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## Current status specifiers for patients at clinical high risk for psychosis

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### ABSTRACT

**Background:** Longitudinal studies of the clinical high risk (CHR) syndrome for psychosis have emphasized the conversion vs non-conversion distinction and thus far have not focused intensively on classification among non-converters. The present study proposes a system for classifying CHR outcomes over time when using the Structured Interview for Psychosis-risk Syndromes and evaluates its validity.

**Method:** The system for classifying CHR outcomes is referred to as “current status specifiers,” with “current” meaning over the month prior to the present evaluation and “specifiers” indicating a set of labels and descriptions of the statuses. Specifiers for four current statuses are described: progression, persistence, partial remission, and full remission. Data from the North American Prodromal Longitudinal Study were employed to test convergent, discriminant, and predictive validity of the current status distinctions.

**Results:** Validity analyses partly supported current status distinctions. Social and role functioning were more impaired in progressive and persistent than in remitted patients, suggesting a degree of convergent validity. Agreement between CHR current statuses and current statuses for a different diagnostic construct (DSM-IV Major Depression) was poor, suggesting discriminant validity. The proportion converting to psychosis within a year was significantly higher in cases meeting progression criteria than in those meeting persistence criteria and tended to be higher than in those meeting full remission criteria, consistent with a degree of predictive validity.

**Discussion:** CHR syndrome current status specifiers could offer a potentially valid and useful description of current clinical status among non-converters. Study in additional samples is needed.

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### 1. Introduction

A prodromal period before the onset of frank schizophrenia has been recognized for at least a century (Bleuler, 1911; Klosterkotter et al., 2008), and over the past two decades a growing body of work has sought to diagnose a prodromal syndrome prospectively (Fusar-Poli et al., 2013). One approach has been to define clinical high risk (CHR) criteria, also known as at-risk mental state or ultra-high risk or risk syndrome (Schultze-Lutter et al., 2011) criteria. Two structured diagnostic interviews, the Comprehensive Assessment of At Risk Mental States

(CAARMS) (Yung et al., 2004) and the Structured Interview for Psychosis-risk Syndromes (SIPS) (McGlashan et al., 2010) have demonstrated reliability and validity (Yung et al., 2005; Addington et al., 2007; Yung et al., 2008; Woods et al., 2009, 2010; Fusar-Poli et al., 2012b).

While CHR criteria consistently have been statistically significant predictors of conversion, it has become more clear over the past decade that the majority of patients meeting the criteria do not go on to become psychotic (Cannon et al., 2008; Ruhrmann et al., 2010; Fusar-Poli et al., 2012a; Nelson et al., 2013). Some of the non-converting patients remain symptomatic over time, and others become symptom-free (Addington et al., 2011). At present, however, existing diagnostic criteria have paid relatively little attention to follow-up classification.

This paper proposes a new classification system for CHR patients when using the SIPS over time. The system is based on diagnostic criteria that establish eligibility for classification and specifiers of

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current status that may vary over follow-up. Data from the first phase of the North American Prodrome Longitudinal Study (Addington et al., 2007) (NAPLS-1) are used to evaluate the validity of the current status distinctions.

## 2. Methods

In the term “current status specifiers,” “current” refers to the month prior to the present evaluation and “specifiers” to a set of labels and descriptions of possible statuses. Although conversion to psychosis could also be considered a current status, the focus of the present paper is not upon the existing SIPS definition of conversion but on new specifiers of current status for patients who have not converted or who have not converted yet. The proposed current status specifiers are influenced by the severity/psychosis/remission specifiers used for affective disorder diagnoses (American Psychiatric Association, 1987, 1994, 2013) and remission criteria proposed for schizophrenia (van Os et al., 2006).

### 2.1. Current status specifiers

The SIPS identifies three CHR syndromes: Attenuated Psychotic Symptoms Syndrome (APSS), Brief Intermittent Psychosis Syndrome (BIPS), and Genetic Risk and Deterioration (GRD), all originally articulated by the Melbourne group (Yung et al., 1996). In previous versions of the SIPS, criteria for each CHR syndrome required recent worsening, and each was scored only as currently present vs not currently present. Different ways of not meeting current worsening criteria (features present but no longer worsening, features no longer present, features never present) were not distinguished.

For each CHR syndrome Fig. 1 outlines criteria for four current status specifiers: progression, persistence, partial remission, and full remission. The current status specifiers may be applied to patients meeting syndromal diagnostic criteria, also in Fig. 1. The syndromal criteria and the current status specifiers are intended to be used together, at initial evaluation and/or at any follow-up assessment. The syndromal diagnosis would apply across course while the current status could vary (for example: APSS currently progressive, or GRD currently in partial remission).

Fig. 1 shows that for APSS and BIPS a CHR diagnosis depends on a history of at least one positive symptom meeting severity, frequency, and attribution criteria. APSS or BIPS progression requires that these criteria be met currently as well as recent worsening; these APSS or BIPS progression criteria are identical to our previously proposed SIPS criteria for APSS and BIPS current presence yes vs no. APSS or BIPS

persistence are similar to APSS or BIPS progression in requiring that syndromal criteria be met currently but differ in that worsening criteria cannot. For APSS or BIPS partial remission two pathways were considered appropriate, following the format for DSM affective disorders in partial remission. For the first pathway, no positive symptom can meet severity and attribution criteria, but for no longer than 6 months. For the second pathway, one or more positive symptoms do currently meet severity and attribution criteria but not frequency criteria. Patients meeting criteria for this second route could potentially remain in partial remission for an indefinite period of time. For APSS or BIPS full remission, no positive symptom has met severity and attribution criteria for longer than 6 months. GRD syndromal and current status criteria are based on indices of genetic risk and changes in global functioning. Criteria for GRD progression differ slightly from our previous criteria for GRD current presence (rationale in Supplementary data).

When patients meet criteria for a current status for one CHR syndrome (e.g. GRD partial remission) but also criteria for a different current status for another CHR syndrome (e.g. APSS progression), the overall CHR syndrome current status is defined according to the rule “progression trumps persistence trumps partial remission trumps full remission.” The supplementary data include pages from SIPS 5.6 providing detail on how syndromal assessments and current status assessments are scored.

### 2.2. Subjects

NAPLS-1 methods have been described in detail previously (Addington et al., 2007). All subjects provided written informed consent, and protocols were approved by institutional review boards at each site. Symptomatic subjects from three groups according to the earlier classification (Woods et al., 2009) were eligible for the present analyses if all 5 SIPS positive symptoms were rated for severity either at baseline, 6 months, and 12 months or at 12, 18, and 24 months. Fig. 2 shows the flow diagram of eligible subjects and reasons for ineligibility.

### 2.3. Classification

Eligible subjects were then classified at each timepoint based as closely as possible on the current status specifier scheme shown in Fig. 1. NAPLS-1 data, however, were not collected prospectively to map onto this criterion set, and therefore certain criteria either could not be applied or required estimation methods. Early versions of the SIPS did not provide for symptom specific frequency ratings, and therefore symptom frequency data were unavoidably missing for some cases.

Term Defined	APSS Syndrome	BIPS Syndrome	GRD Syndrome
<b>Syndromal Diagnosis</b>	Attenuated pos sx ever met criteria for: -severity (rated 3-5 at some time), -frequency ( $\geq 1x/week$ the same month), -attribution (not due to other disorder).	Positive sx ever met criteria for: -severity (rated 6 in some month), -frequency ( $\geq 1x/mo$ ), -attribution (not due to other disorder).	FHx psychosis, or ever SPD. Hx of current or past progression.
<b>Current Status Specifiers</b>	<b>Progression</b>	$\geq 1$ positive sx meets severity, frequency, attribution, and progression ( $\geq 1$ point more than 12 mos ago) criteria.	GAF meets current progression criteria ( $\geq 30\%$ lower than 12 mos ago).
	<b>Persistence</b>	$\geq 1$ positive sx meets severity, frequency, and attribution but not progression criteria.	GAF $< 90\%$ of 12 months prior to first progression.
	<b>Partial Remission</b>	No positive sx have met severity and attribution criteria $\leq 6$ months, OR $\geq 1$ positive sx meet severity and attribution, but not frequency criteria.	GAF $\geq 90\%$ of 12 months prior to first progression, for $\leq 6$ months.
	<b>Full Remission</b>	No positive sx have met severity and attribution criteria $> 6$ months.	GAF $\geq 90\%$ of 12 mos prior to first progression, for $> 6$ months.

**Fig. 1.** Definitions for clinical high risk syndrome and current status specifiers when using the SIPS. SIPS—Structured Interview for Psychosis-risk Syndromes, APSS—Attenuated Psychotic Symptoms Syndrome, BIPS—Brief Intermittent Psychosis Syndrome, GRD—Genetic Risk and functional Decline, pos—positive, sx—symptoms, FHx—family history of, SPD—schizotypal personality disorder, Hx—history of, GAF—Global Assessment of Functioning. N.B. When a patient who meets criteria for two or more specific CHR syndromes now meets criteria for one at a higher level than another (e.g. both APSS progressive and GRD persistent), the higher level current status is given as the overall CHR syndrome status. To be explicit, “progression trumps persistence trumps partial remission trumps full remission.”

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