transcult Psychiatry*. 1998;35(3):357–376. doi:10.1177/136346159803500303
40. Andreasen NC, Arndt S, Alliger R, Miller D, Flaum M. Symptoms of schizophrenia. Methods, meanings, and mechanisms. *Arch Gen Psychiatry*. 1995;52(5):341–351. doi:10.1001/archpsyc.1995.03950170015003
41. Buchanan RW. Persistent negative symptoms in schizophrenia: an overview. *Schizophr Bull*. 2007;33(4):1013–1022. doi:10.1093/schbul/sbl057
42. Andreasen NC. Negative symptoms in schizophrenia. Definition and reliability. *Arch Gen Psychiatry*. 1982;39(7):784–788. doi:10.1001/archpsyc.1982.04290070020005
43. Thorup A, Petersen L, Jeppesen P, et al. Integrated treatment ameliorates negative symptoms in first episode psychosis--results from the Danish OPUS trial. *Schizophr Res*. 2005;79(1):95–105. doi:10.1016/j.schres.2004.12.020
44. Millan MJ, Fone K, Steckler T, Horan WP. Negative symptoms of schizophrenia: clinical characteristics, pathophysiological substrates, experimental models and prospects for improved treatment. *Eur Neuropsychopharmacol*. 2014;24(5):645–692. doi:10.1016/j.euroneuro.2014.03.008
45. Engen MJ, Vaskinn A, Melle I, et al. Cognitive and Global Functioning in Patients With First-Episode Psychosis Stratified by Level of Negative Symptoms. A 10-Year Follow-Up Study. *Front Psychiatry*. 2022;13:841057. doi:10.3389/fpsyt.2022.841057

46. Edwards J, McGorry PD, Waddell FM, Harrigan SM. Enduring negative symptoms in first-episode psychosis: comparison of six methods using follow-up data. *Schizophr Res*. 1999;40(2):147–158. doi:10.1016/s0920-9964(99)00043-2
47. Gee B, Hodgekins J, Fowler D, et al. The course of negative symptom in first episode psychosis and the relationship with social recovery. *Schizophr Res*. 2016;174(1–3):165–171. doi:10.1016/j.schres.2016.04.017
48. Docherty NM. Missing referents, psychotic symptoms, and discriminating the internal from the externalized. *J Abnorm Psychol*. 2012;121 (2):416–423. doi:10.1037/a0026348
49. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull*. 1987;13(2):261–276. doi:10.1093/schbul/13.2.261
50. McGorry PD, Bell RC, Dudgeon PL, Jackson HJ. The dimensional structure of first episode psychosis: an exploratory factor analysis. *Psychol Med*. 1998;28(4):935–947. doi:10.1017/s0033291798006771
51. McCleery A, Ventura J, Kern RS, et al. Cognitive functioning in first-episode schizophrenia: MATRICS Consensus Cognitive Battery (MCCB) Profile of Impairment. *Schizophr Res*. 2014;157(1–3):33–39. doi:10.1016/j.schres.2014.04.039
52. Bora E, Murray RM. Meta-analysis of cognitive deficits in ultra-high risk to psychosis and first-episode psychosis: do the cognitive deficits progress over, or after, the onset of psychosis? *Schizophr Bull*. 2014;40(4):744–755. doi:10.1093/schbul/sbt085
53. Green MF, Kern RS, Heaton RK. Longitudinal studies of cognition and functional outcome in schizophrenia: implications for MATRICS. *Schizophr Res*. 2004;72(1):41–51. doi:10.1016/j.schres.2004.09.009
54. Addington J, Saeedi H, Addington D. The course of cognitive functioning in first episode psychosis: changes over time and impact on outcome. *Schizophr Res*. 2005;78(1):35–43. doi:10.1016/j.schres.2005.05.008
55. Breitborde NJK, Meier M. Cognition in first-episode psychosis: from phenomenology to intervention. *Curr Psychiatry Rev*. 2017;12 (4):306–318. doi:10.2174/1573400512666160927145737
56. Thompson KN, McGorry PD, Harrigan SM. Recovery style and outcome in first-episode psychosis. *Schizophr Res*. 2003;62(1–2):31–36. doi:10.1016/s0920-9964(02)00428-0
57. Ramu N, Kolliakou A, Sanyal J, Patel R, Stewart R. Recorded poor insight as a predictor of service use outcomes: cohort study of patients with first-episode psychosis in a large mental healthcare database. *BMJ Open*. 2019;9(6):e028929. doi:10.1136/bmjopen-2019-028929
58. Strakowski SM, Tohen M, Stoll AL, et al. Comorbidity in psychosis at first hospitalization. *Am J Psychiatry*. 1993;150(5):752–757. doi:10.1176/ajp.150.5.752
59. Wilson RS, Yung AR, Morrison AP. Comorbidity rates of depression and anxiety in first episode psychosis: a systematic review and meta-analysis. *Schizophr Res*. 2020;216:322–329. doi:10.1016/j.schres.2019.11.035
60. Wade D, Harrigan S, Edwards J, Burgess PM, Whelan G, McGorry PD. Course of substance misuse and daily tobacco use in first-episode psychosis. *Schizophr Res*. 2006;81(2–3):145–150. doi:10.1016/j.schres.2005.09.010
61. Strakowski SM, Keck PE, McElroy SL, Lonczak HS, West SA. Chronology of comorbid and principal syndromes in first-episode psychosis. *Compr Psychiatry*. 1995;36(2):106–112. doi:10.1016/s0010-440x(95)90104-3
62. Correll CU, Robinson DG, Schooler NR, et al. Cardiometabolic risk in patients with first-episode schizophrenia spectrum disorders: baseline results from the RAISE-ETP study. *JAMA Psychiatry*. 2014;71(12):1350–1363. doi:10.1001/jamapsychiatry.2014.1314
63. Melle I, Olav Johannesen J, Haahr UH, et al. Causes and predictors of premature death in first-episode schizophrenia spectrum disorders. *World Psychiatry*. 2017;16(2):217–218. doi:10.1002/wps.20431
64. Ventriglio A, Gentile A, Bonfitto I, et al. Suicide in the Early Stage of Schizophrenia. *Front Psychiatry*. 2016;7:116. doi:10.3389/fpsyt.2016.00116
65. Moe AM, Llamocca E, Wastler HM, et al. Risk Factors for Deliberate Self-harm and Suicide Among Adolescents and Young Adults With First-Episode Psychosis. *Schizophr Bull*. 2022;48(2):414–424. doi:10.1093/schbul/sbab123
66. Hor K, Taylor M. Suicide and schizophrenia: a systematic review of rates and risk factors. *J Psychopharmacol*. 2010;24(4 Suppl):81–90. doi:10.1177/1359786810385490
67. Kurdyak P, Mallia E, de Oliveira C, et al. Mortality After the First Diagnosis of Schizophrenia-Spectrum Disorders: a Population-based Retrospective Cohort Study. *Schizophr Bull*. 2021;47(3):864–874. doi:10.1093/schbul/sbaa180
68. Miller TJ, McGlashan TH, Woods SW, et al. Symptom assessment in schizophrenic prodromal states. *Psychiatr Q*. 1999;70(4):273–287. doi:10.1023/a:1022034115078
69. Yung AR, Yuen HP, McGorry PD, et al. Mapping the onset of psychosis: the Comprehensive Assessment of At-Risk Mental States. *Aust N Z J Psychiatry*. 2005;39(11–12):964–971. doi:10.1080/j.1440-1614.2005.01714.x
70. Salazar de Pablo G, Radua J, Pereira J, et al. Probability of Transition to Psychosis in Individuals at Clinical High Risk: an Updated Meta-analysis. *JAMA Psychiatry*. 2021;78(9):970–978. doi:10.1001/jamapsychiatry.2021.0830
71. Addington J, Liu L, Goldstein BI, et al. Clinical staging for youth at-risk for serious mental illness. *Early Interv Psychiatry*. 2019;13 (6):1416–1423. doi:10.1111/eip.12786
72. Fusar-Poli P, Cappucciati M, Borgwardt S, et al. Heterogeneity of Psychosis Risk Within Individuals at Clinical High Risk: a Meta-analytical Stratification. *JAMA Psychiatry*. 2016;73(2):113–120. doi:10.1001/jamapsychiatry.2015.2324
73. Hall RC. Global assessment of functioning. A modified scale. *Psychosomatics*. 1995;36(3):267–275. doi:10.1016/S0033-3182(95)71666-8
74. Schultze-Lutter F, Theodoridou A. The concept of basic symptoms: its scientific and clinical relevance. *World Psychiatry*. 2017;16(1):104–105. doi:10.1002/wps.20404
75. Klosterkötter J, Hellmich M, Steinmeyer EM, Schultze-Lutter F. Diagnosing schizophrenia in the initial prodromal phase. *Arch Gen Psychiatry*. 2001;58(2):158–164. doi:10.1016/j.euroneuro.2014.03.008
76. Rosen JL, Woods SW, Miller TJ, McGlashan TH. Prospective observations of emerging psychosis. *J Nerv Ment Dis*. 2002;190(3):133–141. doi:10.1097/00005053-200203000-00001
77. Bora E, Lin A, Wood SJ, Yung AR, McGorry PD, Pantelis C. Cognitive deficits in youth with familial and clinical high risk to psychosis: a systematic review and meta-analysis. *Acta Psychiatr Scand*. 2014;130(1):1–15. doi:10.1111/acps.12261
78. Addington J, Stowkowy J, Liu L, et al. Clinical and functional characteristics of youth at clinical high-risk for psychosis who do not transition to psychosis. *Psychol Med*. 2019;49(10):1670–1677. doi:10.1017/S0033291718002258

79. Devoe DJ, Braun A, Seredynski T, Addington J. Negative Symptoms and Functioning in Youth at Risk of Psychosis: a Systematic Review and Meta-analysis. *Harv Rev Psychiatry*. 2020;28(6):341–355. doi:10.1097/HRP.0000000000000273
80. Tarbox SI, Addington J, Cadenhead KS, et al. Premorbid functional development and conversion to psychosis in clinical high-risk youths. *Dev Psychopathol*. 2013;25(4 Pt 1):1171–1186. doi:10.1017/S0954579413000448
81. Wastler HM, Cowan HR, Hamilton SA, et al. Variability in suicidal ideation during treatment for individuals at clinical high risk for psychosis: the importance of repeated assessment. *Early Interv Psychiatry*. 2023;17(10):1038–1041. doi:10.1111/eip.13413
82. Wastler HM, Cowan HR, Hamilton SA, et al. Within-Person Relationship between Attenuated Positive Symptoms and Suicidal Ideation among Individuals at Clinical High Risk for Psychosis. *Arch Suicide Res*. 2023:1–14. doi:10.1080/13811118.2023.2269209
83. Taylor PJ, Hutton P, Wood L. Are people at risk of psychosis also at risk of suicide and self-harm? A systematic review and meta-analysis. *Psychol Med*. 2015;45(5):911–926. doi:10.1017/S0033291714002074
84. Solmi M, Soardo L, Kaur S, et al. Meta-analytic prevalence of comorbid mental disorders in individuals at clinical high risk of psychosis: the case for transdiagnostic assessment. *Mol Psychiatry*. 2023;28(6):2291–2300. doi:10.1038/s41380-023-02029-8
85. Cannon TD, Yu C, Addington J, et al. An Individualized Risk Calculator for Research in Prodromal Psychosis. *Am J Psychiatry*. 2016;173(10):980–988. doi:10.1176/appi.ajp.2016.15070890
86. Oliver D, Reilly TJ, Baccaredda Boy O, et al. What Causes the Onset of Psychosis in Individuals at Clinical High Risk? A Meta-analysis of Risk and Protective Factors. *Schizophr Bull*. 2020;46(1):110–120. doi:10.1093/schbul/sbz039
87. Nelson B, Yuen HP, Lin A, et al. Further examination of the reducing transition rate in ultra high risk for psychosis samples: the possible role of earlier intervention. *Schizophr Res*. 2016;174(1–3):43–49. doi:10.1016/j.schres.2016.04.040
88. Fusar-Poli P, Schultze-Lutter F, Cappucciati M, et al. The Dark Side of the Moon: meta-analytical Impact of Recruitment Strategies on Risk Enrichment in the Clinical High Risk State for Psychosis. *Schizophr Bull*. 2016;42(3):732–743. doi:10.1093/schbul/sbv162
89. Wiltink S, Velthorst E, Nelson B, McGorry PM, Yung AR. Declining transition rates to psychosis: the contribution of potential changes in referral pathways to an ultra-high-risk service. *Early Interv Psychiatry*. 2015;9(3):200–206. doi:10.1111/eip.12105
90. Fusar-Poli P. The Clinical High-Risk State for Psychosis (CHR-P), Version II. *Schizophr Bull*. 2017;43(1):44–47. doi:10.1093/schbul/sbw158
91. Carrión RE, McLaughlin D, Goldberg TE, et al. Prediction of functional outcome in individuals at clinical high risk for psychosis. *JAMA Psychiatry*. 2013;70(11):1133–1142. doi:10.1001/jamapsychiatry.2013.1909
92. Kwapil TR, Gross GM, Silvia PJ, Raulin ML, Barrantes-Vidal N. Development and psychometric properties of the Multidimensional Schizotypy Scale: a new measure for assessing positive, negative, and disorganized schizotypy. *Schizophr Res*. 2018;193:209–217. doi:10.1016/j.schres.2017.07.001
93. Stefanis NC, Hanssen M, Smirnis NK, et al. Evidence that three dimensions of psychosis have a distribution in the general population. *Psychol Med*. 2002;32(2):347–358. doi:10.1017/s0033291701005141
94. Addington J, Woods SW, Yung AR, Calkins ME, Fusar-Poli P. Harmonizing the structured interview for psychosis-risk syndromes (SIPS) and the comprehensive assessment of at-risk mental states (CAARMS): an initial approach. *Early Interv Psychiatry*. 2023. doi:10.1111/eip.13401
95. Gross G, Huber G, Klosterkötter J, Linz M. *BSABS: Bonn Scale for the Assessment of Basic Symptoms*. 1st English ed. ShakerVerlag; 2008.
96. Schultze-Lutter F, Addington J, Ruhrmann S, Klosterkötter J. *Schizophrenia Proneness Instrument, Adult Version (SPI-A)*. Giovanni Fioriti Editore; 2007.
97. Schultze-Lutter F, Koch E. *Schizophrenia Proneness Instrument: Child and Youth Version (SPI-CY)*. Fioriti; 2010.
98. First MB, Williams JBW, Karg RS, Spitzer RL. Structured Clinical Interview for DSM-5-Research Version. *Am Psychiatr Assoc*. 2015;2015:1.
99. Endicott J, Spitzer RL. A diagnostic interview: the schedule for affective disorders and schizophrenia. *Arch Gen Psychiatry*. 1978;35(7):837–844. doi:10.1001/archpsyc.1978.01770310043002
100. Kaufman J, Schweder AE. The Schedule for Affective Disorders and Schizophrenia for School-Age Children: present and Lifetime version (K-SADS-PL). In: *Comprehensive Handbook of Psychological Assessment*. Vol. 2. John Wiley & Sons, Inc.; 2004:247–255.
101. Loewy RL, Pearson R, Vinogradov S, Bearden CE, Cannon TD. Psychosis risk screening with the Prodromal Questionnaire — brief Version (PQ-B). *Schizophr Res*. 2011;129(1):42–46. doi:10.1016/j.schres.2011.03.029
102. Addington J, Stowkowy J, Weiser M. Screening tools for clinical high risk for psychosis. *Early Interv Psychiatry*. 2015;9(5):345–356. doi:10.1111/eip.12193
103. Miller TJ, Cicchetti D, Markovich PJ, McGlashan TH, Woods SW. The SIPS screen: a brief self-report screen to detect the schizophrenia prodrome. *Schizophr Res*. 2004;70:78.
104. Ord LM, Myles-Worsley M, Blailes F, Ngiralmau H. Screening for prodromal adolescents in an isolated high-risk population. *Schizophr Res*. 2004;71(2–3):507–508. doi:10.1016/j.schres.2004.03.014
105. Brodey BB, Girgis RR, Favorov OV, et al. The Early Psychosis Screener (EPS): quantitative validation against the SIPS using machine learning. *Schizophr Res*. 2018;197:516–521. doi:10.1016/j.schres.2017.11.030
106. Woods SW, Parker S, Kerr MJ, et al. Development of the PSYCHS: positive SYmptoms and Diagnostic Criteria for the CAARMS Harmonized with the SIPS. *medRxiv*. 2023. doi:10.1101/2023.04.29.23289226
107. Schultze-Lutter F, Klosterkötter J, Ruhrmann S. Improving the clinical prediction of psychosis by combining ultra-high risk criteria and cognitive basic symptoms. *Schizophr Res*. 2014;154(1–3):100–106. doi:10.1016/j.schres.2014.02.010
108. Carpenter WT, van Os J. Should attenuated psychosis syndrome be a DSM-5 diagnosis? *Am J Psychiatry*. 2011;168(5):460–463. doi:10.1176/appi.ajp.2011.10121816
109. Corcoran CM, First MB, Cornblatt B. The psychosis risk syndrome and its proposed inclusion in the DSM-V: a risk–benefit analysis. *Schizophr Res*. 2010;120(1–3):16–22. doi:10.1016/j.schres.2010.03.018
110. Woods SW, Walsh BC, Saksa JR, McGlashan TH. The case for including Attenuated Psychotic Symptoms Syndrome in DSM-5 as a psychosis risk syndrome. *Schizophr Res*. 2010;123(2–3):199–207. doi:10.1016/j.schres.2010.08.012
111. Yang LH, Link BG, Ben-David S, et al. Stigma related to labels and symptoms in individuals at clinical high-risk for psychosis. *Schizophr Res*. 2015;168(1–2):9–15. doi:10.1016/j.schres.2015.08.004
112. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry*. 1998;59(Suppl 20):22–33;quiz 34–57.

113. Hamilton SA, Parris CJ, Breitborde NJK, Stearns WH. Psychotic-spectrum disorders in children and adolescents. In: *Developmental-Behavioral Pediatrics E-Book*. 5th ed. Elsevier Health Sciences. 2022 :549–558.
114. Cassano GB, Pini S, Saettoni M, Rucci P, Dell'Osso L. Occurrence and clinical correlates of psychiatric comorbidity in patients with psychotic disorders. *J Clin Psychiatry*. 1998;59(2):60–68. doi:10.4088/jcp.v59n0204
115. Bleuler E. *Dementia Praecox or the Group of Schizophrenias (J. Zinkin, Translation, 1950)*. International Universities Press; 1911.
116. Wilson C, Kline E, Reeves G, Anthony L, Schiffman J. Blurred Edges: evolving Concepts of Autism Spectrum Disorders and Schizophrenia. *Adolesc Psychiatry*. 2014;4(3):133–146. doi:10.2174/2210676604031409121613l2
117. Jutla A, Foss-Feig J, Veenstra-VanderWeele J. Autism spectrum disorder and schizophrenia: an updated conceptual review. *Autism Res*. 2022;15 (3):384–412. doi:10.1002/aur.2659
118. Wilson CS, Anthony L, Kenworthy L, et al. Feasibility of psychosis risk assessment for adolescents diagnosed with autism. *Autism*. 2020;24 (4):834–850. doi:10.1177/1362361320909173
119. Dossetor DR. 'All That Glitters Is Not Gold': misdiagnosis of Psychosis in Pervasive Developmental Disorders — a Case Series. *Clin Child Psychol Psychiatry*. 2007;12(4):537–548. doi:10.1177/1359104507078476
120. Ribolsi M, Fiori Nastro F, Pelle M, et al. Recognizing Psychosis in Autism Spectrum Disorder. *Front Psychiatry*. 2022;13:768586. doi:10.3389/ fpsyt.2022.768586
121. Van Schalkwyk GI, Peluso F, Qayyum Z, McPartland JC, Volkmar FR. Varieties of misdiagnosis in ASD: an illustrative case series. *J Autism Dev Disord*. 2015;45(4):911–918. doi:10.1007/s10803-014-2239-y
122. Kincaid DL, Doris M, Shannon C, Mulholland C. What is the prevalence of autism spectrum disorder and ASD traits in psychosis? A systematic review. *Psychiatry Res*. 2017;250:99–105. doi:10.1016/j.psychres.2017.01.017
123. Zheng Z, Zheng P, Zou X. Association between schizophrenia and autism spectrum disorder: a systematic review and meta-analysis. *Autism Res*. 2018;11(8):1110–1119. doi:10.1002/aur.1977
124. Carroll LS, Owen MJ. Genetic overlap between autism, schizophrenia and bipolar disorder. *Genome Med*. 2009;1(10):102. doi:10.1186/gm102
125. Vaquerizo-Serrano J, Salazar de Pablo G, Singh J, Santosh P. Autism Spectrum Disorder and Clinical High Risk for Psychosis: a Systematic Review and Meta-analysis. *J Autism Dev Disord*. 2022;52(4):1568–1586. doi:10.1007/s10803-021-05046-0
126. De Haan L, Schirmbeck F, Zink M, eds.. *Obsessive-Compulsive Symptoms in Schizophrenia*. Springer International Publishing; 2015. doi:10.1007/978-3-319-12952-5
127. Achim AM, Maziade M, Raymond E, Olivier D, Mérette C, Roy M-A. How prevalent are anxiety disorders in schizophrenia? A meta-analysis and critical review on a significant association. *Schizophr Bull*. 2011;37(4):811–821. doi:10.1093/schbul/sbp148
128. Bendall S, Jackson HJ, Hulbert CA, McGorry PD. Childhood Trauma and Psychotic Disorders: a Systematic, Critical Review of the Evidence. *Schizophr Bull*. 2007;34(3):568–579. doi:10.1093/schbul/sbm121
129. OConghaile A, DeLisi LE. Distinguishing schizophrenia from posttraumatic stress disorder with psychosis. *CurrOpin Psychiatry*. 2015;28 (3):249–255. doi:10.1097/YCO.0000000000000158
130. Pierre JM. Hallucinations in nonpsychotic disorders: toward a differential diagnosis of "hearing voices. *Harv Rev Psychiatry*. 2010;18(1):22–35. doi:10.3109/10673220903523706
131. Gearon JS, Bellack AS, Tenhula WN. Preliminary Reliability and Validity of the Clinician-Administered PTSD Scale for Schizophrenia. *J Consult Clin Psychol*. 2004;72(1):121–125. doi:10.1037/0022-006X.72.1.121
132. Lu W, Yanos PT, Waynor W, et al. Psychometric properties of post-traumatic stress disorder (PTSD) checklist for DSM-5 in persons with serious mental illness. *Eur J Psychotraumatol*. 2022;13(1):2038924. doi:10.1080/20008198.2022.2038924
133. Barlow DH, Farchione TJ, Sauer-Zavala S, et al. *Unified Protocol for Transdiagnostic Treatment of Emotional Disorders: Therapist Guide*. Second ed. Oxford University Press; 2018.
134. Resick PA, Monson CM, Chard KM. *Cognitive Processing Therapy for PTSD: A Comprehensive Manual*. The Guilford Press; 2017.
135. Breitborde NJK, Moe AM. Early Intervention in Psychosis in the United States: from Science to Policy Reform. *Policy Insights Behav Brain Sci*. 2017;4(1):79–87. doi:10.1177/2372732216683965
136. Moe AM, Rubinstein EB, Gallagher CJ, Weiss DM, Stewart A, Breitborde NJ. Improving access to specialized care for first-episode psychosis: an ecological model. *RMHP*. 2018;11:127–138. doi:10.2147/RMHP.S131833
137. Kline E, Schiffman J. Psychosis risk screening: a systematic review. *Schizophr Res*. 2014;158(1–3):11–18. doi:10.1016/j.schres.2014.06.036
138. Bebbington P, Nayani T. The psychosis screening questionnaire. *Int J Methods Psychiatr Res*. 1995;5(1):11–19.
139. Heuvelman H, Nazroo J, Rai D. Investigating ethnic variations in reporting of psychotic symptoms: a multiple-group confirmatory factor analysis of the Psychosis Screening Questionnaire. *Psychol Med*. 2018;48(16):2757–2765. doi:10.1017/S0033291718000399
140. Owoso A, Ndetei DM, Mbwayo AW, Mutiso VN, Khasakhala LI, Mamah D. Validation of a modified version of the PRIME screen for psychosis-risk symptoms in a non-clinical Kenyan youth sample. *Compr Psychiatry*. 2014;55(2):380–387. doi:10.1016/j.comppsych.2013.10.004
141. Savill M, D'Ambrosio J, Cannon TD, Loewy RL. Psychosis risk screening in different populations using the Prodromal Questionnaire: a systematic review. *Early Interv Psychiatry*. 2018;12(1):3–14. doi:10.1111/eip.12446
142. Simeonova DI, Nguyen T, Walker EF. Psychosis risk screening in clinical high-risk adolescents: a longitudinal investigation using the Child Behavior Checklist. *Schizophr Res*. 2014;159(1):7–13. doi:10.1016/j.schres.2014.07.046
143. Thompson E, Kline E, Reeves G, Pitts SC, Bussell K, Schiffman J. Using parent and youth reports from the Behavior Assessment System for Children, Second Edition to identify individuals at clinical high-risk for psychosis. *Schizophr Res*. 2014;154(1–3):107–112. doi:10.1016/j. schres.2014.02.009
144. Kennedy L, Johnson KA, Cheng J, Woodberry KA. A Public Health Perspective on Screening for Psychosis Within General Practice Clinics. *Front Psychiatry*. 2020;10:1025. doi:10.3389/fpsyt.2019.01025
145. Bernardin F, Gauld C, Martin VP, Laprévote V, Dondé C. The 68 symptoms of the clinical high risk for psychosis: low similarity among fourteen screening questionnaires. *Psychiatry Res*. 2023;330:115592. doi:10.1016/j.psychres.2023.115592
146. Ellman LM, Schiffman J, Mittal VA. Community Psychosis Risk Screening: an Instrument Development Investigation. *J Psychiatr Brain Sci*. 2020;5:e200019. doi:10.20900/jpbs.20200019
147. Millman ZB, Rakhshan Rouhakhtar PJ, DeVylder JE, et al. Evidence for Differential Predictive Performance of the Prime Screen Between Black and White Help-Seeking Youths. *Psychiatr Serv*. 2019;70(10):907–914. doi:10.1176/appi.ps.201800536

148. Schiffman J, Ellman LM, Mittal VA. Individual Differences and Psychosis-Risk Screening: practical Suggestions to Improve the Scope and Quality of Early Identification. *Front Psychiatry*. 2019;10:6. doi:10.3389/fpsyt.2019.00006
149. Wilson C, Smith ME, Thompson E, et al. Context matters: the impact of neighborhood crime and paranoid symptoms on psychosis risk assessment. *Schizophr Res*. 2016;171(1–3):56–61. doi:10.1016/j.schres.2016.01.007
150. Wolny J, Moussa-Tooks AB, Bailey AJ, O'Donnell BF, Hetrick WP. Race and self-reported paranoia: increased item endorsement on subscales of the SPQ. *Schizophr Res*. 2023;253:30–39. doi:10.1016/j.schres.2021.11.034
151. Addington D. The First Episode Psychosis Services Fidelity Scale 1.0: review and Update. *Schizophrenia Bulletin Open*. 2021;2(1):sgab007. doi:10.1093/schizbullopen/sgab007
152. Howes OD, Whitehurst T, Shatalina E, et al. The clinical significance of duration of untreated psychosis: an umbrella review and random-effects meta-analysis. *World Psychiatry*. 2021;20(1):75–95. doi:10.1002/wps.20822
153. Lloyd-Evans B, Crosby M, Stockton S, et al. Initiatives to shorten duration of untreated psychosis: systematic review. *Br J Psychiatry*. 2011;198 (4):256–263. doi:10.1192/bjp.bp.109.075622
154. Oliver D, Davies C, Crossland G, et al. Can We Reduce the Duration of Untreated Psychosis? A Systematic Review and Meta-Analysis of Controlled Interventional Studies. *Schizophr Bull*. 2018;44(6):1362–1372. doi:10.1093/schbul/sbx166
155. Estradé A, Salazar de Pablo G, Zanotti A, Wood S, Fisher HL, Fusar-Poli P. Public health primary prevention implemented by clinical high-risk services for psychosis. *Transl Psychiatry*. 2022;12(1):43. doi:10.1038/s41398-022-01805-4
156. McIlwaine SV, Jordan G, Pruessner M, et al. Does an integrated outreach intervention targeting multiple stages of early psychosis improve the identification of individuals at clinical high risk? *Early Interv Psychiatry*. 2019;13(4):989–992. doi:10.1111/eip.12750
157. López SR, Kopelowicz A, Ullman J, et al. Toward reducing the duration of untreated psychosis in a Latinx community. *J Consult Clin Psychol*. 2022;90(10):815–826. doi:10.1037/ccp0000729
158. Lynch S, McFarlane WR, Joly B, et al. Early Detection, Intervention and Prevention of Psychosis Program: community Outreach and Early Identification at Six U.S. Sites. *Psychiatr Serv*. 2016;67(5):510–516. doi:10.1176/appi.ps.201300236
159. Ramsay Wan C, Broussard B, Haggard P, Compton MT. Criminal justice settings as possible sites for early detection of psychotic disorders and reducing treatment delay. *Psychiatr Serv*. 2014;65(6):758–764. doi:10.1176/appi.ps.201300206