

I. Screening of Ultra High Risk and First Episode

-Overview articles

-Screening instruments: PQ, PQ-B, PQ-16

Self-Report Instruments for Clinical Monitoring of Psychosis Risk States

Kline, E., Thompson, E., Demro, C., Bussell, K., Reeves, G., & Schiffman, J. (2015). Self-Report Instruments for Clinical Monitoring of Psychosis Risk States. *Psychiatric Services*.

Abstract: Objective: Practice guidelines emphasize frequent clinical monitoring of patients at high risk for psychosis. No brief instrument assessing attenuated psychotic symptoms has been validated for this purpose. This study examined use of three self-report questionnaires, which were developed as psychosis risk screeners, for monitoring symptom severity in a naturalistic clinical sample of 54 adolescents. Methods: Self-report measures (Prime Screen–Revised, Prodromal Questionnaire–Brief Version [PQ-B], and Youth Psychosis At-Risk Questionnaire–Brief) and clinician assessments (Structured Interview for Psychosis Risk Syndromes) were administered to participants at baseline and six months. Results: Changes in self-report scores were moderately correlated with changes in clinician ratings. The PQ-B demonstrated slightly better agreement with changes in clinician ratings than the other two measures. Conclusions: Questionnaires developed as psychosis risk screeners could be used for symptom monitoring. Further validation of tools to monitor attenuated symptoms will be a valuable step toward developing an evidence-based approach for treating high-risk youths.

Psychosis Risk Screening: A systematic review

Kline, E., & Schiffman, J. (2014). Psychosis risk screening: a systematic review. *Schizophrenia research*, 158(1), 11-18.

Abstract: Despite the wealth of evidence linking duration of untreated psychosis to critical illness outcomes, most clinicians do not utilize any formal evaluation tools to identify attenuated or emerging psychotic symptoms. Given the costs associated with training and administration, interview-based assessments such as the Structured Interview for Psychosis Risk Syndromes (SIPS) are not likely to be widely adopted for clinical use. The ability to identify high-risk individuals through low-cost, brief methods is essential to the success of scalable prevention efforts. The aim of this article is to present a comprehensive review of the use of self-report forms as psychosis risk “screeners.” A literature search revealed 34 investigations in which authors used a self-report questionnaire as a first-step screener in a clinical high-risk assessment protocol. Information about each screener, including reported psychometric data, is presented within the review. Psychosis risk screeners have been used in diverse samples with the goals of validating assessments, screening populations for clinical referral, recruiting samples of interest for research participation, and estimating symptom prevalence and severity. Screeners focusing on attenuated psychotic experiences appear to measure a reliable construct with variable prevalence in help-seeking and general population samples. Administration of screeners to help-seeking populations can identify enriched samples with substantially elevated likelihood of meeting CHR criteria and transitioning to psychosis over time. More research is needed, however, to establish

reliable norms and screening thresholds, as score elevations indicating a likely high-risk respondent appear to be unreliable across populations and settings.

The Prodromal Questionnaire (PQ)

Loewy, R. L., Bearden, C. E., Johnson, J. K., Raine, A., & Cannon, T. D. (2005). The prodromal questionnaire (PQ): preliminary validation of a self-report screening measure for prodromal and psychotic syndromes. *Schizophrenia research*, 79(1), 117-125.

The PQ is a 92-item self-report questionnaire that takes approximately 20 min to complete. Most items were adapted from the [Schizotypal Personality Questionnaire \(Raine, 1991\)](#) and from probe questions in the SIPS ([Miller et al., 2002](#)); some original items were also added. The items are answered true/false and sum to form four major subscales: 1) Positive symptoms (e.g. unusual thinking and perceptual abnormalities), 2) Negative symptoms (e.g. flat affect and [social isolation](#)), 3) Disorganized symptoms (e.g. odd behavior) and 4) General symptoms (e.g. depression and role functioning). Sample items include “Sometimes I think that people can read my mind,” and “I tend to avoid social activities with other people.”

The Prodromal Questionnaire Brief Version (PQ-B) and 16-Item Prodromal Questionnaire (PQ-16)

Loewy, R. L., Pearson, R., Vinogradov, S., Bearden, C. E., & Cannon, T. D. (2011). Psychosis risk screening with the Prodromal Questionnaire—brief version (PQ-B). *Schizophrenia research*, 129(1), 42-46.

Ising, H. K., Veling, W., Loewy, R. L., Rietveld, M. W., Rietdijk, J., Dragt, S., ... & van der Gaag, M. (2012). The validity of the 16-item version of the Prodromal Questionnaire (PQ-16) to screen for ultra high risk of developing psychosis in the general help-seeking population. *Schizophrenia bulletin*, 38(6), 1288-1296.

II. Clinical Interviews to assess prodromal and psychotic experiences

Prodromal:

-CAARMS

-SIPS/SOPS

-Bonn Scale of Basic Symptoms

FEP:

-PANSS

-BPRS

Symptom Specific:

-PSYRATS (Delusions and Hallucinations)

-Cognitive Assessment of Voices Interview

Comprehensive Assessment of At Risk Mental State (CAARMS)

Alison R. Yung, Alison R. Yung, Hok Pan Yuen, Patrick D. McGorry, Lisa J. Phillips, Daniel Kelly, Margaret Dell'olio, Shona M. Francey, Elizabeth M. Cosgrave, Eoin Killackey, Carrie Stanford, Katherine Godfrey & Joe Buckby (2005) Mapping the onset of psychosis: the Comprehensive Assessment of At-Risk Mental States, *Australian and New Zealand Journal of Psychiatry*, 39:11-12, 964-971

The CAARMS is a semistructured interview schedule designed for use by mental health professionals who are already able to assess and evaluate patients' information. It is designed for repeated use over time, for example, monthly to 6 monthly. The CAARMS includes the following subscales: disorders of thought content (e.g. delusional mood, overvalued ideas and delusions), perceptual abnormalities (e.g. distortions, illusions and hallucinations), conceptual disorganization (e.g. subjectively experienced difficulties with forming thoughts and objective assessment of formal thought disorder), motor changes (e.g. subjectively experienced difficulties with movement and objective signs of catatonia), concentration and attention (assessing both the subjective experience and objective rating), emotion and affect (assessing subjective sense of change in emotions and objective rating of blunting of affect), subjectively impaired energy (a basic symptom) and impaired tolerance to normal stress (a basic symptom).

Structured Interview of Prodromal Symptoms/ Scale of Prodromal Symptoms (SIPS/SOPS)

Miller, T. J., McGlashan, T. H., Woods, S. W., Stein, K., Driesen, N., Corcoran, C. M., ... & Davidson, L. (1999). Symptom assessment in schizophrenic prodromal states. *Psychiatric Quarterly*, 70(4), 273-287.

The first goal of the SIPS and the SOPS is to provide a systematic measure of the presence/absence of prodromal states as outlined by the Australians. The second goal is to measure the severity of prodromal symptoms cross-sectionally and longitudinally, and the third goal is to define the threshold of psychosis operationally. The SOPS consists of five Positive Symptom items, six Negative Symptom items, four Disorganization Symptom items, and four General Symptom items. Each item has a severity scale rating from 0 (Never, Absent) to 6 (Severe/Extreme—and Psychotic, for the positive items). The severity of the prodromal state is judged according to the sum of the ratings from each of the SOPS items and ranges from 0 to 114. Thus, there are severity ratings for the overall scale, each domain of pathology, as well as individual items. The SIPS (available by request from the authors) includes 29 major probes organized according to each positive symptom item in the SOPS. In the SIPS, patients are also rated according to their Global Assessment of Functioning (19) (GAF), a DSM IV Schizotypal Personality Disorder criterion checklist (20), and family history of mental illness. Diagnosis is accomplished using the Criteria for Prodromal States (COPS). The SIPS is used to determine the presence or absence of the prodromal state, the type of prodromal state, and the presence or absence of a psychotic state, and it includes the SOPS and the COPS. The SOPS is used independently to determine the severity of the prodromal state once such a state has been diagnosed.

Bonn Scale of Basic Symptoms (BSABS)

Schultze-Lutter, F., & Klosterkötter, J. (2002). Bonn Scale for the Assessment of Basic Symptoms-Prediction list (BSABS-P). *University of Cologne, Cologne*.

The BSABS is a semi-structured interview consisting of 92 principal items described in a prototypical manner, supplemented by differential-diagnostic guidelines, examples of questions and suggestions of probes. Symptoms are divided into stage 1 and 2 basic symptoms. The stage 2 basic symptoms are found to be more specific to schizophrenia spectrum disorders than to other psychiatric disorders .

Positive and Negative Syndrome Scale (PANSS)

Kay, S. R., Flszbein, A., & Opfer, L. A. (1987). The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophrenia bulletin*, 13(2), 261.

Based on two established psychiatric rating systems, the 30- item PANSS was conceived as an operationalized, drug-sensitive instrument that provides balanced representation of positive and negative symptoms and gauges their relationship to one another and to global psychopathology. It thus constitutes four scales measuring positive and negative syndromes, their differential, and general severity of illness. Study of 101 schizophrenics found the four scales to be normally distributed and supported their reliability and stability. Positive and negative scores were inversely correlated once their common association with general psychopathology was extracted, suggesting that they represent mutually exclusive constructs.

Brief Psychiatric Rating Scale (BPRS)

Rhoades, H. M., & Overall, J. E. (1988). The semistructured BPRS interview and rating guide. *Psychopharmacology Bulletin*, 24(1), 101.

While originally only 16 items, the current and most popular version contains 18 symptom constructs. Each item is rated on a seven-point Likert scale ranging from 0 ('not present') to 6 ('extremely severe'). These constructs were meant to describe the wide variety of symptoms present in psychiatric patients (e.g., 'somatic concern', 'hallucinatory behavior'). Overall and Gorham described their primary purpose as being "the development of a highly efficient, rapid evaluation procedure for use in assessing treatment change in psychiatric patients while at the same time yielding a rather comprehensive description of major symptom characteristics"

Psychotic Symptoms Rating Scale (PSYRATS)

Haddock, G., McCarron, J., Tarrier, N., & Faragher, E. B. (1999). Scales to measure dimensions of hallucinations and delusions: the psychotic symptom rating scales (PSYRATS). *Psychological medicine*, 29(04), 879-889.

The PSYRATS consist of two scales designed to rate auditory hallucinations and delusions respectively (see Appendix 1). The auditory hallucinations subscale (AH) is an 11 item scale. The development of the scale was based on the need for an adequate measure of dimensions of hallucinations which was both comprehensive and easy to administer. The item pool for the scale taps general symptom indices of frequency, duration, severity and intensity of distress and also symptom specific dimensions of controllability, loudness, location, negative content, degree of negative content, beliefs about origin of voices and disruption. A 5-point ordinal scale is used to rate symptom scores (0±4). The items were

chosen following a large number of interviews with hallucinating patients using semi-structured interviews which indicated that a number of dimensions appeared to be unrelated and from psychological intervention work with psychotic patients (see Haddock *et al.* 1998). The delusions subscale (DS) is a six-item scale which assesses dimensions of delusions. The scale items were derived from the literature of phenomenological studies with delusions and from psychological intervention work with psychotic. The items are rated on a five-point ordinal scale (0±4). The items include preoccupation, distress, duration, conviction, intensity of distress and disruption.

Cognitive Assessment of Voices Interview

Chadwick, P., & Birchwood, M. (1994). The omnipotence of voices: A cognitive approach to auditory hallucinations. *British Journal of Psychiatry*, 164, 190±201.

(See attached).

III. Measuring Duration of Untreated Psychosis/ Symptom Onset

-Overview Article

-RPMIP

-CASH

-SOS

Defining, operationalizing and measuring the duration of untreated psychosis: advances, limitations and future directions

Compton, M. T., Carter, T., Bergner, E., Franz, L., Stewart, T., Trotman, H., ... & McGorry, P. D. (2007). Defining, operationalizing and measuring the duration of untreated psychosis: advances, limitations and future directions. *Early Intervention in Psychiatry*, 1(3), 236-250.

Abstract Objective: Substantial converging evidence from schizophrenia researchers indicates that the duration of untreated psychosis (DUP) represents a modifiable predictor of outcome during the early course of schizophrenia. As DUP is increasingly assessed in research settings, focused attention should be given to the complexities of measurement of this critical construct. In this review, three aspects of measurement are addressed: (i) definition of DUP, (ii) operational criteria for the construct, and (iii) methods used for measurement. Recent advances, current limitations and future directions are discussed. Methods: Inclusion of published articles for this systematic review was based on two recent seminal meta-analyses examining associations between DUP and outcomes. Other relevant articles were reviewed to glean information on standardized instruments used to date and limitations regarding measurement of DUP. Results: Whereas the general definition of the DUP construct has been quite consistent across research groups, considerable variability exists in the operationalizations of the onset and endpoint of DUP. Several standardized instruments have been developed to measure DUP, although many articles fail to discuss reliability and validity of measurements. The literature lacks comparative assessments of the relative reliability and validity of the various measures and methods used to assess DUP. Conclusions: Given the importance of DUP and implications for secondary prevention, the complicated measurement issues that arise in quantifying this construct are addressed.

A number of important advances from a variety of research groups have made the systematic assessment of DUP feasible and of great value for early psychosis research. Yet, several limitations must be considered as measurement of DUP progresses.

The Royal Park Multidiagnostic Instrument for Psychosis

McGorry PD, Copolov DL, Singh BS. Royal Park Multidiagnostic Instrument for Psychosis. I. rationale and review. *Schizophr Bull* 1990; 16: 501–15. 66.

McGorry PD, Singh BS, Copolov DL. Royal Park Multidiagnostic Instrument for Psychosis. II. development, reliability and validity. *Schizophr Bull* 1990; 16: 517–36.

The Royal Park Multidiagnostic Instrument for Psychosis (RPMIP) was designed to measure the mode of onset, psychopathology and diagnostic spectrum of first-episode psychosis. This instrument uses multiple sources of information to characterize a number of features from onset until termination of psychotic episodes related to schizophrenia, affective psychosis, atypical psychosis and other psychotic disorders. The interview is typically conducted on two separate occasions within the same acute episode – the first to observe the psychosis at its worst severity, and the second to gather more coherent and reliable information. Each patient interview lasts 1.5–2 h. Data from the informant interview, which lasts approximately 1 h, is integrated to derive best estimates. In terms of inter-rater reliability, most kappa coefficients have been found to be above 0.60, and the mean kappa for single items was 0.70.

The Comprehensive Assessment of Symptoms and History (CASH)

Andreasen NC, Flaum M, Arndt S. The Comprehensive Assessment of Symptoms and History (CASH): an instrument for assessing diagnosis and psychopathology. *Arch Gen Psychiatry* 1992; 49: 615–23.

The Comprehensive Assessment of Symptoms and History (CASH) is a structured interview for psychosis and affective disorders that assesses premorbid functioning, current and past symptoms, treatment, course of illness and sociodemographic variables. Further, the CASH serves as a guide for applying diagnostic criteria. In addition to assessing the presence of specific signs and symptoms, the instrument also rates global severity in particular domains (e.g. global rating of hallucination severity). Both inter-rater and test–retest reliability were shown to be excellent for most items. Using test–retest methods, however, some items had low reliability and were difficult to rate (e.g. severity of positive and negative symptoms during the first 2 years of the illness and negative symptoms during the ‘worst ever’ time frame).

Symptom Onset in Schizophrenia Scale

Perkins DO, Leserman J, Jarskog LF, Graham K, Kazmer J, Lieberman JA. Characterizing and dating the onset of symptoms in psychotic illness: the Symptom Onset in Schizophrenia (SOS) inventory. *Schizophr Res* Jul 7 2000;44(1):1-10.

Prodromal symptoms, including disturbances of perceptions, beliefs, cognition, affect, and behavior, are often the first symptoms of schizophrenia. Little is understood about the initial, prodromal stage of schizophrenia, despite the compelling research and clinical need. The development and psychometric properties of a new, time-efficient instrument to characterize and date the initial symptoms of a psychotic illnesses, the Symptom Onset in Schizophrenia (SOS) scale, is described in this paper. The SOS rates the presence and dates the onset of 16 general prodromal, positive, negative, and disorganized symptoms, as well as a clinician, family, and patient global rating of onset of illness. Inter-rater reliability for the presence of each symptom in 35 patients with schizophrenia, schizoaffective, or schizophreniform disorder was good to excellent, with kappa coefficient >0.7 for 12 items, and >0.5 for all items. Agreement on symptom duration was good to excellent for individual items ($ICC=0.7-1.0$) and for global rating of duration of illness ($ICC=0.97$). Our data indicate that the SOS is a reliable, valid, time-efficient tool useful to retrospectively assess the onset of schizophrenia and related psychotic disorders. Further study is underway to evaluate other psychometric properties of the SOS, including test-retest reliability and predictive validity.

IV. Articles about issues around diagnosis

Diagnostic Stability of ICD/DSM First Episode Psychosis Diagnoses: Meta-analysis.

Fusar-Poli, P., Cappucciati, M., Rutigliano, G., Heslin, M., Stahl, D., Brittenden, Z., ... & Carpenter, W. T. (2016). Diagnostic Stability of ICD/DSM First Episode Psychosis Diagnoses: Meta-analysis. *Schizophrenia bulletin*.

Abstract: BACKGROUND: Validity of current International Classification of Disease/Diagnostic and Statistical Manual of Mental Disorders (ICD/DSM) first episode psychosis diagnoses is essential in clinical practice, research, training and public health. METHOD: We provide a meta-analytical estimate of prospective diagnostic stability and instability in ICD-10 or DSM-IV first episode diagnoses of functional psychoses. Independent extraction by multiple observers. Random effect meta-analysis conducted with the "metaprop," "metaninf," "metafunnel," "metabias," and "metareg" packages of STATA13.1. Moderators were tested with meta-regression analyses. Heterogeneity was assessed with the I² index. Sensitivity analyses tested robustness of results. Publication biases were assessed with funnel plots and Egger's test. FINDINGS: 42 studies and 45 samples were included, for a total of 14 484 first episode patients and an average follow-up of 4.5 years. Prospective diagnostic stability ranked: schizophrenia 0.90 (95% CI 0.85-0.95), affective spectrum psychoses 0.84 (95% CI 0.79-0.89), schizoaffective disorder 0.72 (95% CI 0.61-0.73), substance-induced psychotic disorder 0.66 (95% CI 0.51-0.81), delusional disorder 0.59 (95% CI 0.47-0.71), acute and transient psychotic disorder/brief psychotic disorder 0.56 (95% CI 0.62-0.60), psychosis not otherwise specified 0.36 (95% CI 0.27-0.45, schizophreniform disorder 0.29 (95% CI 0.22-0.38). Diagnostic stability within schizophrenia spectrum psychoses was 0.93 (95% CI 0.89-0.97); changes to affective spectrum psychoses were 0.05 (95% CI 0.01-0.08). About 0.10 (95% CI 0.05-0.15) of affective spectrum psychoses changed to schizophrenia spectrum psychosis. Across the other psychotic diagnoses there was high diagnostic instability, mostly to schizophrenia. INTERPRETATION: There is meta-analytical evidence for high prospective diagnostic stability in schizophrenia spectrum and affective spectrum psychoses, with no significant ICD/DSM differences.

These results may inform the development of new treatment guidelines for early psychosis and impact drug licensing from regulatory agencies.

McLean-Harvard International First-Episode Project: Two-Year Stability of Diagnoses in 500 First-Episode Psychotic Disorder Patients.

Salvatore, P., Baldessarini, R. J., Tohen, M., Khalsa, H. M. K., Sanchez-Toledo, J. P., Zarate Jr, C. A., ... & Maggini, C. (2010). McLean-Harvard International First-Episode Project: Two-Year Stability of Diagnoses in 500 First-Episode Psychotic Disorder Patients. *The Journal of clinical psychiatry*, 72(2), 1-478.

Abstract: Objective: Because clinical and biologic research and optimal clinical practice require stability of diagnoses over time, we determined stability of ICD-10 psychotic disorder diagnoses and sought predictors of diagnostic instability.

Method: Patients from the McLean-Harvard International First-Episode Project, conducted from 1989 to 2003, who were hospitalized for first psychotic illnesses (N = 500) were diagnosed by ICD-10 criteria at baseline and 24 months, on the basis of extensive prospective assessments, to evaluate the longitudinal stability of specific categorical diagnoses and predictors of diagnostic change.

Results: Diagnostic stability averaged 90.4%, ranking as follows: schizoaffective disorder (100.0%) > mania with psychosis (99.0%) > mixed affective episode (94.9%) > schizophrenia (94.6%) > delusional disorder (88.2%) > severe depressive episode with psychotic symptoms (85.2%) > acute psychosis with/without schizophrenia symptoms = unspecified psychosis (all 66.7%) >> acute schizophrenia-like psychosis (28.6%). Diagnoses changed by 24 months of follow-up to schizoaffective disorder (37.5%), bipolar disorder (25.0%), schizophrenia (16.7%), or unspecified nonorganic psychosis (8.3%), mainly through emerging affective features. By logistic regression, diagnostic change was associated with Schneiderian first-rank psychotic symptoms at intake > lack of premorbid substance use.

Conclusions: We found some psychotic disorder diagnoses to be more stable by ICD-10 than DSM-IV criteria in the same patients, with implications for revisions of both diagnostic systems.