

## Bipolar Prodrome Symptom Scale - Abbreviated Screen for Patients

### *Description and validation*

Van Meter, A.; Guinart, D.; Bashir, A.; Sareen, A.; Cornblatt, B.A.; Auther, A.; Carrión, R.E.; Carbon, M.; Jiménez-Fernández, S.; Vernal, D.L.; Walitza, S.; Gerstenberg, M.; Saba, R.; Cascio, N.L.; Correll, C.U.

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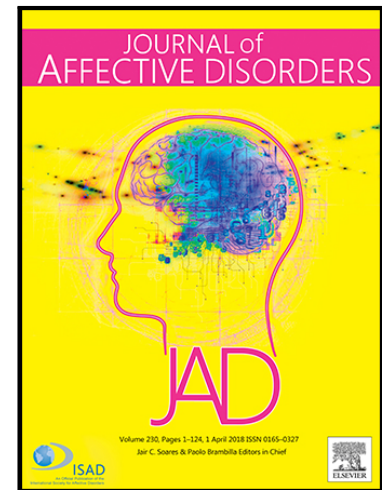
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Bipolar Prodrome Symptom Scale - Abbreviated Screen for Patients:  
description and validation

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### Highlights

- There is no standard tool for measuring the symptoms of the bipolar prodrome, which has limited progress toward early identification
- The clinician-administered Bipolar Prodrome Symptom Interview and Scale–Full Prospective (BPSS-FP) is a valid way to assess for symptoms of the prodrome to bipolar disorder, but takes time and clinical expertise to administer
- The Bipolar Prodrome Symptom Scale–Abbreviated Screen for Patients (BPSS-AS-P) is a screening tool to identify people who would benefit from further evaluation with the BPSS-FP interview
- This study is an important step in the development and validation of a screening tool that could be an efficient way to identify individuals at risk for bipolar disorder

RUNNING HEAD: BPSS-AS-P VALIDATION

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### **Bipolar Prodrome Symptom Scale - Abbreviated Screen for Patients: description and validation**

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## Abstract

### Objective

There is no standard method for assessing symptoms of the prodrome to bipolar disorder (BD), which has limited progress toward early identification and intervention. We aimed to validate the Bipolar Prodrome Symptom Scale–Abbreviated Screen for Patients (BPSS-AS-P), a brief self-report derived from the validated, clinician-rated Bipolar Prodrome Symptom Interview and Scale–Full Prospective (BPSS-FP), as a means to screen and identify people for whom further evaluation is indicated.

### Method

Altogether, 134 participants (aged 12-18 years) were drawn from a study of the pre-syndromal stage of mood and psychotic disorders. All participants had chart diagnoses of a mood- or psychosis-spectrum disorder. Participants were interviewed with the BPSS-FP and completed measures of mania and non-mood psychopathology. Prior to being interviewed, patients completed the BPSS-AS-P. Scores on the BPSS-AS-P were determined by summing the severity and frequency ratings for each item.

### Results

BPSS-AS-P scores were highly reliable (Cronbach's  $\alpha=0.94$ ) and correlated with the interview-based BPSS-FP Mania Symptom Index ( $r=0.55$ ,  $p<.0001$ ). BPSS-AS-P scores had good convergent validity, correlating with the General Behavior Inventory-10M ( $r=.65$ ,  $p<.0001$ ) and Young Mania Rating Scale;  $r=.48$ ,  $p<.0001$ ). The BPSS-AS-P had good discriminant validity, not being correlated with scales measuring positive and negative symptoms of psychotic disorders ( $p$ -values=0.072-0.667).

### Limitations

Findings are limited by the cross-sectional nature of the study by the fact that the participants were all treatment-seeking. Future studies need to evaluate the predictive validity of the BPSS-AS-P for identifying those who develop BD in a community sample.

### Conclusion

BPSS-AS-P has promise as a screening tool for people at risk for BD. Adopting the BPSS-AS-P would support the goal of characterizing the prodrome systematically in order to facilitate research and clinical care.

**Key words:** prodrome, assessment, bipolar disorder, validation

Substantial evidence from retrospective studies suggests that the majority of people with bipolar disorder (BD) experience symptoms prior to the point at which they meet full diagnostic criteria (Correll et al., 2014a; Howes et al., 2010; Martin, 2013; Skjelstad, Malt, & Holte, 2010). Related, following diagnosis, many people report that they are able to recognize when a new episode is impending based on changes in their energy, sleep, or mood, among others (Jackson, Cavanagh, & Scott, 2003; Lam, Wong, & Sham, 2001; Molnar, Feeney, & Fava, 1988). Being able to predict the onset of a new episode is advantageous; people with BD or their families can seek and obtain clinical intervention, which may reduce the severity of the new mood episode and/or the consequences associated with it (Lam & Wong, 1997, 2005; Perry, Tarrier, Morriss, McCarthy, & Limb, 1999). In some instances, it may even be possible to prevent the BD onset (Colom et al., 2009; Lam, Watkins, Hayward, & et al., 2003).

Although monitoring symptoms is recommended for people with BD in order to detect clinical changes and intervene accordingly (Miller, Johnson, & Eisner, 2009; Schwartz, Schultz, Reider, & Saunders, 2016), this approach has not been applied to individuals who are considered at-risk for BD. A meta-analysis found that there are clear mood symptoms prior to both initial and recurrent bipolar mood episodes, and that the duration of the prodrome to the onset of the first mood episode ( $107.9 \pm 91.5$  months) is longer than that of the recurrent prodrome ( $1.1 \pm 1.0$  months; Van Meter, Burke, Youngstrom, Faedda, & Correll, 2016). This finding suggests that there is an opportunity for preventive intervention, but no unified or generally accepted approach to evaluating and treating the BD prodrome exists. In contrast, the prodrome of schizophrenia has been studied extensively, yielding standardized interviews and self-rating scales that facilitate placement into specialized treatment programs for young people experiencing early symptoms of psychosis (Correll, Hauser, Auther, & Cornblatt, 2010; Davies, 2018; Fusar-Poli et al., 2012; Fusar-Poli, Cappucciati, Borgwardt, & et al., 2016; Fusar-Poli et al., 2015; Kline et al., 2015; Loewy, Pearson, Vinogradov, Bearden, & Cannon, 2011; Marshall & Rathbone, 2011; Savill, D'ambrosio, Cannon, & Loewy, 2018).

One of the reasons that the process of defining and treating the BD prodrome lags behind that of the schizophrenia prodrome is that many symptoms associated with the BD prodrome are nonspecific

(e.g., sleep disturbances, diminished ability to think, irritability; Van Meter et al., 2016), making them difficult, in some cases, to distinguish clinically from other disorders, such as depression, ADHD, or oppositional defiant disorder. This is understandable, as the threshold for mania has not yet been met, but it is detrimental for treatment, as inaccurate diagnoses (and the wrong intervention) can persist even as symptoms escalate.

A related factor is that clinical decision-making is imperfect (Lilienfeld & Lynn, 2014; Youngstrom, Choukas-Bradley, Calhoun, & Jensen-Doss, 2014), and clinicians often make invalid diagnostic decisions even for diagnoses with well-defined criteria. Because the symptoms that constitute the prodrome to BD have not yet been well-characterized, the likelihood of it being recognized is very low. Tools that help to focus the clinical decision-making process have demonstrated success at improving the accuracy and efficiency of diagnosing BD when incorporated into the assessment process (Youngstrom et al., 2018; Youngstrom, Genzlinger, Egerton, & Van Meter, 2015; Youngstrom et al., 2017). If a screening tool for the prodrome existed, it could aid in the identification of at-risk cases.

A structured interview, the Bipolar Prodrome Symptom Interview and Scale – Full Prospective (BPSS-FP; Correll et al., 2014b), was developed to facilitate recognition of the prodrome to BD. It has strong reliability and validity to identify people at elevated risk for the onset of a bipolar mood episode. However, the interview requires time and clinical judgment, which makes it impractical to administer to all patients with subthreshold mood symptoms. Consequently, we developed a brief self-report, the 11-item BPSS-Abbreviated Screen for Patients (BPSS-AS-P), based on the BPSS-FP to screen people who may be experiencing prodromal symptoms, in order to identify those who could benefit from further, more detailed, clinician-based assessment. Individuals at the age of highest risk for the onset of BD are among those least likely to engage with mental health services (Heflinger & Hinshaw, 2010; Husky et al., 2012; McGorry, Bates, & Birchwood, 2013); this fact may contribute to the long delays (on average more than ten years; Lish, Dime-Meenan, Whybrow, Price, & Hirschfeld, 1994; Perlis et al., 2004) that are common before people with BD get an accurate diagnosis. This issue highlights the importance of a brief screening tool; if successful at identifying elevated risk for BD, the BPSS-AS-P could be used to screen



for the BD prodrome broadly – in schools or through pediatricians – which would facilitate early identification independent of treatment seeking behavior.

The goal of the present study was to examine the psychometric properties of the BPSS-AS-P in a sample of treatment-seeking young people with symptoms of mood- or psychosis-spectrum disorders. Adolescence is the period during which most people experience the onset of BD (Baldessarini et al., 2012; Bellivier et al., 2014), making this the age range especially relevant for an examination of a tool to identify people at risk. We evaluated the correlation between the short screening tool and the full-length interview. Additionally, we tested the convergent and discriminant validity of the short screening tool.

## Methods

### Participants

Participants were drawn from the ongoing Adolescent Mood Disorder and Psychosis Study (AMDS) study (clinicaltrials.gov: NCT01383915). AMDS is an ongoing longitudinal study that aims to characterize the pre-syndromal stage of mood and psychotic disorders. Participants undergo comprehensive, non-invasive interview/survey assessments every 12 months for up to five years. All participants were recruited from inpatient and outpatient facilities at a single, semi-urban, psychiatric hospital with a catchment population of over three million people, covering Queens, Brooklyn, and counties on Long Island, New York. The present study focuses on the baseline data only. At enrollment, participants were between the ages of 12 and 18 years old. All had chart diagnoses of a mood- or psychosis-spectrum disorder (including DSM-IV diagnoses of Bipolar Disorder I (BD I), Bipolar Disorder II (BD II) BD-Not Otherwise Specified (BP-NOS), mood disorder NOS, Major Depressive Disorder (MDD), depressive disorder NOS, dysthymia, or schizophrenia, schizoaffective disorder, schizophreniform disorder, acute psychotic disorder, or psychotic disorder NOS). The study focused on these diagnoses because young people with mood symptoms (i.e., hypomania, depression, subthreshold manic symptoms) are at high risk for the onset of a manic episode, increasing the likelihood that some participants would experience a manic episode during the study period and enabling us to evaluate the predictive abilities of the BPSS-AS-P. Although this feature limits the generalizability of our results to

other settings (e.g., community mental health, pediatrician offices), given the low rate of mania, even among high-risk samples, we felt that it was important to maximize the number of mania cases at this stage of the BPSS-AS-P development. Additionally, participants with psychotic disorder diagnoses were of interest because they are likely to have a similar level of symptomatology as people with bipolar disorder, but are not at risk for mania, making them a clinically relevant comparison group. Exclusion criteria were minimal; potential participants were not enrolled if they could not speak and read English, if they had an estimated IQ < 70 or a developmental disorder, if they had a current substance use disorder, or if they had a known organic brain condition. This study was approved by the Institutional Review Board at the large academic medical center where it took place; all participants and caregivers provided written informed assent or consent.

### **Procedure**

The participant and a caregiver were each interviewed separately by a trained medical doctor or psychologist in one session (unless the patient was too ill to complete the interviews in one session, in which case the patient interview was completed within the next one-to-three days). The baseline session lasted several hours and included the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID; First, Spitzer, Gibbon, & Williams, 1995), on which DSM diagnoses were based, the clinician-rated Bipolar Prodrome Symptom Scale–Full Prospective (BPSS-FP; Correll et al., 2014b), and the clinician-rated Brief Psychiatric Rating Scale–anchored version (BPRS; Woerner, Mannuzza, & Kane, 1988). The SCID was supplemented with modules from the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version (Kaufman et al., 1997) for disorders of childhood that are not covered in the SCID (e.g., oppositional defiant disorder). Each participant was assigned a research diagnosis following a consensus meeting led by the study principle investigator and last author of this report, a board-certified child and adolescent psychiatrist, at which all sources of information were discussed and integrated. The BPSS-FP assesses putative symptoms and signs of the prodrome to BD and is split into three sections – the Mania Symptom Index, Depression Symptom Index, and General Symptom Index. Each symptom is rated on a six-point scale according to its severity. In a validation

study of the BPSS-FP (Correll et al., 2014b), internal consistency was good to very good for the Mania (Cronbach's  $\alpha = 0.87$ ), Depression (Cronbach's  $\alpha = 0.89$ ), and General Symptom indices (Cronbach's  $\alpha = 0.74$ ). Inter-rater reliability was high for the total score (ICC = 0.939), as well as for the Mania (ICC = 0.934), Depression (ICC = 0.985), and General (ICC = 0.981) indices. Correlations were large ( $\rho \geq 0.50$ ) between the Mania Index and other measures of manic symptoms. Related, correlations were small ( $\rho = 0.10$  to  $< 0.30$ ) between the Mania Index and measures of depressive symptoms. Furthermore, the discriminant validity of the BPSS-FP and its subscales was high. The BPRS, a clinician-rated measure of current psychotic symptoms, consists of 18 items, rated 1-7, that form five factor scales – Withdrawal-Retardation, Thinking Disturbance, Anxious-Depression, Hostile-Suspiciousness, and Activation. Reliability for participant BPRS factor scores was high (Cronbach's  $\alpha = 0.91-0.97$ ). Caregivers were interviewed about the participant's family history of mental health disorders using the Family Interview for Genetic Studies (FIGS; Maxwell, 1992).

Additionally, before the clinician administered BPSS-FP, we administered the Bipolar Prodrome Symptom Scale – Abbreviated Screen for patients (BPSS-AS-P) to screen for the presence of attenuated and/or subsyndromal mania symptoms. The BPSS-AS-P (see appendix) was developed as a self-rated companion scale of the clinician-administered BPSS-FP. BPSS-FP (Correll et al. 2014b) is a semi-structured interview that was developed based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria for BD and MDD, as well as established rating scales for mania, depression, and other psychopathology. In addition, the BPSS-FP development was based on the BPSS-Retrospective (Correll et al. 2014a), which was informed by a review of existing literature regarding risk factors and early symptoms of BD, published scales and interviews for the assessment of the psychotic prodrome and character traits, input from experts in the areas of the schizophrenia prodrome and BD, and open questioning of youth with BD and their caregivers regarding emerging subthreshold symptoms prior to the onset of a first syndromal bipolar manic, mixed, and major depressive episode. The BPSS-AS-P contains 10 BPSS-FP mania index items that directly map on the DSM-IV and DSM-5 mania criteria and that were rephrased from interviewer-based language to allow patient-reported self-rating. The General index item “mood lability” was added, as mood lability is a

common symptom during the bipolar prodrome (Van Meter et al. 2016; Hafeman et al. 2016). The BPSS-AS-P originally had 14 items, but we only analyzed the 11 items that match the 10-item the Mania Symptom Index from the BPSS-FP plus the General Symptom Index item “mood lability.” We excluded the items targeting “being more social and outgoing or flirtatious,” “being dressed more colorfully or unusually, or putting on more make-up,” and “being more creative than usual,” which had been added as exploratory items based on another utilized bipolar high-risk assessment schedule (Leopold et al, 2012), as these items are not contained in the BPSS-FP.

Participants also completed questionnaires to assess their personal history, functioning, and symptoms of psychopathology. The 10-item mania checklist from the General Behavior Inventory (GBI-10M; Youngstrom, Van Meter, Frazier, Youngstrom, & Findling, *in press*; Youngstrom, 2008) is a screening tool for the diagnosis of bipolar disorder; in multiple studies, it has demonstrated excellent sensitivity to differences in manic symptoms (Findling et al., 2009; Youngstrom et al., 2013). It was also used as the basis of inclusion for the Longitudinal Assessment of Manic Symptoms study (LAMS; Horwitz et al., 2010). The GBI-10M was completed *about the past month* by the participant; reliability for the self-report was excellent (Cronbach’s  $\alpha=0.92$ ). The other measure of mania was the Young Mania Rating Scale (YMRS; Young, Biggs, Ziegler, & Meyer, 1978). The YMRS includes ten items that are rated by the interviewer about the *past month*, based on his/her impressions of the participant. In our sample, the YMRS had adequate reliability, Cronbach’s  $\alpha=0.80$ .

### **Data analytic plan**

The goal of this study was to validate the patient self-report BPSS-AS-P, and to determine whether it has utility as a screening tool to identify individuals who might be at risk for developing bipolar disorder, who could then be further evaluated with an interview like the BPSS-FP. Although the BPSS-FP evaluates symptoms across multiple domains (mania, depression, general symptoms), the BPSS-AS-P focuses on ten items assessing mania-related symptoms and one question on mood lability, which is part of the general symptom index of the BPSS-FP (Correll et al., 2014b). Consequently, we focused on mania-related measures and on the Mania Symptom Index of the BPSS-FP to validate the

BPSS-AS-P. We also performed an exploratory factor analysis of the BPSS-AS-P severity items. IRT analyses used a rating scale model to estimate item characteristics and reliability across levels of the mania trait.

We evaluated different score thresholds of the BPSS-AS-P in order to determine which best mapped onto the mania score from the BPSS-FP. The BPSS-AS-P consists of 11 items, each of which is rated on its severity (0=no impact, 5=severe impact) and its frequency (0=not at all, 5=almost all the time). First, we created a raw score, summing both the severity and frequency ratings across items; this is the raw summed total score. Next, we looked at the summed severity ratings (raw severity score) and summed frequency ratings (raw frequency score) separately. We then created a priori, based on clinical considerations of progressively severe and frequent, and, possibly, more specific states, four threshold scores; *threshold one* (mild severity-mild frequency) is a count of the items that were rated at least a 3 on severity (some impact) and at least a 2 on frequency (once a month). *Threshold two* (mild severity-moderate frequency) is a count of the items that were rated at least a 3 on severity (some impact) and at least a 3 on frequency (once a week). *Threshold three* (moderate severity-mild frequency) is a count of the items that were rated at least a 4 on severity (a lot of impact) and at least a 2 on frequency (once a month). *Threshold four* (moderate severity-moderate frequency) is a count of the items that were rated at least a 4 on severity (a lot of impact) and at least a 3 on frequency (once a week).

Given that our sample included both prepubertal youth and adolescents, who – based on age – are at different levels of risk for the onset of BD and may have different clinical presentations (Birmaher et al., 2009; Goldstein et al., 2017), and because there is some limited evidence of sex differences in symptom presentation (Duax, Youngstrom, Calabrese, & Findling, 2007; Sibisi, 1990; Wozniak et al., 2013), we evaluated whether any of the scores produced by the methods described above were influenced by age or sex, in order to determine whether it was necessary to control for these variables in subsequent analyses.

Next, each method of scoring was compared with the Mania Symptom Index severity score from the participant's BPSS-FP interview using Pearson's correlation. Additionally, although the purpose of

the BPSS-AS-P is not diagnosis, as it is intended to identify those at risk for BD, we expected it to distinguish those with BD from patients with other diagnoses. In order to test this hypothesis, we performed receiver operating characteristic (ROC) analyses using each of the BPSS-AS-P scoring methods and compared these to the performance of the interview score using Venkatraman's permutation test (Venkatraman, 2000; Venkatraman & Begg, 1996), which evaluates equality of two ROC curves by examining the absolute difference between the two at each point along the curves (Venkatraman & Begg, 1996). Following these analyses (correlations and ROC), if one scoring method emerged as the most effective and efficient, we planned to focus on that one for the remaining analyses for simplicity and clarity.

Cronbach's alpha was calculated to determine the internal reliability of the BPSS-AS-P. Because individuals experiencing symptoms of mania may have limited insight, we also examined the association between self-reported BPSS-AS-P and the parent interview BPSS-FP; a strong association between the self-report and parent interview would support the utility of the BPSS-AS-P. Next, we tested the convergent and divergent validity of the BPSS-AS-P by comparing scores to other common screening or rating tools for BD (GBI-10M, YMRS) and to another measure of non-bipolar psychopathology (BPRS total score and subscales).

## Results

### Demographic and descriptive variables

The sample included 134 people who completed the BPSS-AS-P at baseline. The average age at baseline was 15.6 (1.4), 73% were female, 60% were White, 17% were Black, 10% were Asian, and 13% identified as Other. The majority of the participants were diagnosed with depressive disorders (60%), 24% had a bipolar disorder diagnosis, 16% had other, non-mood disorder diagnoses (see Table 1). There were no statistically-significant differences in demographic or clinical characteristics between the groups.

### Evaluation of thresholds for "caseness"

Each item on the BPSS-AS-P is rated on both severity (how pronounced the symptoms are and and/or much functioning is impacted) and frequency (how often the symptom occurs). See Table 2 for

average scores on the BPSS-AS-P, as well as the other clinical scales. We evaluated how well the self-report correlated with the BPSS-FP Mania Symptom Index at different thresholds, as described in the Analytic Plan. Correlations ranged from 0.45 (for the moderate thresholds of both the severity and frequency ratings) to 0.53 (for the raw summed frequency and combined severity and frequency ratings), all  $p$ -values were  $<0.0001$  (Table 3).

We also evaluated the diagnostic efficiency of each threshold using receiver operating characteristic analysis; AUCs ranged from 0.64 (for the moderate severity-moderate frequency threshold) to 0.73 for the raw summed total score. The AUC for the BPSS-FP Mania Symptom Index severity score was 0.82; Venkatraman's test indicated this was significantly better than the AUCs for thresholds three and four ( $p$ -values $<0.05$ ). Similarly, the AUC for the raw summed BPSS-AS-P severity and frequency ratings was significantly better than the AUCs for thresholds three and four ( $p$ -values $<0.05$ ).

Given that summing the severity and frequency ratings to create a single score is among the simplest approaches to scoring, and because this approach performed as well as or better than the other evaluated scoring methods, there did not seem to be any benefit to using a more complicated scoring algorithm. Subsequent analyses focused on this raw summed total score.

Neither age nor sex were related to any of the scores produced for the BPSS-AS-P (as described above), consequently, we did not control for demographic factors in subsequent analyses.

### **Factor and item response theory analyses**

The factor structure of the BPSS-AS-P was evaluated using exploratory factor analysis with principal axis factoring and promax rotation. The Kaiser-Meyer-Olkin measure of indicated "meritorious" sampling adequacy ( $KMO=0.89$ ; Kaiser, 1974) and Bartlett's test of sphericity was significant ( $X^2(55)=508.48, p<0.0001$ ; Snedecor & Cochran, 1989). Both the scree plot and eigenvalues suggested a two-factor solution, which explained 57% of the variance. One factor was indicated by five items (#1, 3, 4, 5, 8) related to positive aspects of mania (e.g., elated mood, increased energy); it explained 46% of the variance. The other factor was indicated by six items (#2, 6, 7, 9, 10, 11) related to the negative aspects of mania (e.g., irritability, risky behavior); it explained 11% of the variance.

The IRT model was also estimated using the rating scale model; the BPSS-AS-P severity items fulfilled the Rasch model for unidimensionality ( $X^2(14)=22.92, p=.062$ ), and the model fit the data well (RMSEA =.03). Additionally, items were invariant across those with a diagnosis of BD and those without;  $X^2(14)=19.08, p=.162$ . Person separation reliability was good, 0.88.

### Reliability

Calculating Cronbach's alpha for the summed severity and frequency items, the reliability was excellent ( $\alpha=0.94$ ).

### Convergent and discriminant validity

In addition to comparing the BPSS-AS-P to the clinician-rated BPSS-FP Mania Symptom Index, we also examined how well it correlated with the parent BPSS-FP Mania Symptom Index; the scales were moderately correlated ( $r=0.44, p<0.0001$ ). We also examined correlations between the BPSS-AS-P and other commonly used screening tools for mania. The summed score of the BPSS-AS-P was highly correlated with the self-report GBI-10M ( $r=0.65, p<0.0001$ ) and moderately correlated with the clinician-rated YMRS ( $r=0.48, p<0.0001$ ).

We also evaluated the discriminant validity of the BPSS-AS-P by comparing the raw summed total score to the five symptom scales of the BPRS. None of the correlations between the BPSS-AS-P and the BPRS total score or subscales were statistically significant ( $rs=-0.09-0.18; ps=.072-.667$ ), indicating that the content of the BPSS-AS-P does not overlap with scales measuring the positive and negative symptoms associated with psychotic disorders.

### Discussion

Bipolar disorder is challenging to diagnose (Berk, Berk, Moss, Dodd, & Malhi, 2006; Bruchmüller & Meyer, 2009; Youngstrom, Birmaher, & Findling, 2008); consequently, many individuals experience long delays before appropriate treatment is administered (Berk et al., 2006; Berk et al., 2010; Drancourt et al., 2013; Elanjithara, Frangou, & McGuire, 2011; Lish, Dime-Meenan, Whybrow, Price, & Hirschfeld, 1994; Perlis et al., 2004). Improving methods for early identification and intervention are



important goals, but have been stymied by lack of consistency in the measurement and description of the prodrome and by the reliance on retrospective reports of prodromal symptoms (Faedda et al., 2014; Van Meter et al., 2016). The BPSS-FP was developed to address these challenges and has demonstrated strong psychometric properties for the identification of the prodrome to bipolar disorder. However, this interview-based tool requires significant time and clinical skill to administer. In contrast, the BPSS-AS-P is brief and can be administered broadly in order to identify individuals who might be at-risk and would benefit from further evaluation with the interview.

The goal of the present study was to validate the BPSS-AS-P as tool to screen for degrees of symptoms of mania in a clinical sample. We found that the BPSS-AS-P parallels scores from lengthy and time consuming, clinician-based interview of patients using the full-length interview version of the BPSS, and that it correlates well with other measures of manic symptoms, as completed by the patient, his/her caregiver, and a clinician.

The 11 items of the BPSS-AS-P focus on manic symptoms and mood lability. Although previous work suggests that not all symptoms common during the prodrome are specific to mania (Van Meter et al., 2016), non-manic symptoms are likely to overlap with other disorders, making them less helpful in identifying those at risk for a manic episode. The specificity of the 11 items is indicated by the high correlations we found with other manic symptom scales. Additionally, because we compared scores on the BPSS-AS-P with the YMRS, a clinician-rated measure, we see that the BPSS-AS-P – a self-report – captures symptoms in a way that corresponds well with clinical impressions. This feature is important; the prodrome is most likely to occur during adolescence or early adulthood, and broad screening will be more feasible if there is a brief, self-report tool that eliminates the need to interview each youth directly.

Our results also indicate that the BPSS-AS-P has good discriminative validity – scores were not correlated with the BPRS scales measuring the positive and negative symptoms of psychotic disorders. This is a key finding; many have speculated that, at the prodromal stage, it is difficult or impossible to distinguish those likely to develop mania from those likely to develop schizophrenia or another non-mood psychotic disorder, but in our study, the BPSS-AS-P appears to be specific to mania. Additionally, the

results of the IRT and factor analyses are consistent with a unidimensional trait; although a two-factor structure fit best, the second factor explained a minimal amount of variance. Interestingly, these results are consistent with other work that has identified different components of mania (Topor et al., 2013; Benazzi & Akiskal, 2003), and with patients' experiences, which can vary from "irritable" to "elated" presentations.

Being able to rely on self-report could also facilitate the adoption of the BPSS-AS-P by other research groups. As noted above, the use of many different tools to measure the prodrome to BD has limited our understanding of this critical phase of illness development (Van Meter et al., 2016). Related, the referral source is likely to influence patient characteristics in important ways; for example, participants with a family history of illness may be likely to experience symptoms earlier than their peers (Johnson, Andersson-Lundman, Åberg-Wistedt, & Mathé, 2000; Post et al., 2017; Post et al., 2014). In order to improve the characterization of the prodrome to BD, including its key symptom profiles and duration, it is necessary to collect data in a systematic way from diverse populations. The BPSS-AS-P offers a simple and fast way by which to identify those who would benefit from further evaluation and whose data will be instrumental to informing future efforts to identify the prodrome, in order to intervene before an individual experiences the full consequences of BD.

**Limitations.** Predicting who is likely to develop mania is an ambitious goal; an important next step in this pursuit is the longitudinal follow-up of individuals who have completed the BPSS-AS-P. Although our results suggest strong associations between the BPSS-AS-P, the BPSS-FP, and other measures of mania, the data are still cross-sectional, so we do not yet know how well the BPSS-AS-P predicts who will go on to have a manic or hypomanic episode. In addition to the lack of longitudinal data, our findings are limited by the fact that our data were from individuals already experiencing significant symptoms and seeking treatment. The sample in which a screening tool is validated influences its performance (Youngstrom et al., 2018; Youngstrom et al., 2015), and it is important to evaluate the psychometric properties of the BPSS-AS-P in people who are not yet in clinical care before undertaking

broad screening efforts. Moreover, due to the lengthy baseline assessments, we did not ask patients and families to return for test-retest reliability testing of the BPSS-AS-P.

### **Conclusion**

In spite of clear evidence that early intervention is associated with better outcomes for individuals with bipolar disorder (Berk et al., 2007; Elanjithara et al., 2011), progress has been slow to characterize the prodrome to BD in a way that facilitates identification and intervention. The BPSS-FP was developed to identify people at risk for BD, but it requires significant time and clinical resources. The BPSS-AS-P offers a valid way to screen people for bipolar risk and to identify those who would benefit from further evaluation. In this initial validation study, the BPSS-AS-P showed strong convergent and divergent validity. Using this tool across populations to identify those who may be at risk for mania, especially longitudinally, is the necessary next step in the goal of reducing the long delay most patients experience before getting the treatment they need to achieve the quality of life they deserve.

Table 1.

*Clinical characteristics across diagnostic groups\**

	Full sample	Bipolar spectrum disorder	Depressive disorder	No mood disorder
<i>n</i>	134	32	81	21
Mean (SD)				
Age	15.63(1.4)	15.84(1.3)	15.60(1.4)	15.39(1.6)
N (%)				
Female <sup>1</sup>	95 (70.9)	25 (78.1)	59 (73.8)	11 (61.1)
White <sup>2</sup>	71 (59.7)	17 (58.6)	45 (61.6)	9 (52.9)
Black <sup>2</sup>	20 (16.8)	5 (17.2)	11 (15.1)	4 (23.5)
Hispanic <sup>3</sup>	24 (32.4)	8 (42.1)	15 (33.3)	1 (10.0)
Asian <sup>2</sup>	12 (10.0)	1 (3.4)	8 (10.9)	3 (17.6)
Family history of bipolar disorder	13 (9.7)	5 (15.6)	5 (6.1)	3 (14.2)
Bipolar I	7 (5.2)	7 (21.8)	0 (0.0)	0 (0.0)
Bipolar II	6 (4.4)	6 (18.7)	0 (0.0)	0 (0.0)
Bipolar NOS	19 (14.1)	19 (59.3)	0 (0.0)	0 (0.0)
Major depressive disorder	64 (47.7)	0 (0.0)	64 (79.0)	0 (0.0)
Other depressive disorder	17 (12.6)	0 (0.0)	17 (20.9)	0 (0.0)
Attention deficit/hyperactivity disorder	12 (8.9)	10 (31.2)	0 (0.0)	2 (9.5)
Anxiety disorder or OCD	10 (7.4)	3 (9.3)	3 (3.7)	4 (19.0)
Disruptive behavior disorder	17 (12.6)	5 (15.6)	11 (13.5)	1 (4.7)
Eating disorder	2 (1.4)	0 (0.0)	2 (2.4)	0 (0.0)

<sup>1</sup> – data missing for four people<sup>2</sup> – data missing for 15 people<sup>3</sup> – data missing for 60 people

\* there were no statistically-significant differences between any of the groups on these characteristics

Table 2.

*Rating scale scores across diagnostic groups*

	Bipolar spectrum disorder	Depressive disorder	No mood disorder			
<i>n</i>	32	81	21			
	Mean (SD)			Cohen's d BD vs DD	Cohen's d BD vs NMD	Cohen's d DD vs NMD
Age	15.84(1.3)	15.60(1.4)	15.39(1.6)	0.17, $p=.712$	0.31, $p=.541$	0.14, $p=.838$
Patient-Rated Instruments	Mean (SD)					
BPSS-AS-P severity	30.87(12.8)	17.26(10.7)	20.00(12.8)	1.16, $p<.0001$	0.85, $p=.003$	-0.23, $p=.604$
BPSS-AS-P frequency	30.00(11.6)	18.19(10.8)	21.23(10.5)	1.05, $p<.0001$	0.79, $p=.014$	-0.29, $p=.492$
BPSS-AS-P total	59.91(24.0)	34.38(20.5)	41.24(22.3)	1.15, $p<.0001$	0.81, $p=.007$	-0.32, $p=.401$
GBI-10M	25.48(7.8)	17.26(7.1)	18.77(8.2)	1.10, $p=.021$	0.84, $p<.0001$	0.20, $p=.779$
Parent-rated Instruments	Mean (SD)					
Patient BPSS-FP Mania Index severity	24.23(14.4)	9.44(7.3)	16.38(11.7)	1.37, $p<.0001$	0.60, $p=.132$	-0.73, $p=.160$
Clinician-rated Instruments	Mean (SD)					
Patient BPSS-FP Mania Index severity	32.28(13.8)	13.49(8.8)	17.06(12.1)	1.66, $p<.0001$	1.17, $p<.0001$	-0.34, $p=.425$
BPRS Thinking Disturbance	5.15(2.6)	3.95(2.0)	3.18(0.6)	0.52, $p=.038$	1.21, $p=.026$	-0.60, $p=.491$
BPRS Withdrawal-Retardation	3.11(1.3)	3.14(1.7)	3.10(1.6)	-0.02, $p=.997$	0.01, $p=1.0$	-0.02, $p=.997$
BPRS Hostile-Suspiciousness	6.04(2.4)	4.51(2.3)	4.00(2.0)	0.65, $p=.013$	0.91, $p=.040$	-0.23, $p=.778$
BPRS Anxious-Depression	9.96(3.7)	11.40(3.3)	7.36(4.2)	-0.41, $p=.177$	0.66, $p=.102$	-1.07, $p=.002$
BPRS Activation	5.5(2.3)	4.35(1.8)	4.00(1.7)	0.554, $p=.028$	0.75, $p=.082$	-0.20, $p=.843$

## BPSS-AS-P VALIDATION 19

Patient YMRS	17.30(9.5)	5.31(5.4)	4.82(3.1)	1.61, $p<.0001$	1.98, $p<.0001$	-0.12, $p=.972$
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*Note:*

BD – Bipolar disorder diagnosis

DD – Depressive disorder diagnosis

NMD – No mood disorder diagnosis

BPSS-AS-P – Bipolar Prodrome Symptom Scale–Abbreviated Screen for Patients

BPSS-AS-P – Bipolar Prodrome Symptom Scale–Abbreviated Screen for Informant

BPSS-FP – Bipolar Prodrome Symptom Scale–Full Prospective

GBI-10M – General Behavior Inventory-10-item Mania scale

YMRS – Young Mania Rating Scale

BPRS – Brief Psychiatric Rating Scale

Table 3.

*Comparisons between the BPSS-FP Mania Index severity score and BPSS-AS-P scoring options*

	BPSS-AS-P severity	BPSS-AS-P frequency	BPSS-AS-P total	BPSS-AS-P Threshold one <sup>1</sup>	BPSS-AS-P Threshold two <sup>2</sup>	BPSS-AS-P Threshold three <sup>3</sup>	BPSS-AS-P Threshold four <sup>4</sup>
Correlation with BPSS-FP Mania Index severity score	.51***	.55***	.55***	.49***	.49***	.46***	.46***
AUC (95% CI)	.71 (.59-.83)	.70 (.58-.82)	.73 (.61-.84)	.69 (.58-.81)	.68 (.56-.80)	.65 (.54-.77)	.64 (.52-.76)

\*\*\*  $p < .0005$

<sup>1</sup> at least a 3 on severity (some impact) and at least a 2 on frequency (once a month)

<sup>2</sup> at least a 3 on severity (some impact) and at least a 3 on frequency (once a week)

<sup>3</sup> at least a 4 on severity (a lot of impact) and at least a 2 on frequency (once a month)

<sup>4</sup> at least a 4 on severity (a lot of impact) and at least a 3 on frequency (once a week)

Note:

BPSS-AS-P – Bipolar Prodrome Symptom Scale–Abbreviated Screen for Patients

BPSS-FP – Bipolar Prodrome Symptom Scale–Full Prospective

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## Appendix

**The BPSS-Abbreviated Screen – Patient (BPSS-AS-P)**

Pt. #. \_\_\_\_\_ Date \_\_\_\_\_ Office ID # \_\_\_\_\_

The following screen contains statements that might or might not relate to your personal experiences. We are asking you about the **presence and impact** of these experiences, as well as about **how often** they occur. Please focus on the **last year**.

Within the past year:	<b>Severity:</b> How much has the experience had a <b>positive or negative</b> impact on your <b>functioning</b> ?						<b>Frequency:</b> How often has the experience occurred in the <b>past year</b> ?					
Please read each statement carefully and circle the answer that <b>BEST</b> describes your experiences <b>IN THE PAST YEAR</b> .  Please complete each part of this questionnaire.	Not at all	Yes, no impact	Yes, little impact	Yes, some impact	Yes, a lot impact	Yes, severe impact	Not at all	A few times/year	About once /month	About once /week	About 50% of the time	Almost all the time
1. I have felt <u>unusually</u> upbeat, super-happy, or like on top of the world; or got really silly or goofy.	0	1	2	3	4	5	0	1	2	3	4	5
2. I have felt particularly cranky, grouchy, or irritable, or got easily annoyed, or blew up at people.	0	1	2	3	4	5	0	1	2	3	4	5
3. I have felt better than others, or particularly gifted or talented, or made very ambitious plans	0	1	2	3	4	5	0	1	2	3	4	5
4. I have had times when I needed much less sleep than usual and was still fully rested and energetic. (i.e. I did not need to take a nap or go to bed early on the following day)?	0	1	2	3	4	5	0	1	2	3	4	5
5. I have been particularly talkative, spoke very rapidly or very loudly, or was difficult to interrupt.	0	1	2	3	4	5	0	1	2	3	4	5
6. I felt that my ideas come and go unusually easy and fast, that I am changing topics quickly, or that my mind is racing.	0	1	2	3	4	5	0	1	2	3	4	5
7. I felt unusually easily distracted by things around me, or needed more time than I usually do to complete tasks due to distractibility.	0	1	2	3	4	5	0	1	2	3	4	5
8. I felt unusually energetic or motivated, got things done more easily or faster, or got involved in more activities than usual.	0	1	2	3	4	5	0	1	2	3	4	5
9. I felt unusually restless or fidgety, could not sit still, or had to pace.	0	1	2	3	4	5	0	1	2	3	4	5
10. I either felt the urge to do things that could potentially be dangerous, or was involved in or actively sought out risky activities.	0	1	2	3	4	5	0	1	2	3	4	5
11. I felt that my mood changed a great deal from one moment or one day to the other (happy, sad or irritable), or that my mood goes up and down for no apparent reason.	0	1	2	3	4	5	0	1	2	3	4	5