APPROVAL SHEET

Title of Thesis: Preliminary Validation of a New Measure of Duration of Untreated psychosis: The SIPS-DUP

Name of Candidate: John Fitzgerald

Master of Arts, 2021

July Am

Thesis and Abstract Approved:

Jason Schiffman, Ph.D. Professor Human Services Psychology Program

Date Approved: 8/9/21

NOTE:*The Approval Sheet with the original signature must accompany the thesis or dissertation. No terminal punctuation is to be used.

- Andorko, N. D., Fitzgerald, J., Roemer, C., Solender, E., Petti, E., Rakhshan
 Rouhakhtar, P., McNamara, K. E., Smith, M. E., Buchanan, R. W., Schiffman, J.,
 & DeVylder, J. (2021). Social work training to reduce duration of untreated
 psychosis: Methodology and considerations of a web-based training for
 community providers. *Early Intervention in Psychiatry*. https://doi.org/10.1111/eip.13178
- DeLuca, J. S., Andorko, N. D., Chibani, D., Jay, S. Y., Rakhshan Rouhakhtar, P. J.,
 Petti, E., Klaunig, M. J., Thompson, E. C., Millman, Z. B., Connors, K. M.,
 Akouri-Shan, L., Fitzgerald, J., Redman, S. L., Roemer, C., Bridgwater, M. A.,
 DeVylder, J. E., King, C. A., Pitts, S. C., Reinblatt, S. P., ... Schiffman, J.
 (2020). Telepsychotherapy with youth at clinical high risk for psychosis: Clinical issues and best practices during the COVID-19 pandemic. *Journal of Psychotherapy Integration*, *30*(2), 304-331. https://doi.org/10.1037/int0000211
- Millman, Z. B., Gallagher, K., Demro, C., Schiffman, J., Reeves, G. M., Gold, J. M., Rakhshan Rouhakhtar, P. J., Fitzgerald, J., Andorko, N. D., Redman, S., Buchanan, R. W., Rowland, L. M., & Waltz, J. A. (2020). Evidence of reward system dysfunction in youth at clinical high-risk for psychosis from two eventrelated fMRI paradigms. *Schizophrenia Research*, 226, 111-119. https://doi.org/10.1016/j.schres.2019.03.017

ABSTRACT

Title: PRELIMINARY VALIDATION OF A NEW MEASURE OF DURATION OF UNTREATED PSYCHOSIS: THE SIPS-DUP John C. Fitzgerald

Directed By: Jason Schiffman, Ph.D, Professor, Department of Psychology, Human Services Psychology Program

A growing body of research suggests that, for those who develop a psychotic illness, early detection of symptoms and initiation of treatment is associated with improved clinical and functional outcomes, as well as reductions of positive symptoms (experiences that are in excess of otherwise typical functioning, and include hallucinations, delusions, and/or disorganized behavior) and intensive service use (e.g., emergency room and inpatient hospitalization). Early intervention is also cost effective and instills a more positive and helpful impression of the mental health system (Lucksted et al., 2015). In studies exploring both immediate and distal effects of the first episode of psychosis, researchers have found that the duration of untreated psychosis (DUP), the time between the emergence of psychotic symptoms and adequate treatment, may impact illness course and treatment response (Kane et al., 2016). Although there are several instruments frequently used to measure DUP in people within their first episode of psychosis, these are primarily derived from approaches that consider fully manifested psychosis as the point of reference at which evaluation should be initiated. Given the possibility of identifying psychosis risk prior to full threshold symptoms, and the benefits of a short DUP, there is compelling rationale to improve upon measurement strategies of DUP. The current study evaluated the validity of a new tool designed to assess DUP based on a

modified version of the Structured Interview for Psychosis-risk Syndromes (SIPS), the gold-standard interview for assessing risk for psychosis. Consistent with other measures of DUP, the new measure was associated with various positive and negative symptoms of psychosis, indicating some preliminary construct validity for the tool. This initial psychometric validation provides support for a measure that possesses methodological advantages relative to existing tools of DUP measurement.

PRELIMINARY VALIDATION OF A NEW MEASURE OF DURATION OF

UNTREATED PSYCHOSIS: THE SIPS-DUP

By

John C. Fitzgerald

Thesis submitted to the Faculty of the Graduate School of the University of Maryland, Baltimore County, in partial fulfillment of the requirements for the degree of Masters of Arts 2021 © Copyright by

John C. Fitzgerald 2021

Acknowledgments

This work was supported in part by funding from the Maryland Department of Health and Mental Hygiene, Behavioral Health Administration through the Center for Excellence on Early Intervention for Serious Mental Illness (OPASS# 14-

13717G/M00B4400241).

I would like to thank my family, whose relentless dedication to the helping professions inspired my path. Thank you to my mentor, Jason Schiffman, whose insight, scholarship, and patience have been pivotal throughout my graduate career. I am also appreciative of the support from my committee members, Steven Pitts and Shari Waldstein, who shared my enthusiasm and provided invaluable input along the way. Thank you to my YouthFIRST lab mates and the lab staff, who make the culture of this team unlike any other.

Most importantly, thank you to the participants and families who chose to disclose their experiences. Without you, science does not progress.

Acknowledgments	ii
Table of Contents	iii
List of Tables	iv
Preliminary Validation of a New Measure of Duration of Untreated Psychosis:	
The SIPS-DUP	1
Psychosis	1
Development of Psychosis	2
Operational Definitions of DUP	8
Development of a New DUP Measure	19
Present Study	22
Specific Aims and Hypotheses	23
Method	24
Participant Eligibility and Recruitment	24
Measures	25
Procedures	29
Results	29
Data Analysis Plan	29
Preliminary Analyses	30
Primary Analyses	31
Race	
Discussion	37
BPRS Total Score	37
Positive Symptoms	38
General Psychonathology	39
Psychomotor Flattening	40
Expressive Language	40
Volition and Role Functioning.	
Non-significant Findings	
Mechanisms Between SIPS-DUP assessed DUP and Symptoms	
Utility of the SIPS-DUP Interview	
Limitations	45
Future Directions	48
Appendix A: SIPS-DUP Interview	50
Appendix B: Scale for the Assessment of Negative Symptoms	66
Appendix C: Brief Psychiatric Rating Scale	73
References	81

Table of Contents

List of Tables

Table 1. Descriptions of Administration, Reported Interrater Reliabilities, Number	
of Studies Included in Meta-Analysis, and DUP's Predictive Validity of	
Symptoms, Per Measure	11
Table 2. Zero-Order and Partial Correlations Between DUP and BPRS Item Scores	32
Table 3. Zero-Order and Partial Correlations Between DUP and BPRS Item Scores	33
Table 4. Mean BPRS Differences by Race	35
Table 5. Mean SANS Differences by Race	36

•

Preliminary Validation of a New Measure of Duration of Untreated Psychosis: The SIPS-DUP

Psychosis

An episode of psychosis is characterized by an array of atypical cognitive processes, behavioral patterns, belief systems, and/or perceptual experiences that may lead to distorted perceptions of reality and reduction of overall functioning. The development of these experiences may manifest as unwarranted paranoia (e.g., others being out to harm them), grandiosity (i.e., inflated sense of self or ability), ideas of reference (i.e., ambiguous experiences being perceived as personally significant), or hallucinations (e.g., hearing or seeing things that others do not see or hear) on a regular basis (American Psychiatric Association, 2013). These "positive" symptoms (so named as they represent behavioral excess) contribute to a diagnosis of psychosis once they manifest for a significant portion of time over the course of at least one month, while negatively impacting social, occupational, or other areas of functioning. Psychosis is also characterized by the presence of "negative" symptoms, which are deficits in what would otherwise be typical behavior, including anhedonia, blunted affect, decreased sociability, impoverished speech, and avolition.

The effects of positive and negative symptoms extend beyond these initial stressors (e.g., fear from hallucinations, difficulty with recall due to impoverished speech, etc.) and may be associated with various types of functional impairment, psychiatric comorbidities, and aversion to help-seeking (Buckley, Miller, Lehrer, & Castle, 2009; Dixon, Goldman, Srihari, & Kane, 2018; Skeate, Jackson, Wood, & Jones, 2002). For example, if one develops an unwarranted belief system that authority figures are "out to get them" during an episode of psychosis, they may experience a subsequent increase in social withdrawal or other anxious symptoms, contributing to a decline in functioning and perhaps an aversion to help-seeking behavior, with treatment aversion leading to more symptoms creating a negative and iterative cycle.

While on the surface it might seem that an initial episode of psychosis begins unambiguously, it is actually much more complicated and tends to develop more slowly than an acute "break." These symptoms do not necessarily arrive en masse, but rather sporadically and over time, making reliable detection of a first episode a common barrier to treatment. Moreover, psychiatric comorbidities such as depression or anxiety may hinder one's willingness to disclose positive symptoms, while behavioral shifts such as withdrawal or decline in academic performance may be incorrectly attributed to normative changes in early adulthood (Spear, 2000). In these situations, misdiagnosis can be of particular concern given the insidious nature of psychosis and the importance of targeted care. This, and other sources of poor identification and help-seeking (e.g., stigma, lack of community awareness, lack of personal insight, disconnect with social support networks, etc.), can often lead to delays in care after a person has developed psychosis (Gayer-Anderson & Morgan, 2013; McGlashan, 1999). On average, psychosis remains untreated for approximately one to three years in the United States (Addington et al., 2015), necessitating a more thorough understanding for how psychosis develops and how to detect it earlier.

Development of Psychosis

Psychosis etiology. With an average onset of around 22 and 25 years old for men and women respectively, approximately 100,000 young people in the US will experience a first episode of psychosis each year (NIMH, 2015). Psychosis is often conceptualized

2

within the "diathesis-stress model" of illness development, which posits that the onset of a psychotic episode may be attributed to a combination of innate and environmental factors (Howes & Murray, 2014; van Os, Rutten, & Poulton, 2008). This model suggests that psychosis is first precipitated by a genetic predisposition, as heritability research suggests that identical twin and parent/child dyads have a 48% and 13% likelihood of sharing a diagnosis, respectively (Gottesman, 1991). The onset of a first episode may then be triggered, or worsened, by environmental stressors that are perceived threats to one's well-being (Jones & Fernyhough, 2007). These threats to homeostasis may include traumatic events (e.g., observed or experienced instances of abuse or disaster) or major life adjustments (e.g., immigration and possible subsequent discrimination), as those with psychosis report experiencing significantly more stressful events than those without (Norman & Malla, 1993).

Considering the negative effects of psychosis and its complex etiology, early detection of symptoms is critical to understanding illness development. The psychosis state is often preceded by a sub-threshold form of positive symptoms, referred to in the North American literature as clinical high risk (CHR), and is characterized by more attenuated symptoms that are not marked by the degree of frequency, interference/distress, or progression of illness that characterizes diagnosable psychosis (Jackson, McGorry, & Dudgeon 1995; McGorry, Yung, & Phillips, 2003). Understanding the CHR phase is particularly important considering that approximately 26% of those meeting criteria for CHR will go on to develop psychosis within two years (Fusar-Poli et al., 2015). This link between risk and subsequent psychosis makes the CHR phase of illness important to early detection efforts, however, assessments borne out of the CHR

literature have generally gone unused as a measure to detect psychosis onset or the amount of time that one goes untreated.

First episode psychosis. The designation of prevention and early intervention in psychosis as a high priority within the field (McGorry, Killackey, & Yung, 2008) has led to a more comprehensive understanding of consumers' (i.e., help-seekers who have successfully begun treatment) experiences regarding first episode psychosis, as well as pathways into treatment services. As a result, increased attention on consumers whose symptoms meet criteria for full-threshold psychosis has prompted researchers to specifically investigate 1) which markers are predictive of poorer outcomes and 2) what can be done with this information to mitigate the negative effects of psychosis. This has led to investigation of an emerging construct in psychosis research known as the "duration of untreated psychosis" (DUP). DUP research has utilized various measures to determine psychosis onset and subsequent admission into treatment, with findings suggesting that minimizing DUP often leads to improved outcomes (Marshall et al., 2005).

Duration of untreated psychosis. DUP has been a construct of interest for researchers across various domains, including neuroimaging (Lappin et al., 2006; Malla, Bodnar, Joober, & Lepage, 2011; van Erp et al., 2016), electrophysiology (Nagai et al., 2013), and pharmacological intervention (Altamura, Buoli, & Serati, 2011). Clinically, DUP research has suggested that negative clinical impacts of illness are significantly reduced when symptoms are identified early in the course of illness and treatment initiated as early as possible (Penttilä, Jääskeläinen, Hirvonen, Isohanni, & Miettunen, 2014). This "critical period" hypothesis suggests that reductions in social and role functioning, as well as exacerbation of positive and negative symptoms, are likely to occur when appropriate treatment is not pursued in the first 2-3 years of psychosis onset (Birchwood, Todd, & Jackson, 1998).

Negative effects of prolonged DUP. Despite variability in how psychosis and treatment are operationally defined, research has generally shown that lower DUP is associated with fewer losses in occupational functioning, reduced hospitalizations, and better clinical outcomes (Kane et al., 2016; Marshall et al., 2005; Penttilä et al., 2014). In a nation-wide study of 404 outpatient participants, DUP was found to be associated with positive symptom levels at intake, suggesting that this severity may continue to increase until treatment is initiated (Addington et al., 2015). These trends have been sustained in individual symptom domains, with DUP being associated with intensity of positive symptoms individually (i.e., hallucinations, delusions, and disorganized behavior; Birnbaum, Wan, Broussard, & Compton, 2015), as well as severity of negative symptoms at treatment baseline (Boonstra et al. 2012). Prolonged DUP has also been linked to decline in areas of social functioning, including increased social isolation (Drake, Haley, Akhtar, & Lewis, 2000) and breakdown of social support systems (Gayer-Anderson & Morgan, 2013). The most robust study of DUP and early psychosis intervention stems from a 34-site randomized clinical trial that compared a specialized first episode program model to non-specialized community treatment (Kane et al., 2015). The authors found significantly greater improvements in symptomatology and quality of life in those who had shorter DUPs and were receiving specialized care, highlighting the importance of swift intervention.

In addition to cross-sectional assessment of DUP and outcome measures at treatment baseline, longitudinal measurement of symptoms has also informed the trajectory of symptom development as it pertains to early intervention and reduced DUP. Research using both a baseline and 1-year follow-up has found more pronounced improvements in positive symptoms (Barnes et al., 2008; Gumley et al., 2014; Larsen, Moe, Vibe-Hansen, & Johannessen, 2000; Sullivan et al., 2018) and negative symptoms (Boonstra et al., 2012; de Haan, Van der Gaag, & Wolthaus, 2000; Elsheshtawy & Hussein, 2015; Tabo et al., 2017) among those with shorter DUP. Long-term follow-up studies have confirmed that longer DUP is still associated with positive symptomatology at 10-year follow-up (Austin et al., 2015) and positive, negative, and general psychopathological symptoms at 15 years (Bottlender et al., 2003). These findings underscore the importance of assessing DUP as a risk factor for increased symptom severity and decreased functioning, and specifically how these effects may be sustained over time. Research on psychosis intervention has demonstrated across several studies that early treatment can mitigate some of these effects, however, a more standardized and specific method of measuring onset and DUP may help to better compare findings across samples of people with emerging psychosis.

Barriers to treatment engagement within DUP. Several factors at the illness level may contribute to longer DUP, including a lack of insight (Compton, Goulding, Gordon, Weiss, & Kaslow 2009; Cuesta, Peralta, Campos, & Garcia-Jalon, 2011) and misattribution of psychotic symptoms (e.g., spirits or demons; Bourgou, Halayem, & Hayalem, 2012; Chilale, Silungwe, Gondwe, & Masulani-Mwale, 2017). Because lack of insight is itself a symptom of psychosis, those experiencing this illness may not acknowledge the need for mental health services, thereby increasing DUP and potentially isolating friends or family that could help with treatment-seeking. Alternatively, this delay may also be *enabled* by friends or family who attribute symptoms to factors such as personality traits or coinciding life stressors that are believed to account for the psychotic symptoms (Tanskanen et al., 2011). For example, if the symptoms are seen only as an exacerbation of their typical characteristics (e.g., a normally "shy" adolescent developing negative symptoms), then those involved in the person's care may not be sensitive to the underlying psychopathology (Compton et al., 2015).

Difficulty in detecting psychosis is further complicated by its relatively low base rate of occurrence and high likelihood of psychiatric comorbidity. Considering that over 90% of consumers with a first episode report depression as a precipitant to their psychosis (NICE, 2014), it may initially be overlooked by providers. Research has also found that as those presenting with affective psychosis (i.e., psychosis associated with a significant mood component) have a significantly shorter DUP than those with nonaffective (Large, Nielssen, Slade, & Harris, 2008). If help-seeking is more likely to occur when other presenting concerns exist, this may suggest that: 1) consumers may feel a stronger stigma around seeking help for psychosis relative to other psychiatric conditions, 2) psychosis-only symptoms may be misattributed to other phenomena (e.g., hallucinations due to suspected substance use, disorganized behavior due to impulsivity in young adulthood, etc.), and/or 3) the lack of insight stemming from psychosis might delay care. Internalized self-stigma may enable the person to accept negative and stereotyped attitudes about psychosis, which reduce feelings of self-empowerment (Brohan, Elgie, Sartorius, & Thornicroft, 2010) and perpetuate a cycle of delaying

treatment (Strkalj Ivezić, Sesar, & Mužinić, 2017). While many of these barriers will require efforts around de-stigmatization and mental health education, improvement upon clinical DUP measures may help to identify people earlier in the course of illness.

Operational Definition(s) of DUP

An accurate measure of DUP is reliant upon precise and accurate measures of two dates: 1) psychosis onset, and 2) treatment of psychosis. The field has approached evaluating these two dates in a variety of ways. This variability, as well as limitations inherent within the various approaches to assessing DUP, creates issues with respect to accurate and reliable evaluation of the DUP construct within and across studies. In subsequent consideration, all references to DUP will denote the amount of elapsed time between the two onset dates; psychosis to treatment. Predictably, differences in DUP arise with respect to definitions of either, or both, of those two dates.

Assessing onset of illness. Although DUP itself has been investigated at length, the methodology in how these data are collected has varied, making comparisons across studies difficult and calling into question the relative validity of different methods of DUP evaluation (Addington, Van Mastrigt, & Addington, 2004; Esterberg & Compton, 2012; Jeppesen et al., 2008). Date of psychosis onset has been defined through a number of strategies including chart reviews (Altamura et al., 2015), unstructured qualitative interviews (de Haan, Linszen, Lenior, De Win, & Gorsira, 2003), and longer psychosis-specific interviews (Cuesta et al., 2012). A meta-analysis reporting on the most commonly used methods of eliciting DUP found that, out of 94 research groups reporting DUP, twelve different measures for psychosis onset (i.e., clinical interviews, chart reviews, and nine psychosis onset-specific measures published in English [one psychosis

onset-specific measure not published in English is excluded in the current review]) were used (Register-Brown & Hong, 2014).

Chart reviews. The use of chart review in documenting psychosis onset allows researchers to understand the participant's experience as it happened in real time (at least as well as it was documented) via historical providers. Chart review assessments of DUP allow for the collection of large, comprehensive samples of participants across a variety of settings, including those who may not have matriculated into any psychosis-specific treatment. Conversely, such documentation is not necessarily designed for research and should be interpreted cautiously if used to make inferences about the progression of illness. Onset calculated from clinical records carries with it a lack of standardization, considering it may be based only on available records and is subject to clinical rater biases in what the provider might interpret as psychosis threshold.

Diagnostic interviews. General diagnostic interviews have also been employed to evaluate psychosis onset. These interviews provide probes to quickly assess the presence of many diagnoses and generally do not require training in psychosis detection, allowing access for a wider range of clinicians to collect information about psychosis onset. Despite the structured nature of this approach, however, most of these tools were not designed with the intent of establishing DUP. The Structured Clinical Interview for DSM-5 (SCID-5; First, Williams, Karg, & Spitzer, 2015), for instance, assesses symptoms' presence dichotomously without providing nuanced measures of when symptoms truly cross over from sub-threshold to threshold. Focusing primarily on overarching diagnoses, specific attention may not be given to the frequency, impairment, and conviction needed to assess symptoms of psychosis, reducing the precision of psychosis onset identification.

Illness onset-specific measurement tools and DUP. Several assessments have been designed to specifically document the date of psychosis onset as either a primary or secondary goal. These include The Royal Park Multidiagnostic Instrument (RPMIP; McGorry, Copolov, & Singh, 1990), the Beiser Scale (Beiser & Erickson., 1993), the Comprehensive Assessment of Symptoms and History (CASH; Andreasen, 1992), the Circumstances of Onset of Symptoms and Relapse Schedule (CORS; Norman, Malla, Verdi, Hassall, & Fazekas, 2004), the Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein, & Opler, 1987), the Interview for the Retrospective Assessment of Onset Schedule (IRAOS; Häfner et al., 1992), the Symptom Onset in Schizophrenia (SOS; Perkins et al., 2000), and the Personal and Psychiatric History Schedule (PPHS; Jablensky et al., 1992). These measures vary in their administration length, interview style, definition of onset, interviewee, reliability, validity and frequency of use, but all incorporate a measure of psychosis onset. While use of these measures has contributed to the field's understanding of DUP, all suffer from limitations. Table 1 includes data on reliability, number of studies used, and predictive validity for several of the most commonly used psychosis onset assessments for measuring DUP, which were taken from a recent review on variability in DUP measures (Register-Brown & Hong, 2014). This table was based on information from that review and is expanded to include information on how symptoms are queried, definitions of onset, and the type of respondent used.

Despite these measures' ability to assess DUP, several key limitations exist. All struggle with variations in one or more of the following features: 1) how information

Table 1.

Descriptions of Administration, Reported Interrater Reliabilities, Number of Studies Included in Meta-Analysis, and DUP's Predictive Validity of Symptoms, Per Measure.

	Duration Respond		ndent Studies	Reliability estimates			Predictive validity	
Instrument		Respondent		DUP	Sx	Тх	Positive	Negative
Royal Park Multidiagnostic Instrument for Psychosis (RPMIP; McGorry, Copolov, & Singh 1990)	Method: Dichotomous probes used to determine presence/non-presence of symptoms. Psychosis Onset: Emergence of the first sustained psychotic symptom at threshold level.							
Singh, 1990)	4-7 hrs	Subject	6	$\kappa = 0.79$	$\kappa = 0.79$	NI	0.31**	0.29**
Beiser Scale (Beiser & Erickson., 1993)	Method: Open-ended interview questions. Psychosis Onset: Following interview, content analysis used to determine date of first sympto presence via standardized checklist.							om
	0.5 hrs	Subject, peer, or family member	11	CC = 0.79-0.98	ICC = 0.94-0.98	ICC = 0.95	0.28**	0.33**
Comprehensive Assessment of Symptoms and History (CASH; Andreasen, 1992)	nent of SymptomsMethod: Dichotomous probes used to determine presence/non-presence of symptoms.dreasen, 1992)Psychosis Onset: Date at which conviction of positive symptom is "firmly held."							
	2 hrs	Subject	4	CC = 0.87-1.00	ICC = 0.96	ICC = 0.96-1.00	0.12	0.02
Circumstances of Onset of Symptoms and Relapse Schedule (CORS; Norman et al., 2004)	 Method: Dichotomous probes used to determine presence/non-presence of symptoms. 1., Psychosis Onset: Date when the patient first experienced symptoms of psychosis (hallucinati delusions and/or grossly disorganized behavior or thinking) that had duration of at least 						ons, 1 week.	
	1.5 hrs	Subject	7	ICC = 0.71-0.98	NI	NI	0.22**	0.18*
Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein, & Opler, 1987)	Method: Semi-structured interview that uses open-ended questions to determine symptom presence. Symptoms are then rated along continuum of intensity. Psychosis Onset: Date when positive symptoms become marked manifestations that distinctly impact functioning.							
	0.5 hm	Subject	10	ICC =	NI	NI	0.11	0.20*
	0.5 ms	Subject	10	0.9-0.99	111	181	0.11	0.20**

Table 1 (cont.)

				Reliability estimates			Predictive validity		
Instrument	Duration	Respondent	Studies	DUP	Sx	Тх	Positive	Negative	
Interview for the Retrospective Assessment	Method: D	Method: Dichotomous probes used to determine presence/non-presence of symptoms.							
of Onset Schedule (Häfner et al., 1992)	Psychosis Onset: Date when there began to be a clear increase in symptom intensity, where the symptoms led to a clear change in behavior, with associated changes in the patient's experient social competence.							he nce and/or	
	15 - 2	Subject peer or		κ=	PA =	PA =			
	hrs	family member	11	0.6-0.95	77%	80-100%	0.15*	0.10*	
Symptom Onset in Schizophrenia (SOS; Perkins et al., 2000).	Method: D Psychosis	Method: Dichotomous probes used to determine presence/non-presence of symptoms. Psychosis Onset: Date when symptoms cross predetermined frequency threshold.							
	0.5 hrs	Subject	7	ICC = 0.99	ICC = 1.0	NI	NI	0.27**	
Psychiatric and Personal History (PPHS; Jablensky et al., 1992)	Method: D Psychosis	Method: Dichotomous probes used to determine presence/non-presence of symptoms. Psychosis Onset: Date when patient first experienced symptom.							
	0.5 - 1	Subject, peer, or		ICC =					
	hrs	family member	4	0.90	NI	NI	NI	NI	

about symptoms is probed, 2) the operational definition of psychosis onset, and 3) the field definition (or lack thereof) of treatment onset.

Symptom probing. Some psychosis-specific (IRAOS; Häfner et al., 1992; RPMIP; McGorry, Copolov, & Singh, 1990; PPHS; Jablensky et al., 1992) and general (SCID; First et al., 2015) clinical interviews that assess psychosis onset use dichotomous approaches for symptom presence (i.e., present or not present). This approach helps to quickly outline a consumer's presenting symptoms, but may not be nuanced enough to distinguish subthreshold from threshold psychosis, and may therefore lead to an imprecise determination of onset. As people may have experienced psychotic-like symptoms without meeting diagnostic criteria, a more continuous approach may help in improving overall accuracy, and in particular, reduce false positives. For example, the RPMIP assessment of persecutory delusions inquires whether "anybody has been giving [the participant] a hard time or trying to hurt [them]" or "accusing [them] of things," but does not include any follow-up inquiries that would help determine whether these symptoms meet criteria for subthreshold (e.g., occurring infrequently with occasional conviction) or threshold psychosis (e.g., functionally impairing, frequent, and held with significant conviction). Pinpointing psychosis onset with the RPMIP would rely more heavily on the clinical judgment of the interviewer, which may vary based on personal interpretation and training background, than if probing were facilitated with more nuanced prompts and gradations of symptoms. This cursory approach may sacrifice some standardization in the assessment of psychosis or risk status.

A second concern in some measures is the reliance on qualitative content. The Beiser Scale (Beiser & Erickson., 1993), which is among the more frequently used

psychosis onset measures, provides open-ended questions to consumers or family members to develop a narrative about the onset of psychotic illness. Using these qualitative narratives, raters then review the content to pinpoint a date of psychosis onset. Although this does allow the participant to recount their first episode in their own words, it also sacrifices standardization. Because this interview does not include structured, psychosis-specific probes, much of the information needed to determine onset depends on the amount and quality of information volunteered by the interviewee, which may increase the risk of omitting important information. Similarly, the PANSS (Kay et al., 1987) and the CORS (Norman et al., 2004) are also semi-structured interviews that use open-ended questions to determine symptom presence. The tone of the PANSS is intended to be more conversational than a direct assessment of clinical functioning, and requires the administrator to code the open-ended responses on a Likert-type scale of severity after the conclusion of the interview. Because these questions lack specific follow-up to clarify or quantify an interviewee's response, specifying frequency or severity may be difficult, and threaten reliability and validity.

Psychosis onset. The definition of psychosis onset also varies across measures and may be overly ambiguous for accurate ratings on both Likert-type and dichotomous ratings of symptoms in the absence of additional symptom specifiers. For example, symptoms on the PANSS are rated along a 7-point Likert-type scale, where anchors suggest that symptoms rated a 4 (i.e., "only occasionally or intruding on daily life only to a moderate extent") or lower are considered clinical-high risk (CHR), while symptoms at a 5 (i.e., "marked manifestations that distinctly impact one's functioning") or higher are considered to meet psychosis threshold. These anchors do not include quantifiable

specifiers (e.g., a specified amount of time during the day that hallucinations occur, the degree to which delusions are believed, etc.), which may lead to reduced standardization for follow-up questions and scoring.

Another concern in these measures is the inconsistent and selective use of symptom duration and impairment in determining psychosis presence, which may inappropriately label those who are not in need of services. For example, consumers who experience regular positive symptoms, but are otherwise well-adjusted in their level of quality of life and functioning, may be inaccurately given a psychosis diagnosis according to some measures. This approach can be seen in the CORS measure, which requires that any positive symptom be occurring for one week or more to meet onset criteria, regardless of whether it is functionally impairing or not. Similarly, the determination of psychosis presence in the SOS also relies solely on frequency, which is further complicated by the fact the required duration depends on the type of symptom. For example, "ideas of reference" that are considered "sporadic" (i.e., "has had the symptom at least once but less than five times, or did not have the symptoms occur at least twice within a 1-month period") meet criteria for psychosis, whereas a higher "recurrent" frequency (i.e., "has had the symptom throughout the day for many days and the symptoms have lasted for at least 1 month") is required for the "suspiciousness" scale. Neither measure assesses for a specific degree of impact on functioning, which is traditionally required for an axis I diagnosis. Applying a label to those not impacted by their psychiatric experiences may be stigmatizing. Moreover, the ambiguity in how frequency is operationalized (e.g., "only occasionally," "many days") may also reduce reliability across raters.

Additionally, psychosis determined by dichotomous probes found in the Beiser Scale (Beiser & Erickson., 1993), the RPMIP (McGorry, Copolov, & Singh, 1990), and the IRAOS (Häfner et al., 1992) is also limiting. The Beiser Scale uses a checklist of symptoms to assess unstructured interview reports, eliciting dates of onset based on interview content. This method allows consumers to recall their experiences in their own words, which can be helpful for those who have difficulty with clinical terminology, but again heavily depends on the interviewee's recall. The RPMIP also uses a checklist of symptoms' presence/non-presence, requesting "start" dates for each symptom endorsed, a relatively insensitive approach. Additionally, creators of the RPMIP explain that its use was primarily intended for inpatient use and community providers. Thus, evidence for the RPIMP in non-inpatient settings is lacking, and the authors themselves note that its generalizability to the community is uncertain (McGorry, Copolov, & Singh, 1990). The IRAOS also uses a dichotomous approach in its probing but does require that endorsed symptoms be associated with behavioral changes or a reduction in functioning or social connectedness/competence. It does not describe what this reduction might look like or provide a quantification of how to measure it, relying on the administrator to make that determination informally.

Assessing onset of treatment. Similar to the *illness onset* criticisms outlined above, there is not a gold standard in DUP research as to what constitutes *treatment onset*. Several meta-analyses assessing the impact of DUP on outcomes have noted a range of definitions for treatment onset including: 1) initiation of first treatment (Addington et al., 2004) or admission into psychosis-specific program (Amminger, 2002); 2) initiation of first antipsychotic (Black et al., 2001; Ho et al., 2003); or 3) first hospitalization (Craig et al., 2000; Crow, MacMillan, Johnson, & Johnstone, 1986; Haas & Sweeny, 1992), each of which can complicate research assessment for several reasons.

Initiation of first treatment or admission into a general or psychosis-specific mental health program does not guarantee a therapeutic effect, as it is largely reliant on the level of engagement by the consumer. Similarly, the use of "initiation of an antipsychotic" as a measure of treatment may include those who will terminate treatment before experiencing therapeutic effects of the medication, which can take as long as six weeks to impact symptoms (Lally & MacCabe, 2015). Therefore, it is possible that those taking medication for an insufficient amount of time may follow the same symptomatic trends as those who are continuously unmedicated. Finally, like the aforementioned treatment modalities, involuntary hospitalization may help to stabilize consumers experiencing a first episode of psychosis, but may not serve as adequate treatment. In fact, involuntary hospitalizations may have iatrogenic long-term effects related to psychopathology and functioning as compared to voluntary hospitalization (Opjordsmoen et al., 2010).

Currently available assessments vary in their degree of specifying treatment onset. Despite being two of the more frequently used assessments for measuring DUP, the PANSS interview and SOS have been designed only as symptom ratings (used for psychosis onset), which has required research groups to supplement the interviews with customized definitions of treatment onset. These have included the first noticeable clinical response to medication (Larsen et al., 2000), first hospitalization (Compton et al., 2011; Flanagan & Compton, 2012), or one month of adequate antipsychotic dosage (Winsper et al., 2013), which complicates the comparison of efforts for measuring DUP across samples. Similarly, many of the groups using the RPMIP do not document their methods for assessing treatment onset (Alvarez-Jimenez et al., 2012; Harrington, Neffgen, Sasalu, Sehgal, & Woolley, 2013), suggesting variability in this interview's definition of DUP.

For those assessments that explicitly probe for treatment onset in their original forms, there still exists some lack in the quality of information provided. Similar to its assessment of symptom onset, the Beiser Scale uses content analysis of open-ended questions to determine the date of when treatment was first sought, but does not probe any further about the course of treatment. This has led Beiser Scale research groups to formulate their own methods of determining treatment onset, which have included first antipsychotic treatment (Clarke et al., 2006; Foley et al., 2007; Hill et al., 2010) and first hospitalization (Verdoux et al., 2001). The CORS is more operationalized than other measures, labelling treatment as "receiving antipsychotic medication that would lead, in most cases, to a clinically sufficient response in non-chronic, non-treatment-resistant people" (Norman et al., 2004). Despite this guidance, this definition may still create an unclear judgment call for non-prescribers. The CASH, like other global diagnostic interviews, inquires more broadly about whether or not the interviewee is currently, or has ever been, prescribed an antipsychotic. Follow-up probes assess the number of total months they may have been prescribed, but do not specify either the date of first administration or if it was taken continuously. As a result, several of the studies reviewed used the "initiation" of an antipsychotic as the onset of treatment, which may not accurately capture the date of therapeutic response.

Development of a New DUP Measure

Limitations in current measures of DUP include overreliance on chart reviews, dichotomous probing of complex symptoms, loose definitions of frequency or duration criteria, and inattention to duration and functional impairment interplay. The standardization of a DUP measure is further complicated by the fact that many current measures do not include a tool to document any form of treatment onset, requiring that interviews incorporate their own treatment onset measure to elicit a DUP. An improved measure would provide: 1) a sensitive symptom assessment with a continuum of severity and frequency and 2) an easily measured and generally accepted metric for treatment onset, which would aid in the standardization of DUP.

Structured Interview for Psychosis-Risk Syndromes (SIPS). One measure that may have potential to contribute to a standardized definition of illness onset is the Structured Interview for Psychosis-Risk Syndromes (SIPS; Miller et al., 2003). Unlike traditional psychosis-onset measures, the SIPS stems from research measuring a continuum of symptom severity in those at risk for, or experiencing, psychotic symptoms. The SIPS was designed to measure the level of conviction, frequency, and functional impairment of symptoms, many of which are lacking in the majority of measures in the DUP literature. Moreover, the SIPS is better able to probe at the lower end of symptom expression than other psychosis-focused measures and can comprehensively assess for symptoms along a continuum of psychosis-risk. It is also the most commonly used measure of psychosis risk in North America (Goulding et al., 2013).

The SIPS uses a detailed list of probes to detect the presence of positive symptoms, which includes 21 items assessing unusual thoughts and delusional ideas, 5

items assessing suspiciousness/persecutory ideas, 5 items assessing grandiose ideas, 14 items assessing perceptual abnormalities, and 3 items assessing disorganized communication. After the presenting symptoms are established, follow-up probes are used to determine if these symptoms meet criteria for a CHR syndrome or full-threshold psychosis. The most common CHR diagnosis is "attenuated psychosis syndrome" (APS), where a consumer endorses regular experiencing of positive symptoms, but with a level of conviction or impact to functioning that scores below the diagnostic threshold for psychosis (Tsuang et al., 2013). Alternatively, a diagnosis of "Brief Intermittent Psychotic Syndrome (BIPS)" suggests that the severity of symptoms would meet criteria for psychosis, but are too brief and not dangerous or disorganizing enough to meet the frequency threshold. Finally, the SIPS also has a third categorization that focuses on psychosis-risk syndromes in those with genetic risk and who have experienced a decline in global functioning. This "Lifetime Genetic Risk and Functional Decline" (GRD) syndrome specifically includes those with a reported 30% or greater reduction in global functioning and have either: 1) a first degree relative with a psychotic disorder or 2) meet criteria for Schizotypal Personality Disorder (SPD). The SIPS is designed to detect these three different manifestations of CHR. Importantly, in addition to assessing these three risk syndromes, the SIPS is also designed to measure the onset of psychosis.

To meet criteria for psychosis, the SIPS requires that positive symptoms are held with conviction (belief that the symptom is real [with no doubt] at least intermittently) and interfere with thinking, feeling, social relations, and/or behavior. In addition, symptoms must also be disorganizing (posing a threat to one's reputation, e.g., wearing foil on head), dangerous (e.g., jumping in front of traffic), or frequent (i.e., occurring at least 1 hour/day at an average frequency of 4 days/week over 1 month). These combined criteria ensure that the diagnostic process excludes consumers that may have experienced prolonged symptoms but are not severely affected, or have experienced an acute occurrence of psychosis symptoms that could potentially remit without intervention. Unlike other measures' diagnosis for psychosis, the SIPS criteria closely reflect criteria set forth by the DSM, making it an ideal candidate for measuring DUP.

SIPS-DUP Interview. The SIPS holds important advantages in the evaluation of psychosis onset (a necessary component to establish DUP), including its comprehensiveness with respect to possible psychosis symptoms, attention to the full psychosis spectrum on a continuous scale, sensitivity to subtle changes in illness that mark early expression of psychosis (e.g., severity, frequency, interference, distress, conviction), a highly standardized administration format, and inclusion of a working definition of psychosis reflective of that in the DSM. However, the SIPS' length and lack of treatment onset measurement prevents it from efficiently and comprehensively measuring DUP in its original form.

With these strengths in mind, a modified "SIPS-DUP Interview" was designed by our team to maintain the benefits inherent to the SIPS (i.e., documentation of psychosis onset, use of multiple probes to assess individual symptoms, continuous measurement to distinguish psychosis from CHR symptoms, ability to probe at the lower end of symptom expression, and a structured interview format to ensure standardization and reliability), while also improving the measurement of DUP relative to existing options. To do this, the SIPS-DUP was modified to conclude with a "DUP Interview" portion that uses clinical interview probes to ascertain dates that specific symptom indicators may have occurred, including first observance of a symptom's presence by another person, first ER/hospitalization, and first time seen by mental health care provider for symptoms of psychosis. Next, the SIPS-DUP Interview documents five markers of treatment onset date, including first dose of antipsychotics, first completed course of antipsychotics for 1 month or more, first visit for mental health issues, first non-medication treatment, and first non-antipsychotic but psychotropic medication. These modifications are intended to address the limitations documented in the existing DUP measurement strategies.

Present Study

Although the association between DUP and clinical outcomes has been wellestablished using a variety of assessments, there is reason to believe that use of the SIPS-DUP Interview may help correct for some shortcomings inherent in these measures. The ability for the SIPS-DUP to sensitively measure change from the prodromal to full psychosis phase of illness, use multiple probes to thoroughly assess symptoms, and deliver a structured and reliable interview may help the field better understand which components of illness are most affected by DUP. Additionally, given the value of early detection in the risk stage of illness to help minimize DUP, using a measure with roots in identifying early signs prospectively, versus a tool designed to assess existing psychosis, may help facilitate links between systems of care that serve those at risk with aspects of systems of care that serve people in their first episode of psychosis.

The current study aimed to measure the ability of the SIPS-DUP Interview to predict the clinical impact of longer DUP in overall positive and negative symptom scores, while also exploring what effect DUP may have at the symptom level. Unlike many studies measuring participants at treatment baseline, however, this study enrolled young adults currently in treatment for 1-3 years following a first episode of psychosis.

Specific Aims and Hypotheses

Aim 1: Assess the relation between the SIPS-DUP Interview and positive symptoms. The first aim of this study was to assess the degree to which DUP, as measured by the SIPS-DUP Interview, was associated with positive symptomatology (e.g., strange beliefs, delusional thoughts, suspiciousness, grandiose ideas, hallucinatory experiences) of psychosis during treatment, as measured by total and individual scores on the Brief Psychiatric Rating Scale (BPRS).

Hypothesis 1A. It was hypothesized that longer SIPS-DUP assessed DUP would be predictive of more severe overall positive symptomatology, as measured by BPRS total score.

Exploratory Hypothesis 1B. It was hypothesized that the degree to which SIPS-DUP assessed DUP would be positively associated with individual items on the BPRS would vary based on the item being assessed. Specifically, the correlations of SIPS-DUP assessed DUP with individual symptoms (i.e., items on the BPRS) were estimated to assess patterns of relations between specific symptoms and SIPS-DUP assessed DUP.

Aim 2: Explore the relation between the SIPS-DUP Interview and negative symptoms. The second aim of this study was to assess the degree to which DUP, as measured by the SIPS-DUP Interview, was associated with negative symptomatology (e.g., blunted affect, alogia, avolition, asociality) of psychosis during treatment, as measured by total and individual scores on the Scale for the Assessment of Negative Symptoms (SANS). *Hypothesis 2A.* It was hypothesized that longer DUP would be predictive of more severe overall negative symptomatology, as measured by SANS total score.

Exploratory Hypothesis 2B. It was hypothesized that the degree to which SIPS-DUP assessed DUP was positively associated with individual items on the SANS would vary based on the item being assessed. Specifically, the correlations of SIPS-DUP assessed DUP with individual symptoms (i.e., items on the SANS) were estimated to examine patterns of relations between specific symptoms and SIPS-DUP assessed DUP.

Method

Participant Eligibility and Recruitment

The current study was part of an ongoing research collaboration between the University of Maryland, Baltimore's Department of Psychiatry and the University of Maryland, Baltimore County's Department of Psychology, which aims to track the clinical, neuropsychological, and neurological markers of participants between the ages of 12 and 45 who are within their first year of treatment at a first episode program in the Baltimore area. Consumers were invited to participate if they met the following requirements: had a reported history of hallucinations or delusions, were enrolled in clinical services, were considered clinically stable enough for research by their treating therapist, and could communicate well enough to effectively answer interview questions. Research staff coordinated recruitment with programs' clinical staff to ensure eligibility criteria were met, at which point study staff offered them the opportunity to participate in the research. All consumers meeting these criteria were offered the opportunity to participate in the study. The final sample was comprised of 27 participants in which the average age was 22, identified gender was predominantly male (81%), and mean duration of untreated psychosis (DUP) was approximately 46 weeks.

Measures

Structured Interview of Prodromal Syndromes – Duration of Untreated **Psychosis Interview (SIPS-DUP Interview).** The original Structured Interview for Psychosis-risk Syndromes (SIPS; Miller et al., 2003) is designed to measure the presence of 19 symptoms within four individual domains of the psychosis spectrum: positive, negative, disorganizing, and other general symptomatology. These 19 items are measured using a 7-point Likert-type scale, which ranges from 0 ("absent") to 6 ("severe and psychotic" for positive symptoms, or "extreme" for negative, disorganized, and general symptoms). The positive symptom domain is used to determine psychosis presence where, if a symptom is endorsed, follow-up qualifiers are used to determine the frequency, distress level, degree of interference (e.g., behavioral, functional), and degree of conviction. A psychosis rating requires that the symptom be rated a 6, and meet either a frequency criterion (i.e., at least one hour per day at an average frequency of four days per week over one month) or a distress/interference criterion (i.e., symptom must be either seriously disorganizing or dangerous). Research on the SIPS interrater reliability (Miller et al., 2003) has revealed a rater agreement of 93% (kappa = 0.81, 95% CI = 0.55-0.93). In terms of ability to predict the eventual onset of psychosis, approximately 26% of those deemed CHR using the SIPS will cross the threshold for full psychosis in the first two years of illness onset (Fusar-Poli et al., 2015).

The SIPS-DUP Interview is a modified version of the SIPS interview that includes three major changes. The first modification was the use of only positive
symptom probes in the SIPS-DUP Interview; the original SIPS measures an array of positive, negative, disorganizing, and other general symptoms. The SIPS-DUP Interview's primary purpose in this study was to establish psychosis onset, eliminating the need for the assessment of non-positive symptoms. The second modification was the paring down of these positive symptom probes, where item-level analyses eliminated probes that were either 1) not a significant predictor of psychosis or 2) highly correlated with other items tapping into the same construct (i.e., "copycat" items), which resulted in a retention of 31 of the original 48 probes. The final and most notable change was the integration of a novel section that collected information on the date of first symptom to cross psychosis threshold and date of treatment for psychosis (described below).

The SIPS-DUP Interview was administered as a standardized, structured interview, where interviewees are first provided 31 positive symptom probes in a yes/no response format. For probes that are endorsed, follow-up inquiries are used to determine if a psychotic intensity is present. This includes the use of "anchor questions," which aim to bolster the participant's recall of when certain symptoms emerged (e.g., inquiring what season it was, what year in school something happened, or if it was around a particular holiday) when insight is limited. To determine psychotic presence, participants must endorse a specific degree of conviction (i.e., believing the symptom to be real at least intermittently) and interference (i.e., the symptom affecting one's thinking, feeling, social relations, or behavior) in their symptoms. If the symptoms meet these thresholds, further follow-up questions are administered to determine if these symptoms meet full criteria for psychosis. Full psychosis is reached when symptoms are either dangerous (e.g., physically dangerous toward life or physical health) or disorganizing (apparent and impairing odd or bizarre behavior that impacts one's dignity or reputation); or occurring at a frequency of at least one hour per day over the course of at least four days per week, with this level of frequency occurring for at least one month.

The final portion of this measure is used to document DUP. To do so, the date of earliest full-threshold symptom is first identified from the probes to document exactly when psychosis began. Next, to determine the end of one's DUP, participants are asked when treatment was adequately obtained (defined in this study as 30 days of continuous antipsychotic treatment). DUP is therefore operationalized as the amount of time between 1) onset of earliest full-threshold symptoms and 2) the reception of adequate treatment.

Brief Psychiatric Rating Scale (BPRS). The BPRS is a 22-item clinicianadministered semi-structured interview designed to assess the positive, negative, and affective symptoms of psychosis (Overall & Gorham, 1962). The BPRS measures the frequency and severity of symptoms over the past week using a 7-point Likert-type scale with anchors ranging from 1 ("not present") to 7 ("extremely severe"). It is composed of questions based on content (e.g., reported depression, anxiety, anhedonia) and observable symptoms (e.g., blunted affect, poverty of speech). This measure has established satisfactory sensitivity in its ability to detect changes in symptom severity (Faustman & Overall, 1999), and reports of reliability have demonstrated moderate inter-rater reliability ranging from .66 to .88 (Ventura, Green, Shaner, & Liberman, 1993). Concurrent validity of the BPRS has been established through comparison of other measures, including the Hamilton Rating Scale for Depression (r = .79; Craig, Richardson, Pass, & Bregman, 1985), Scale for the Assessment of Negative Symptoms (r = .85; Gur et al., 1991), and the Brief Symptoms Inventory (r = .56; Morlan & Tan, 1998).

Scale for the Assessment of Negative Symptoms (SANS). The SANS is a 23item clinician-administered semi-structured interview designed to assess only the negative symptoms of psychosis (Andreasen, 1989). It consists of five domains: Affective Flattening or Blunting, Alogia, Avolition-Apathy, Anhedonia-Asociality, and Attentional Impairment. Included in the total SANS score are both individual items scores and global scores for each of the five domains. In this study, the SANS was used to assess the frequency and severity of negative symptoms over the prior week. Each item measures symptoms on a 6-point Likert-type scale ranging from 0 ("not present") to 5 ("present and severe"). Interrater reliability of the SANS has ranged from moderate to high (ICC = 0.60 - 0.84; Andreasen, 2008). Interrater reliability improves within each of the domains (0.86 - 0.93), with reliability of the overall score being very good (0.92); Andreasen, 2008). Test-retest reliability of the SANS total score has been measured at 0.45, while the measures of individual domains have ranged from 0.13 - 0.40(Andreasen, 2008). Internal consistency of the SANS within individual domains has also demonstrated satisfactory reliability (Cronbach α = Alogia, 0.63; Affective Flattening, 0.83; Avolition-Apathy, 0.74; Anhedonia-Asociality, 0.77; Attention, 0.75; Andreasen, 2008).

Duration of Treatment. The duration of treatment was defined as the total number of days between the participant's date of admission into their first episode psychosis program and the date of their being administered the outcome measures. These dates were taken from their medical record and research record, respectively.

Procedures

Consumers who chose to participate in the study were brought to a university research center to provide informed consent, which included an "evaluation to sign consent" to ensure full understanding of research procedures. For minors, this process consisted of providing assent to research while the corresponding guardian provides informed consent. Participants, or their guardians, also completed a HIPAA authorization form to allow research staff to review relevant medical records from participants' respective first episode programs. These medical record reviews were used to assess participants' duration of treatment. Following the informed consent process, participants were administered the study battery of clinical assessments and surveys, which included the BPRS, SANS, and SIPS-DUP Interview. The current project was begun with an initial recruitment target of 55 participants. Due to challenges in recruiting, this target was not met and a significantly smaller sample of 27 participants was used for analyses.

Results

Data Analysis Plan

Given the small sample size of 27 participants, reliance on traditional null hypothesis significance testing (e.g., inferring relations given p < .05) may be misleading and not reveal meaningful findings. For example, given the sample size, correlation statistics smaller than .39 (considered a "large" effect size; Cohen, 1988) would have *p*levels greater than .05, resulting in a decision to retain the null. As such, statistical inferences in this study were based on effect size, where any correlation or partial correlation that was at least .27 (ignoring sign) was interpreted as a meaningful effect. This threshold approaches a "medium" strength association, as coefficients of .10, .30, and .50 represent small, medium, and large magnitudes, respectively (Cohen, 1988).

Because the variations in duration of treatment (DT) and age of participants may conflate the relation of DUP with the outcomes, both variables were controlled for in the study. DT was calculated by totaling the amount of time, in weeks, between the beginning of treatment and the administration of outcome measures. Controlling for DT helped to evaluate the SIPS-DUP assessed DUP impact on outcomes while controlling for extended periods of time between the initiation of treatment and the administration of the SIPS-DUP measure.

Hypotheses 1A and 2A assessed whether previous findings associating DUP with positive and negative symptomatology would be replicable using the SIPS-DUP Interview. These hypotheses were tested through use of partial correlations, assessing the degree of association between DUP and positive and negative symptomatology, as measured by BPRS and SANS total scores, while controlling for age and duration of treatment (i.e., time between enrolling into treatment and administration of research measures). Hypotheses 1B and 2B were also explored through estimation of the partial correlations of DUP with BPRS item scores and SANS item scores, controlling for duration of treatment and age.

Preliminary Analyses

Demographics

The study included 27 participants who consented. The sample was comprised of 12 Black participants (44%), 13 White participants (48%) and two Asian-American

participants (7%) of which 5 (18%) identified as female and 22 (81%) male, and were approximately 22 years old (SD = 3.18).

Assumptions

Correlation and partial correlation analyses require that specific criteria are met to ensure that the sample is appropriate for analysis. These criteria include that there is a linear relation between predictor and outcome, that there are no appreciable outliers, and the variables approximate a normal distribution. Prior to conducting primary analyses, variable distributions were examined for consistency with these assumptions.

Measures of normality for predictor (DUP, duration of treatment, and age) and outcome variables (BPRS total scores, BPRS individual items, SANS total scores, and SANS individual items) were evaluated. Variables with skewness > | 2 | and/or kurtosis > | 7 | were considered moderately or severely non-normally distributed (Curran, West, & Finch, 1996). Ten variables exceeded these suggested guidelines and were transformed using natural log. Of these transformed variables, only DUP, BPRS Grandiosity, and BPRS Poverty of Speech appeared normally distributed following transformation. Seven variables, BPRS Conceptual Disorganization, BPRS Mannerisms, BPRS Uncooperativeness, BPRS Excitement, BPRS Disorientation, BPRS Inappropriate Affect, and SANS Blocking, continued to exceed guidelines following transformation and were not included in any remaining analyses.

Primary Analyses

Hypothesis 1

Partial correlations were estimated to determine the relation of DUP with the BPRS total score and individual items while controlling for age and duration of treatment. Table 2 provides both the zero-order (non-controlled) and partial correlations

between DUP and the 15 BPRS items.

Table 2.

	Covariates			DUP		
BPRS Items	Age	BPRS _{DT}	Zero-order	Partial	р	
Total Score	02	05	.49	.51	.009	
Conceptually grouped as positiv	e symp	toms				
Unusual Thought Content	12	13	.52	.57	.003	
Suspiciousness	.10	.06	.51	.53	.007	
Hallucinations	05	12	.47	.49	.013	
Grandiosity	18	.16	.27	.37	.072	
Guilt	.02	.41	.24	.36	.078	
Conceptually grouped as psycho	omotor	flattening				
Tension	22	.17	45	40	.048	
Motor Retardation	.03	20	.34	.23	.279	
Poverty of Speech	26	09	23	19	.351	
Blunted Affect	02	09	.03	.02	.934	
Conceptually grouped as genero	al psych	opathology				
Anxiety	.18	02	.48	.46	.021	
Hostility	.12	16	.46	.43	.030	
Depressiveness	.10	22	.34	.29	.153	
Emotional Withdrawal	.34	.11	15	24	.244	
Somatic Concern	.32	.09	.06	.00	.991	

Zero-Order and Partial Correlations Between DUP and BPRS Item Scores

Within a given cluster, items ordered based on magnitude of partial correlation

As the covariates were not strongly related to DUP, the zero-order and partial correlations for a given variable are predictably quite similar. For ease in considering the relations, I conceptually grouped the BPRS items as falling into one of three categories: a) positive symptoms, b) psychomotor flattening, and c) general psychopathology. As can be seen from Table 2, all five of the positive symptom items and most (three of five) of the general psychopathology items were related to DUP. Moreover, most of the significant relations in each of these domains were typically in the moderate-strong to strong range (> .40). Only one item (Tension) met traditional significance criterion in the

psychomotor flattening category and unexpectedly, it was negatively related to DUP.

Hypothesis 2

Aim 2 sought to determine whether there were statistically significant associations

between DUP SANS total scores and individual items via partial correlations. Table 3

displays the relations between DUP and the 17 SANS items.

Table 3.

	Covariates			DUP		
SANS Items	Age	SANS _{DT}	Zero-order	Partial	р	
Total Score	.10	29	09	18	.381	
Conceptually grouped as affecti	ve flatte	ening or blunt	ing			
Paucity of Expression	08	13	21	22	.288	
Unchanging Facial Expression	.13	06	.21	.17	.408	
Decreased Spontaneity	.12	18	08	15	.472	
Lack of Vocal Inflections	.15	24	.12	.04	.832	
Affective Non-Responsivity	.19	.05	.07	.03	.879	
Poor Eye Contact	.19	.02	.07	.03	.877	
Conceptually grouped as alogia						
Poverty of Speech	21	09	33	32	.124	
Poverty of Content of Speech	.06	18	.35	.32	.113	
Increased Latency	.36	.09	.00	08	.707	
Conceptually grouped as avoliti	on-ana	thv				
Grooming	21	07	29	27	.199	
Concentually grouped as role fu	nction					
Role Functioning Level	- 06	- 30	- 28	- 35	088	
Role Functioning Quality	.03	21	23	30	.148	
Anergia	17	25	27	30	.150	
	7.					
Conceptually grouped as asocia	lity-ani	nedonia	20	17	401	
Ability Intimacy	.21	.04	.20	.17	.421	
Anhedonia	.15	26	.20	13	.531	
Sexuality	19	26	02	02	.911	
Asociality	.52	.06	.10	03	.905	

Zero-order and Partial Correlations Between DUP and SANS Item Scores

Within a given cluster, items ordered based on magnitude of partial correlation

DUP was significantly associated with all measures within the Role-Functioning and Avolition-Apathy domains, along with two measures of Alogia (Poverty of Speech, Poverty of Content of Speech). Interestingly, with the exception of Poverty of Speech, all of these significant associations were negative, suggesting increased DUP is associated with lower negative symptomatology.

Race

It is noted that race was not controlled for in this study for two reasons. It was not theoretically predicted a priori and, given only two participants endorsed Asian-American, it would have resulted in dropping nearly 10% of the sample. However, research has suggested that race is related to these symptoms of psychosis, particularly differences between Black and White participants (Anglin et al., 2019; Millman et al., 2019). To help further understand these differences, and to contextualize the findings of the current study, descriptive statistics were estimated for Black and White participants as well as determining an estimate of Cohen's *d* corresponding to the mean difference. Cohen's *d* can appropriately be thought of as a standardized mean difference with proposed guidelines of 0.20, 0.50, and 0.80 corresponding to small, moderate, and large, respectively.

Examining statistics in Tables 4 and 5 suggests that the mean difference was moderate (or greater) on four of the positive symptoms and four of the negative symptoms. Importantly, in all instances Black participants were rated higher on these symptom measures. Moreover, of the 34 items, Black participants were rated higher on 24 of them. The only symptom in which White participants were rated higher that had a small-to-moderate effect size was Depressiveness (d = 0.44). Given the somewhat robust race differences, the primary analyses presented above were conducted again controlling for race (in which the two Asian-American participants were dropped). Examination of the findings controlling for race were consistent with those presented in Tables 2 and 3 and were thus not provided here.

Table 4.

	White participants	Black participants	Cohen's d
BPRS Items	M(SD)	M(SD)	
Total Score	33.85 (10.05)	38.67 (7.39)	0.54
Somatic Concern	1.77 (1.09)	2.92 (1.16)	1.02
Hallucinations	1.46 (1.39)	2.58 (2.19)	0.62
Emotional Withdrawal	2.00 (1.00)	2.58 (1.16)	0.54
Depressiveness	2.38 (1.56)	1.75 (1.29)	0.44^{a}
Blunted Affect	2.31 (1.25)	2.67 (1.44)	0.27
Suspiciousness	1.69 (1.25)	1.92 (1.08)	0.19
Grandiosity	0.12 (0.22)	0.17 (0.27)	0.19
Guilt	2.08 (1.55)	1.83 (1.11)	0.18 ^a
Motor Retardation	2.00 (0.82)	2.17 (1.19)	0.16
Unusual Thought Content	2.00 (1.73)	1.83 (1.40)	0.11 ^a
Poverty of Speech	0.12 (0.25)	0.10 (0.23)	0.10 ^a
Tension	1.85 (1.21)	1.92 (1.16)	0.06
Hostility	2.08 (1.66)	2.17 (1.40)	0.06
Anxiety	2.92 (1.04)	2.92 (1.56)	0.00

Mean BPRS Differences by Race

^a Black participants rated lower on these measures

Cohen's d values of .20, 0.50, and 0.80 correspond to small, moderate, and large, respectively

Table 5.

Mean SANS Differences by Race

	White participants	Black participants	
SANS Items	M (SD)	M (SD)	Cohen's d
Total Score	19.15 (11.64)	22.17 (11.22)	0.26
Increased Latency	0.38 (0.65)	1.08 (1.08)	0.79
Affective Non-Responsivity	0.23 (0.44)	0.92 (1.16)	0.79
Blocking	0.00 (0.00)	0.25 (0.62)	0.58
Poverty of Content of Speech	0.31 (0.85)	0.83 (1.27)	0.49
Paucity of Expression	1.08 (1.26)	1.75 (1.48)	0.49
Poor Eye Contact	1.46 (1.20)	1.92 (1.24)	0.37
Ability Intimacy	0.54 (0.97)	0.92 (1.08)	0.37
Poverty of Speech	0.46 (0.97)	0.83 (1.34)	0.32
Current Role Level	2.62 (2.40)	1.92 (2.02)	0.31 ^a
Current Role Level Outpatient	2.31 (2.59)	1.58 (2.19)	0.30 ^a
Grooming	0.69 (1.03)	1.00 (1.21)	0.28
Decreased Spontaneity	1.00 (1.00)	0.75 (0.97)	0.25 ^a
Unchanging Facial Expression	1.46 (1.33)	1.75 (1.48)	0.21
Physical Anergia	1.54 (1.45)	1.67 (1.44)	0.09
Lack of Vocal Inflections	1.46 (1.61)	1.58 (1.51)	0.08
Anhedonia	0.92 (1.04)	0.83 (1.11)	0.08^{a}
Sexuality	1.38 (1.89)	1.25 (1.96)	0.07^{a}
Asociality	1.31 (1.32)	1.33 (1.44)	0.02

^a Black participants rated lower on these measures Cohen's *d* values of .20, 0.50, and 0.80 correspond to small, moderate, and large, respectively

Discussion

This study evolved from previous research linking prolonged DUP with poorer outcomes, including more pronounced symptomatology, higher likelihood of rehospitalization, and reduced occupational functioning. Although DUP has been wellestablished as a relatively strong predictor of outcomes, the method for assessing DUP is largely unstandardized and may benefit from a more unified approach. The goal for the current study was to first see whether use of the SIPS-DUP Interview could replicate previous findings. Additionally, a more exploratory goal sought to determine whether SIPS-DUP assessed DUP may also be linked to more specific symptoms at the item level of the BPRS and SANS. Unless otherwise stated, DUP will specifically refer to SIPS-DUP assessed DUP in the remaining discussion.

In an effort to obtain a clearer perception of the link between DUP and clinical symptom measures, partial correlation analyses were employed, controlling for age and duration of treatment. DUP in this sample was significantly and positively associated with BPRS items of Unusual Thought Content, Suspiciousness, Hallucinations, Grandiosity, Guilt, Anxiety, Hostility, Depressiveness, and Total Score, as well as with SANS Poverty of Content of Speech. DUP was also negatively correlated with BPRS Tension and the SANS items Poverty of Speech, Grooming, Role Functioning Level, Role Functioning Quality, and Anergia, which had not been theoretically predicted.

BPRS Total Score

Use of the SIPS-DUP Interview when assessing the effect of DUP on BPRS total score generally reflected findings from studies using similar measures. DUP remained a strong predictor of BPRS total scores, even when controlling for age and duration of treatment. This finding is in line with previous studies measuring associations between DUP and BPRS total scores during treatment using other measures of DUP (Cechnicki, Hanuszkiewicz, Polczyk, & Bielanska, 2011; Üçok, Polat, Genç, Çakır, & Turan, 2004), as well as studies that assess other types of symptom severity partway through treatment (Howes et al., 2021), and provides preliminary support for the SIPS-DUP measure as a tool for assessing DUP.

Positive Symptoms

The association between DUP and positive symptomatology was also observed across a range of individual BPRS items. Five positive symptom items (i.e., Suspiciousness, Hallucinatory Behavior, Unusual Thought Content, Guilt, and Grandiosity) were significantly associated with DUP and had moderate or large relations. These findings suggest that the five positive symptoms may intensify in participants with more prolonged DUP and corroborate the existing literature.

Although mechanisms behind these links were not assessed, the associations between DUP and Suspiciousness, Unusual Thought Content, Grandiosity, Guilt, and Hallucinations were significant, with the first four of these items representing various types of delusions. One hypothesis for the link between DUP and delusional experiences is that such belief systems may stem from unhelpful irregularities in cognition (e.g., biases and the ability to correct incorrect judgments, jumps to conclusions, etc.; Bell, Halligan, & Ellis, 2006), leading them to proliferate until they are challenged by effective therapy. For example, cognitive-behavioral therapy introduces alternative explanations for unhelpful cognitions may help dispel implausible belief systems and replace them with more evidence-based explanations. If this therapy is delayed, belief systems may go unchallenged for extended periods of time, which might then lead to delusions as measured by the BPRS. In contrast, if therapy is introduced more proximally to the onset of therapy, consumers may benefit from early efforts to stem unhelpful cognitions.

General Psychopathology.

While much of the DUP literature has focused on active phase symptoms and functional outcomes, less might be known about other psychological concerns, and several possibilities exist as to why DUP was significantly associated with Anxiety, Depression and Hostility. First, a longer period of psychotic illness may lead to increased anxiety or depression as the progression of the illness becomes more apparent and potentially debilitating. Because longer DUP might signify a lack of knowledge about, or confidence in, treatment, it stands to reason that hopelessness may segue into more generalized types of psychopathology. Similarly, an elevation in one's hostility may also be a downstream effect of hallucinatory or delusional experiences, which has been found in prior studies (Faay & van Os, 2020).

Conversely, it may be that these symptoms are not necessarily by-products of DUP, but rather serve as sequalae to the onset of psychosis itself. In fact, those eventually meeting criteria for clinical high risk are often referred initially for anxious or depressive symptoms (Stowkowy, Colijn, & Addington, 2012), suggesting that other types of psychopathology may precede psychosis onset. Considering the high rates of co-occurrence between general psychopathology and psychosis (McAusland et al., 2015; Millman, Gold, & Mittal, 2019), further research into how these types of symptomatology interact may be necessary.

Psychomotor Flattening

One minor finding was the SIPS-DUP's significant association with Tension (i.e., "motor restlessness [agitation]"), which was included under the "Psychomotor Flattening" domain. Unlike the other three items in this category, BPRS Tension refers to a motor *excess* and was negatively correlated with DUP, suggesting that DUP may be associated with a more relaxed clinical presentation. In terms of why this link exists, a behavioral approach might suggest that those exhibiting calmer behaviors may not draw the same clinical concern as those with more excessive or agitative behaviors, thereby minimizing the likelihood that others will identify these people as needing treatment. Alternatively, it may be that longer DUP leads to a more exacerbated flatness. Although no study to date has found that DUP uniquely and exclusively contributes to this psychomotor flattening, several meta-analyses have found that DUP may have a direct effect on negative symptom severity when controlling for premorbid factors (Marshall et al., 2005; Perkins, 2005). One study found that shorter-DUP participants may experience decreases in negative symptom severity throughout treatment while longer-DUP participants experience increases, suggesting that these experiences may be inconstant.

Expressive Language

These findings also found that DUP was positively correlated with impoverished speech content (e.g., nebulous, overabstract, overconcrete or repetitive) and negatively with quantity (e.g., brief, concrete, or unelaborated), both of which are characteristics of "formal thought disorder" in schizophrenia. Formal thought disorder occurs in approximately 20% of patients and, like other symptoms, can be conceptualized as positive (e.g., impoverished content) and negative (e.g., impoverished quantity) in

nature. For example, patients have also been differentiated from healthy controls based on deficits in "speech connectedness" (i.e., organized expressive language with in analyzed speech samples; Spencer et al., 2021) and premorbid expressive language abilities (Bearden et al., 2000).

Although research on the effect of DUP on language abilities is sparse, these findings are consistent with some evidence that DUP may be uniquely associated with more "positive" thought disorder (Birnbaum et al., 2015). One potential explanation is that, due to this symptom's emergence prior to psychosis onset (Bearden et al., 2000; Mouridsen & Hauschild, 2008), it may obscure others' ability to detect aberrations and facilitate help. Moreover, the genetic underpinnings of expressive language deficits in schizophrenia-related disorders (Asarnow et al., 2002; Welham et al., 2010) may make it difficult for parents with similar difficulties to identify these deficits in their children.

Volition and Role Functioning

Another important marker in psychosis assessment is how one remains motivated and pursues vocational success. In the current study, DUP was negatively associated with measures of vocational functioning, anergia, and grooming, which contrasts with most of the current research indicating that longer DUP often results in poorer outcomes in these domains (Kane et al., 2016). However, much of this research on the effects of DUP and role functioning has been collected in community settings where a wider range of these clinical ratings may occur. Unlike community-based studies, clients in the current sample participated in voluntary research and may represent a higher range of more motivated individuals. Moreover, it may be the case that participants prioritized their schooling or employment over seeking treatment, suggesting that there may be a subset of people who delay treatment for reasons related to high role-functioning or motivation.

Non-significant Findings

A significant link was not detected between DUP and the BPRS items of Motor Retardation, Poverty of Speech, Blunted Affect, Emotional Withdrawal, and Somatic Concern. There was also no significant link between DUP and SANS items of Paucity of Expression, Unchanging Facial Expression, Decreased Spontaneity, Lack of Vocal Inflections, Affective Non-Responsivity, Poor Eye Contact, Increased Latency, Ability for Intimacy, Anhedonia, Sexuality, or Asociality.

There are several possible explanations for the null findings, including a lack of statistical power as a result of few participants, as well as use of construct measurements that are not theoretically related between the SIPS-DUP Interview tool and these outcome measures. The latter may be especially true for negative symptom items, as psychosis onset is predicated on positive symptoms meeting a predetermined threshold, potentially making relations between DUP and positive symptoms inherently stronger than DUP with other types of outcomes. It may also be the case that these clinical measures were intended to assess the full spectrum of psychosis (i.e., from first episode to the more chronic), where some symptoms may not become as prevalent until later in the illness.

Mechanisms between SIPS-DUP assessed DUP and Symptoms

Although the mechanisms linking DUP and various clinical symptoms were not examined in this study, the literature offers several hypotheses. One proposed hypothesis is the "neurotoxic" effect of psychosis. This theory suggests that the progression of untreated psychosis can result in measurable degeneration of brain structures involved in symptom development (Goff et al., 2018; Lappin et al., 2006), but that antipsychotic medication may help to slow or stop this process. However, evidence for the neurotoxic theory remains inconclusive (Anderson, Voineskos, Mulsant, George, & McKenzie, 2014).

Another suggestion is that those with a longer DUP represent a subset of the population with "a more severe form of schizophrenia, typified by an early and insidious onset, poor premorbid functioning, and treatment resistance" (Jonas et al., 2020). These first two characteristics make it understandably difficult to identify the emergence of a first episode, where more robust changes in behavior may make psychosis more detectable. Further, other studies have identified tendencies for long-DUP clients to have a smaller social network and be more withdrawn, leading them to a longer DUP (Drake et al., 2000; Larsen, Johannessen, & Opjordsmen, 1998). Taken together, these hypotheses suggest that both innate characteristics and surrounding environmental factors may contribute to the link between DUP and symptoms.

Also, more recent research has suggested that DUP findings may simply be an artifact of study design (Jonas et al., 2020). Termed "lead-time bias," this phenomenon refers to the idea that differences in symptom severity may be more a function of *when* people are assessed rather than the length of their untreated psychosis. It postulates that people generally experience a similar rate of decline following the onset of psychosis, but that short-DUP clients, who seem to be doing relatively better at the beginning of treatment, simply have not fully experienced this decline yet. Future DUP research

would do well to include frequent and sensitive re-assessment of symptoms at baseline and throughout treatment.

Future use of the SIPS-DUP Interview in this research may help clarify the effects of premorbid functioning, symptom types, and other variables on the link between DUP and outcomes. This measure's capture of the full psychosis continuum may be particularly helpful in explaining the differential effects of acute and insidious onset of illness given its ability to detect changes between low risk, clinical high risk, and full-threshold psychosis. Additionally, the concision of the SIPS-DUP Interview allows it to be easily readministered over multiple timepoints, which may help the field better understand the effect of lead-time bias for people well into their treatment.

Utility of the SIPS-DUP Interview

These findings corroborate previous research suggesting a strong link between DUP and positive symptom-related outcomes and less robust associations with negative symptoms (Kane et al., 2016). Further research into the emergence of negative symptomatology may provide a clearer understanding of whether this pattern of findings is theoretically stable or an artifact due, in part, to the overwhelming focus on positive symptoms as the first marker of full-threshold psychosis in the field.

While we cannot suggest the SIPS-DUP Interview to be psychometrically superior to other measures of DUP, the ability for it to be frequently re-assessed and effectively probe at the lower end of symptoms expression could help to fill the gaps in understanding symptoms during both illness and treatment. Recurring administrations of the SIPS-DUP Interview during treatment may help neutralize concerns around leadtime bias and ideally inform the field on the utility of the SIPS-DUP Interview as a tool for assessing DUP. Use of the SIPS-DUP Interview at the item level may also help clarify the psychological symptoms most affected by DUP and underscore the importance of facilitating treatment as quickly as possible.

Limitations

This study was impacted by several limitations, the largest of which was the small sample size (n = 27). This resulted in underpowered analyses, requiring that both significant and null findings be interpreted cautiously. In an effort to avoid Type II error, a correlation coefficient was used to identify the threshold for "significant" findings, as traditional hypothesis testing was potentially over-conservative. Additionally, several variable distributions could not be made normal even following transformations, resulting violated statistical assumptions that prevented the running of certain analyses.

The lack of a longitudinal design prevented us from fully understanding the impact of treatment, as participants were measured only once, at a random point, within their first year of treatment. Although duration of treatment was controlled for, measuring symptom change over time could provide information into how DUP affects the trajectory of symptoms as well. This is especially important considering the variability of symptom severity in those first entering treatment and the potential impact of lead-time bias. If lead-time bias is a confounding issue in this study, future research may benefit from follow-up measures well after the onset of treatment in order to understand the impact of prolonged DUP and treatment resistance.

The voluntary nature of the study may also skew these data, as participants had the choice to opt into research through their respective clinical programs. As a result, it is possible that those agreeing to participate were characteristically different from the general first episode population. The motivation or agreeableness demonstrated by those choosing to participate in research may be representative of broader volitional characteristics, which may lead this research sample to be more likely to seek treatment, thus having a lower DUP, and thus limiting generalizability. A more ideal design would have the SIPS-DUP Interview and clinical ratings occur as part of their treatment, which would help to capture a more representative sample.

Another important measurement limitation is the use of the BPRS total score as a proxy for positive symptom severity. While the BPRS does include many items traditionally associated with positive symptoms, it is also composed of other symptom domains (e.g., Blunted Affect, Disorientation, Uncooperativeness, etc.) that may have detracted from its overall utility as a positive symptom measure. This dilution of a positive symptom sum may have affected the validity of these analyses, and the use of a more positive symptom-specific measure may have reduced statistical noise.

In terms of the generalizability of this research, it is important to understand that the majority of DUP research traditionally focuses on the consumer's symptom levels when they first begin treatment, whereas the clinical ratings in this study (i.e., BPRS and SANS) did not reflect a "true" baseline. The duration of treatment may have introduced other factors impacting these ratings, such as benefits of antipsychotic medication, psychosocial strategies to help reduce symptom impact, insight about one's illness, etc. Controlling for duration of treatment may help account for some variance, but cannot be expected to remove all statistical noise when assessing the relation between DUP and clinical symptom severity. Moreover, this delayed administration of the SIPS-DUP Interview and clinical ratings may be confounded not only by treatment factors, but also the increase in time elapsed since the first episode, which may negatively affect a participant's ability to recall specific dates in which symptoms cross over the psychosis threshold. This recall may already be difficult due to confusion or disorganization during the episode, and asking participants to recall these events long after treatment has begun may increase the difficulty of accurately eliciting onset dates for psychosis and psychosis treatment. Additionally, successful, long-term treatment may distort one's view of their initial symptoms if they have become accustomed to being asymptomatic.

The current study also did not measure convergent validity of the SIPS-DUP Interview, as correlating its findings along with established measures of DUP would have helped determine the degree to which this measure taps into the targeted construct. Although we believe that innovations within the SIPS-DUP Interview improve the capture of DUP from a technical perspective (e.g., probing at the lower end of symptom expression, providing multiple probes for each symptom, etc.), analyses comparing it to other measures of DUP would have provided a more objective view of its ability.

Taking the findings at face value, a refined measurement of DUP may help inform direct care. First, identifying which components of mental well-being are most impacted by DUP can provide clinicians individualized expectations when treating those with psychosis. For example, someone with longer DUP may exhibit more anxiety, requiring the clinician to adapt their symptomatology probing techniques. Second, refined measurement of DUP may afford a more refined understanding of symptom emergence (e.g., from low- to high- to full-threshold psychosis), which would allow for more individualized and efficacious dialogue. Finally, to the extent that a better understanding of DUP is related to severity of outcomes, it is the case that the refined measurement of DUP would impact treatment protocols earlier in the process, thus providing the appropriate levels of treatment to the affected individual sooner in the process. Again, these are translational aspects of the current study based on the results as observed. Given the implications of any of the examples provided, it is of importance that research into the measurement of DUP continue with independent and notably larger samples to confirm the findings.

Future Directions

Validation of the SIPS-DUP Interview as an acceptable measure of DUP may also benefit from several improvements. First, it is critical that future studies obtain sample sizes large enough to conduct traditional hypothesis testing that can elicit more reliable results. Likewise, more diverse samples along the full continuum of care (e.g., inpatient hospitalization, partial hospitalization, outpatient treatment, etc.) and in various geographical and cultural areas may help clarify whether the SIPS-DUP is applicable beyond the current study's context. To this end, it may also be useful for future studies to integrate the SIPS-DUP Interview into routine clinical care instead of voluntary research, as the latter may lead to self-selection biases.

Additionally, future SIPS-DUP Interview studies may also be improved through a more standardized outcome administration schedule. Although duration of treatment did not significantly impact most findings in the current study, the variability may make it difficult to ascertain exactly when relations between DUP and outcomes begin to form. Further, longitudinal assessment may help the field understand how these variables relate to one another at treatment onset and whether these relations change as a result of treatment. It will also be important for future studies using the SIPS-DUP Interview to use measures that are specific to the intended constructs. The current study's use of the BPRS total score as a proxy for positive symptom severity may have resulted in Type II error, considering that some items may not necessarily map onto the positive symptom experience. If possible, use of multiple types of negative and positive symptom outcome measures may help researchers understand specifically what relations might exist between DUP and symptoms at the individual item level. Additionally, integration of multiple types of DUP measure could also help determine the relation between SIPS-DUP assessed DUP and other tools capturing DUP, providing a measure of convergent validity.

Appendix A

Rationale for using the Structured Interview for Psychosis-Risk Syndromes (SIPS) to track psychosis onset

Measuring the duration of untreated psychosis (DUP) among FEP clients is essential to EIP efforts. Despite the obvious need and importance, the field has not come to a consensus as to how to measure DUP. Additionally, understanding symptom development during the CHR phase may lead to more effective interventions at the earliest stages of illness. To track both psychosis onset, as well as risk symptoms, it seems logical to use one comprehensive tool designed to be sensitive to at-risk phases of illness as well as psychosis onset.

The Structured Interview for Psychosis-Risk Syndromes (SIPS) is an assessment tool designed to screen individuals for attenuated positive symptoms that are characteristic of the CHR population, while also distinguishing between those at CHR from those with diagnosable psychosis. The SIPS assesses five positive symptom categories rated on a scale ranging from symptom absence (0) to psychotic intensity symptoms (6), with scores from 3 to 5 falling in the at-risk range. The following psychosis symptoms are included in the SIPS: 1) unusual thought content/delusional ideas, 2) suspiciousness or persecutory ideas, 3) grandiose ideas, 4) perceptual abnormalities/hallucinations, and 5) disorganized communication. These symptoms map on to hallmark characteristics of psychosis that are evaluated by other commonly used assessment tools in the field, making it an appealing option to integrate both CHR and FEP efforts.

The SIPS guides clinicians in making distinctions between attenuated and psychotic intensity symptoms by outlining clear criteria for diagnosis and providing specific probes and anchors to thoroughly assess and rate symptoms. A rating of "psychotic" on the SIPS refers to "severe" symptoms, clearly present, accompanied by conviction and functional interference, critical components of true psychosis. Conviction is defined as a belief that the symptom is real (with no doubt), at least intermittently, and functional interference is defined as persistent interference in thinking, feeling, social relations or behavior since symptom onset. In addition to these criteria, a diagnosis of psychosis requires that one (or more) psychotic intensity symptom was either seriously disorganizing/dangerous or occurred regularly over a one month period (i.e. at least 1 hour per day at an average frequency of 4 days per week). Applying these same criteria for psychosis across CHR and FEP populations will allow for a standardized definition of onset, helping to maximize consistency in tracking symptom progression and course of illness.

We created the following SIPS-derived tools to help facilitate DUP identification:

- SIPS PSYCHOSIS IDENTIFICATION: CLINICIAN INSTRUCTIONS. Contains directions for clinicians using the SIPS Psychosis Identification tools to assess DUP for clients entering the FEP clinic.
- 2) SIPS PSYCHOSIS IDENTIFICATION: PROBE WORKSHEET. Contains specific probes from the SIPS along with follow-up probes that allow for the determination as to whether a positive endorsement meets criteria for psychosis. Likely used when the client is new to the assessor and a comprehensive gathering of information is required.
- 3) SIPS PSYCHOSIS IDENTIFICATION: ASSESSMENT TOOL. Contains the SIPS definition of attenuated and full threshold psychosis, as well as SIPS derived anchors for symptom severity, frequency anchors, and probes for symptom onset. Likely used to document psychosis onset and attenuated symptom onset (optional).
- DUP INTERVIEW. Contains symptom information that was captured from the above two tools. Probes specifically about treatment and is used to identify the onset of treatment.

SIPS PSYCHOSIS IDENTIFICATION: CLINICIAN INSTRUCTIONS

The following instructions are intended to guide clinicians in using the SIPS Psychosis

Identification Assessment Tool and Probe Worksheet to determine the duration of untreated psychosis (DUP) and complete the DUP Interview form.

The Assessment Tool is the primary form to be used for evaluating and summarizing

psychotic symptoms using SIPS criteria to determine duration of untreated psychosis (DUP). This form briefly describes the experiences and behaviors captured by each of the five positive symptoms included in the SIPS (P1: unusual thought content/delusional ideas, P2: suspiciousness/persecutory ideas, P3: grandiosity, P4: perceptual abnormalities, and P5: disorganized communication). P1-P5 should be rated on a scale from 0 (absent) to 6 (severe/psychotic) according to the anchors provided for each symptom category.

A score "0", "1", or "2" indicates that the symptom is either absent (0), or insignificant/inconsequential (1: questionably present, or 2: mild).
A score of "3", "4", or "5" indicates that the symptom is present in an attenuated form. These psychosis-risk scores indicate that the symptom is recurrent, and noticed by the individual (likely causing some impairment), but doubt as to whether the symptom is real remains intact (or can be induced).
A score of "6" indicates that the symptom is "severe/psychotic", meaning that it is clearly present and accompanied by conviction and functional interference. Conviction is a belief that the symptom is real (with no doubt), at least intermittently. Functional interference is persistent interference in thinking, feeling, social relations or behavior since symptom onset.
A "psychotic" rating (6) on one or more positive symptoms indicates psychosis if the symptoms were either A) seriously disorganizing or dangerous, or B) occurred for at least 1 hour per day at an average frequency of 4 days per week over 1

month. If criteria for psychosis is met, the date that the symptom first met criteria should be recorded.

The Probe Worksheet can be used in conjunction with the assessment tool and includes specific probes to evaluate each of the SIPS positive symptoms. The probe worksheet helps to guide the clinician in thoroughly evaluating P1-P5 and is especially helpful if limited clinical knowledge is available for the client (e.g., those new to our system). Specific criteria for psychosis are included for each probe and should be evaluated for all symptoms of psychotic intensity. For all symptoms indicating psychosis, record the earliest date that symptom met criteria for psychosis. Of all the symptoms that have ever met criteria for psychosis, record the *earliest* psychosis onset date as well as the earliest date that symptom was present in an attenuated form.

Directions for use: When evaluating new clients who were not previously assessed at the high-risk clinic, clinicians should conduct an interview utilizing the full probe worksheet in order to complete the assessment form. If a client is referred from the high-risk clinic, previous assessment information from the SIPS may be used to determine date of onset for attenuated symptoms. The pre-collected SIPS information can also be used to guide

clinicians in assessing symptoms previously endorsed by the client. In this case, it may not be necessary to rely on the probe worksheet to guide the interview, instead, the clinician can assess only relevant symptoms.

SIPS PSYCHOSIS IDENTIFICATION: PROBE WORKSHEET

P. POSITIVE SYMPTOMS

Present: Check if symptom is endorsed at an attenuated or psychotic level of intensity either currently or at any point in the past.

Psychotic Intensity: Indicates that the symptom is or was present and accompanied by conviction and interference.

Conviction: Belief that the symptom is real (with no doubt) at least intermittently.

Interference: Symptom interferes persistently with thinking, feeling (e.g., causes distress), social relations, and/or behavior.

Disorganizing or Dangerous or Frequent: Symptom is/was ever seriously disorganizing or dangerous *OR* symptom meets frequency criteria for psychosis (symptom occurrence of at least 1 hour/day at an average frequency of 4 days/week over 1 month).

Frequency: Record minutes/hours per day, days per week, weeks per month, at highest frequency. Psychosis Onset Date: Earliest date psychotic symptom became 1) disorganizing/dangerous *OR* 2) met psychosis frequency criteria.

<u>P. 1. UNUSUAL THOUGHTS/DELUSIONAL IDEAS</u>		Psychotic Intensity		Disorganizing or Dangerous or Frequent		Frequency	Psychosis Onset Date
1.1. Have you had the feeling that something odd is going on or that something is wrong that you can't explain?		Y	N	Y	N		
1.2. Have you ever been confused at times whether something you have experienced is real or imaginary?		Y	N	Y	N		
1.3. Do familiar people or surroundings ever seem strange? Confusing? Unreal? Not a part of the living world? Alien? Inhuman? Evil?		Y	N	Y	N		
1.4. Does your experience of time seem to have changed? Unnaturally faster or slower?		Y	N	Y	N		
1.5. Have you felt that you are not in control of your own ideas or thoughts?		Y	N	Y	N		
1.6. Do you ever feel as if your thoughts are being said out loud so that other people can hear them?		Y	N	Y	N		
1.7. Do you ever think that people might be able to read your mind?		Y	N	Y	N		
1.8. Do you ever think that you can read other people's minds?		Y	N	Y	N		
1.9. Do you ever feel the radio or TV is communicating directly to you?		Y	N	Y	N		
1.10. Do you have strong feelings or beliefs that are very important to you, about such things as religion, philosophy, or politics?		Y	N	Y	N		

P. 1. UNUSUAL THOUGHTS/DELUSIONAL IDEAS F	Present	Psyc Inter	hotic 1sity	Disorga or Dan or Fre	unizing gerous quent	Frequency	Psychosis Onset Date
1.11. Do you daydream a lot or find yourself preoccupied with stories, fantasies, or ideas? Do you ever feel confused about whether something is your imagination or real?		Y	N	Y	N		
1.12. Do other people tell you that your ideas or beliefs are unusual or bizarre? If so, what are these ideas or beliefs?		Y	N	Y	N		
1.13. Do you ever feel you can predict the future?		Y	N	Y	N		
1.14. Do you ever worry that something might be wrong with your body or your health?		Y	N	Y	N		
1.15. Have you ever felt that you might not actually exist? Do you ever think that the world might not exist?		Y	N	Y	N		
<u>P. 2. SUSPICIOUSNESS/PERSECUTORY</u> IDEAS							
2.1. Do you ever feel that people around you are thinking about you in a negative way? Have you ever found out later that this was not true or that your suspicions were unfounded?		Y	N	Y	N		
2.2. Have you ever found yourself feeling mistrustful or suspicious of other people?		Y	N	Y	N		
2.3. Do you ever feel that you have to pay close attention to what's going on around you in order to feel safe?		Y	N	Y	N		
2.4. Do you ever feel like you are being singled out or watched?		Y	N	Y	N		
2.5. Do you ever feel people might be intending to harm you?Do you have a sense of who that might be?		Y	N	Y	N		
P. 3. GRANDIOSE IDEAS				1			1
3.1. Do you feel you have special gifts or talents? Do you feel as if you are unusually gifted in any particular area? Do you talk about your gifts with other people?		Y	N	Y	N		

Running Head: PRELIMINARY EVIDENCE OF A NEW MEASURE

P. 4. PERCEPTUAL ABNORMALITIES/HALLUCINATIONS Present	Psyc Inte	hotic nsity	Disorg or Dan or Fre	anizing gerous equent	Frequency	Psychosis Onset Date
4.1. Do you ever feel that your mind is playing tricks on you?	Y	N	Y	N		
4.2. Do you ever think you hear sounds and then realize that there is probably nothing there?	Y	N	Y	N		
4.3. Do you ever hear your own thoughts as if they are being spoken outside your head?	Y	N	Y	N		
4.4. Do you ever hear a voice that others don't seem to or can't hear? Does it sound clearly like a voice speaking to you as I am now? Could it be your own thoughts or is it clearly a voice speaking out loud?	Y	N	Y	N		
4.5. Have you ever seen unusual things like flashes, flames, vague figures or shadows out of the corner of your eye?	Y	N	Y	N		
4.6. Do you ever see things that others can't or don't seem to see?	Y	N	Y	N		
4.7. Have you noticed any unusual bodily sensations such as tingling, pulling, pressure, aches, burning, cold, numbness, vibrations, electricity, or pain?	Y	N	Y	N		
4.8. Do you ever smell or taste things that other people don't notice?	Y	N	Y	N		
P. 5. DISORGANIZED COMMUNICATION						
5.1. Do people ever tell you that they can't understand you? Do people ever seem to have difficulty understanding you?	Y	N	Y	N		
5.2. Are you aware of any ongoing difficulties getting your point across, such as finding yourself rambling or going off track when you talk?	Y	N	Y	N		

Summary:

S1a. Record the earliest psychosis onset date:

S1b. Indicate which symptom first met criteria for psychosis by recording the corresponding question number and provide a brief description of the symptom:

 After identifying the earliest psychosis onset date, probe further to pinpoint the earliest date that symptom occurred at an attenuated level (i.e. it was distressing or interfering, but would not meet criteria for psychosis because it was less frequent or present without conviction).

S2a. Attenuated symptom onset date: _____

S2b. Provide a brief description of the attenuated symptom:

SIPS PSYCHOSIS IDENTIFICATION: ASSESSMENT TOOL

Rate the most severe experience endorsed for each symptom domain. Psychotic Intensity (rating of 6): Indicates that the symptom is/was present with conviction and interference.

Conviction: Belief that the symptom is real (with no doubt) at least intermittently.

Interference: Symptom interferes persistently with thinking, feeling (e.g., causes distress), social relations, and/or behavior.

For each symptom rated psychotic (6), assess the following psychosis criteria:

Disorganizing/Dangerous: Is the symptom seriously disorganizing or dangerous, or was it ever in the past?

Frequency: Has the symptom occurred for at least 1 hour/day at an average frequency of 4 days/week for 1 month?

If a psychotic symptom has ever met either of the above psychosis criteria, psychosis onset should be recorded.

Date of Psychosis Onset: What is the earliest date that the symptom met psychosis criteria? If possible, for each symptom domain that meets criteria for psychosis, pinpoint the earliest date that symptom occurred at an attenuated level. Use the anchors provided to evaluate attenuated symptoms. Note: symptoms of psychotic intensity (rated 6) that do not meet criteria for psychosis (e.g., symptoms that are less frequent and not seriously disorganizing or dangerous) should be considered attenuated symptoms.

P. 1. UNUSUAL THOUGHT CONTENT/DELUSIONAL IDEAS

a. Perplexity and delusional mood. Mind tricks, such as a sense that something odd is going on or puzzlement and

confusion about what is real or imaginary. Familiar feels strange, confusing, ominous, threatening, or has special

meaning. Sense that self, others, the world have changed. Changes in perception of time, déjà vu experience.

b. Non-persecutory ideas of reference.

c. First rank phenomenology. Mental events such as thought

insertion/interference/withdrawal/broadcasting/

telepathy/external control/radio and TV messages.

d. Overvalued beliefs. Preoccupation with unusually valued ideas (religion, meditation, philosophy, existential

themes). Magical thinking that influences behavior and is inconsistent with subculture norms (e.g., being

superstitious, belief in clairvoyance, uncommon religious beliefs).

e. Unusual ideas about the body, guilt, nihilism, jealousy and religion. Delusions may be present but are not well

organized and not tenaciously held.

Rate the individual's most severe rating:

0	1	2	3	4	5	6
Absent	Questionably	Mild	Moderate	Moderately	Severe but Not	Severe and
	Present			Severe	Psychotic	Psychotic
	"Mind tricks" that	Overly interested	Unanticipated	Sense that ideas/	Experiences	Delusional
	are puzzling.	in fantasy life.	mental events that	experience/	familiar,	conviction (with
	Sense that	Unusually valued	are puzzling,	beliefs may be	anticipated.	no doubt) at least
	something is	ideas/ beliefs.	unwilled, but not	coming from	Doubt can be	intermittently.
	different.	Some	easily ignored.	outside oneself or	induced by	Interferes
		superstitions	Experiences seem	that they may be	contrary evidence	persistently with
		beyond what	meaningful	real, but doubt	and others'	thinking, feeling,
		might be	because they will	remains intact.	opinions.	social relations,
		expected by the	recur and will not	Distracting,	Distressingly real.	and/or behavior.
		average person	go away.	bothersome. May	Affects daily	
		but within	Functions mostly	affect	functioning.	
		cultural norms.	as usual.	functioning.		

Most severe rating: _____ Date of most severe rating: _____

Rating based on (provide brief description):_____

Frequency of symptom: $\Box \ge 1$ h/d, ≥ 4 d/wk, ≥ 1 x/mo; $\Box \ge$ several minutes/d, ≥ 1 x/mo; $\Box \ge 1$ x/wk in past mo; \Box none

If ever rated "6": a) Disorganizing/Dangerous? Yes No b) Frequency $\geq 1 \text{ h/d}$, $\geq 4 \text{d/wk}$ over 1 month? Yes No

c) Date of Psychosis Onset (date that criterion a or b was first achieved):

P. 2. SUSPICIOUSNESS/PERSECUTORY IDEAS

- a. Persecutory ideas of reference.
- b. Suspiciousness or paranoid thinking.

c. Presents a guarded or even openly distrustful attitude that may reflect delusional conviction and intrude on the

interview and/or behavior.

Rate the individual's current symptom severity as well as the most severe past rating:

0	1	2	3	4	5	6
Absent	Questionably	Mild	Moderate	Moderately	Severe but Not	Severe and
	Present			Severe	Psychotic	Psychotic
	Wariness.	Concerns about	Concerns that	Thoughts of	Beliefs about	Delusional
		safety.	people are	being the object	danger from	paranoid
		Hypervigilance	untrustworthy	of negative	hostile intentions	conviction (no
		without clear	and/or may	attention. Sense	of others.	doubt) at least
		source of danger.	harbor ill will.	that people may	Skepticism and	intermittently.
			Sense of unease	wish harm. Self-	perspective can	Frightened,
			and need for	generated	prevail with non-	avoidant,
			vigilance (often	skepticism	confirming	watchful.
			unfocused).	present. Pre-	evidence or	Interferes
			Mistrustful.	occupying,	other's opinion.	persistently with
			Recurrent (yet	distressing. May	Anxious,	thinking, feeling,
			unfounded) sense	affect daily	unsettled. Daily	social relations,
			that people might	functioning. May	functioning	and/or behavior.
			be thinking or	appear defensive	affected. Guarded	
			saying negative	in response to	presentation may	
			things about	questioning.	diminish	
			person.		information	
					gathered in the	
					interview.	

Most severe rating: _____ Date of most severe rating: _____

Rating based on (provide brief description):_____

Frequency of symptom: $\Box \ge 1$ h/d, ≥ 4 d/wk, ≥ 1 x/mo; $\Box \ge$ several minutes/d, ≥ 1 x/mo; $\Box \ge 1$ x/wk in

past mo; □ none

If ever rated "6": a) Disorganizing/Dangerous? Yes No b) Frequency $\geq 1 \text{ h/d}$, $\geq 4 \text{d/wk}$ over 1 month? Yes No

c) Date of Psychosis Onset (date that criterion a or b was first achieved): _____

P. 3. GRANDIOSE IDEAS

- a. Exaggerated self-opinion and unrealistic sense of superiority.
- b. Some expansiveness or boastfulness.
- c. Occasional clear-cut grandiose delusions that can influence behavior.

Rate the individual's current symptom severity as well as the most severe past rating:

0	1	2	3	4	5	6
Absent	Questionably	Mild	Moderate	Moderately	Severe but Not	Severe and
	Present			Severe	Psychotic	Psychotic
	Private thoughts	Mostly private	Notions of being	Beliefs of talent,	Compelling	Delusions of
	of being better	thoughts of being	unusually gifted,	influence, and	beliefs of superior	grandiosity with
	than others.	talented,	powerful, or	abilities.	intellect,	conviction (no
		understanding or	special and have	Unrealistic goals	attractiveness,	doubt) at least
		gifted.	exaggerated	that may affect	power, or fame.	intermittently.
			expectations.	plans and	Skepticism and	Interferes
			May be expansive	functioning, but	modesty can only	persistently with
			but can redirect to	responsive to	be elicited by the	thinking, feeling,
			the everyday on	other's concerns	efforts of others.	social relations,
			own.	and limits.	Affects	or behavior.
					functioning.	

Most severe rating: _____ Date of most severe rating: _____

Rating based on (provide brief description):_____

Frequency of symptom: $\Box \ge 1 \text{ h/d}, \ge 4 \text{d/wk}, \ge 1 \text{x/mo}; \quad \Box \ge \text{several minutes/d}, \ge 1 \text{x/mo}; \quad \Box \ge 1 \text{ x/wk in past mo;} \quad \Box \text{ none}$

If ever rated "6": a) Disorganizing/Dangerous? Yes No b) Frequency $\geq 1 \text{ h/d}$, $\geq 4 \text{d/wk}$ over 1 month? Yes No

c) Date of Psychosis Onset (date that criterion a or b was first achieved): _____

P. 4. PERCEPTUAL ABNORMALITIES/HALLUCINATIONS

a. Unusual perceptual experiences. Heightened or dulled perceptions, vivid sensory experiences, distortions, illusions.

b. Pseudo-hallucinations or hallucinations into which the subject has insight (is aware of their abnormal nature.)

c. Occasional frank hallucinations that may minimally influence thinking or behavior.

		2	1			0
0	1	2	3	4	5	6
Absent	Questionably	Mild	Moderate	Moderately Severe	Severe but Not	Severe and Psychotic
	Present				Psychotic	
	Minor, but	Unformed	Recurrent,	Illusions or	Hallucinations	Hallucinations
	noticeable	perceptual	unformed,	momentary formed	experienced as	perceived as real and
	perceptual	experiences/	images (e.g.,	hallucinations that	external to self	distinct from the
	sensitivity	changes that	shadows, trails,	are ultimately	though skepticism	person's thoughts.
	(e.g.	are noticed	sounds, etc.),	recognized as	can be induced by	Skepticism cannot be
	heightened,	but are not	illusions, or	unreal yet can be	others.	induced. Captures
	dulled,	considered to	persistent	distracting, curious,	Mesmerizing,	attention, frightening.
	distorted, etc.).	be significant.	perceptual	unsettling. May	distressing. Affects	Interferes persistently
			distortions that	affect functioning.	daily functioning.	with thinking, feeling,
			are puzzling			social relations, and/or
			and			behavior.
			experienced as			
			usual.			

Rate the individual's current symptom severity as well as the most severe past rating:

Most severe rating: _____ Date of most severe rating: _____

Rating based on (provide brief description):_____

Frequency of symptom: $\Box \ge 1 \text{ h/d}, \ge 4 \text{d/wk}, \ge 1 \text{x/mo}; \quad \Box \ge \text{several minutes/d}, \ge 1 \text{x/mo}; \quad \Box \ge 1 \text{ x/wk in past mo;} \quad \Box \text{ none}$

If ever rated "6": a) Disorganizing/Dangerous? Yes No b) Frequency $\geq 1 \text{ h/d}$, $\geq 4 \text{d/wk}$ over 1 month? Yes No

c) Date of Psychosis Onset (date that criterion a or b was first achieved): ____
P. 5. DISORGANIZED COMMUNICATION

a. Odd speech. Vague, metaphorical overelaborate, stereotyped.

b. Confused, muddled, racing or slowed down speech, using the wrong words, talking about things irrelevant to

context or going off track.

c. Speech is circumstantial, tangential or paralogical. There is some difficulty in directing sentences toward a goal.

d. Loosening or paralysis (blocking) of associations may be present and make speech hard to follow or unintelligible.

Rate	the	ind	ivi	dua	l's	current	svm	ptom	severit	v as	well	as	the	most	sev	vere	past r	ating:
							~			J								

0	1	2	3	4	5	6
Absent	Absent Questionably		Moderate	Moderately	Severe but Not	Severe and
	Present			Severe	Psychotic	Psychotic
	Occasional word	Speech is slightly	Incorrect words,	Speech is clearly	Speech tangential	Communication
	or phrases doesn't	vague, muddled,	irrelevant topics.	circumstantial	(i.e. never getting	persistently loose,
	make sense.	overelaborate or	Goes off track,	(i.e. eventually	to the point).	irrelevant or
		stereotyped.	but redirects on	getting to the	Some loosening	blocked and
			own.	point). Difficulty	of associations or	unintelligible
				in directing	blocking. Can	when under
				sentences toward	reorient briefly	minimal pressure
				a goal. Sudden	with frequent	or when the
				pauses. Can be	prompts or	content of the
				redirected with	questions.	communication is
				occasional		complex. Not
				questions and		responsive to
				structuring.		structuring of the
						interview.

Most severe rating: _____ Date of most severe rating: _____

Rating based on (provide brief description):_____

Frequency of symptom: $\Box \ge 1 \text{ h/d}, \ge 4 \text{d/wk}, \ge 1 \text{x/mo}; \quad \Box \ge \text{several minutes/d}, \ge 1 \text{x/mo}; \quad \Box \ge 1 \text{ x/wk in past mo;} \quad \Box \text{ none}$

If ever rated "6": a) Disorganizing/Dangerous? Yes No b) Frequency $\geq 1 \text{ h/d}$, $\geq 4 \text{d/wk}$ over 1 month? Yes No

c) Date of Psychosis Onset (date that criterion a or b was first achieved):

Date symptom first met attenuated criteria (score \geq 3 but not meeting psychosis criteria):

DUP INTERVIEW

This form should be completed using symptom information obtained on the SIPS Psychosis Identification Assessment Tool and Probe Worksheet

Patient Name: _____, _____,

Date of Intake: ____/ ___/ ____/

PLEASE USE EITHER AGE OR DATE IN ALL ITEMS ON THIS FORM

1. <u>Psychosis onset interview</u> (All dates or ages should be accurate to the <u>week</u> if possible. If not, the month or year.)

Complete items 1a-1b using items S1a and S2a from the SIPS Psychosis Identification Assessment Tool

Using the earliest date reported, indicate the dates of onset and the associated symptoms

Onset of		Date		Age ^b	Base (Based on Symptom Category (check all that apply)				
	Month	Day ^a	Year		P1	P2	P3	P4	P5	
1a Psychosis										
1b Attenuated										
Symptom										

When did the following occur:	Month	Day ^a	Year	Age ^b
1c. First time family or others				
observed a symptom of psychosis				
1d. First ER visit/hospitalization for				
behavior problem				
1e. First seen for mental health care				
for symptoms of psychosis				
(regardless of treatment given)				

Specify:

Yes No Psychotic symptoms are better explained by another disorder or condition (use information obtained through diagnostic interviews and/or other assessment to verify).

If yes, symptoms are better explained by:

2. <u>Treatment onset</u> (All dates or ages should be accurate to the <u>week</u> if possible. If not, the month or year.)

When did the following occur:	Month	Day ^a	Year	Age ^b
2a. First dose of antipsychotics given				
2b. First completed a course of antipsychotics				
treatment for 1 month or more				
2c. First visit for mental health issues				
(including therapy, counseling, primary care).				
Specify issue:				
2d. First given non-medication treatment				
(therapy, counseling, alternative medicine)				
2e. First non-antipsychotic but psychotropic				
medication given				

a. Estimate the day within a week if possible. If day is not available, enter 99

b. Only use age if month and year are unknown.

DUP Evaluation Instructions:

Duration of untreated psychosis (DUP) is defined by the weeks between <u>psychosis onset</u> (item 1a) and the time <u>adequate initial treatment</u> has been given as defined by the first completed antipsychotics therapy for 1 month or more (item 2b).

From		MM	DD	YY	AGE
Item 1b					
Item 2b	-				
DUP	=				

3. <u>DUP</u> (in weeks) _____

Note: When sufficient information is not available for accurate date of psychosis onset or date of adequate treatment, briefly state below the information used to estimate the DUP.

<u>Psychosis onset</u> is defined as the date at which one (or more) positive symptom first reached psychotic intensity *and* was either seriously disorganizing/dangerous *or* occurred regularly over a one month period as defined by the Structured Interview for Psychosis-Risk Syndromes (SIPS). These determinations can be facilitated by accompanying worksheets (SIPS Psychosis Identification Assessment Tool and Probe Worksheet plus instructions).

- Psychosis is defined by having at least one of five positive symptoms: unusual thought content/delusional ideas, suspiciousness or persecutory ideas, grandiose ideas, perceptual abnormalities/hallucinations, or disorganized communication.
- A rating of "psychotic" on the SIPS refers to "severe" symptoms, clearly present, plus conviction and functional interference.
 - Conviction is defined as a belief that the symptom is real (with no doubt), at least intermittently.
 - Functional interference is defined as persistent interference in thinking, feeling (e.g., causes distress), social relations or behavior since symptom onset.
- A "psychotic" rating on one or more positive symptoms indicates psychosis if the symptoms were *either* A) seriously disorganizing or dangerous, *or* B) occurred for at least 1 hour per day at an average frequency of 4 days per week over 1 month.
- Multiple sources from patients, relatives, schools, and clinical records can be used for the assessment.

Appendix B

SANS (Scale for the Assessment of Negative Symptoms)

Form Version:

AFFECTIVE FLATTENING OR BLUNTING

Affective flattening or blunting manifests itself as a characteristic impoverishment of emotional expression, reactivity, and feeling. Affective flattening can be evaluated by observation of the patient's behavior and responsiveness during a routine interview. The rating of some items may be affected by drugs, since the Parkinsonian side-effects of phenothiazines may lead to mask-like faces and diminished associated movements. Other aspects of affect, such as responsivity or appropriateness, will not be affected, however.

1. Unchanging Facial Expression

The patient's face appears wooden, mechanical, frozen. It does not change expression, or changes less than normally expected, as the emotional content of discourse changes. Since phenothiazines may partially mimic this effect, the interviewer should be careful to note whether or not the patient is on medication, but should not try to "correct" his/her rating accordingly. Additionally, many patients may have initial anxiety about being interviewed and may therefore act in a "formal" manner during the beginning of the interview. Therefore, when rating facial expression, more emphasis should be given to the subject's facial expressiveness after he/she has had a chance to "warm up" to the interview. For subjects who still have decreased facial expressiveness after an appropriate "warm up" period, the interviewer should prompt the subject by smiling or telling a joke to see if the patient responds.

- 0 =Not at all. Patient is normal or labile.
- 1 =Questionable decrease.
- 2 = Mild. Slight decrease in the range of facial expression during the interview.
- 3 = Moderate. Range of facial expression is definitely restricted but there is some spontaneous expressiveness during the interview.
- 4 = Marked. Facial expression is wooden and/or unchanging except in response to prompting.
- 5 = Severe. Facial expression is wooden throughout the entire interview even when prompted.
- 2. _____ Decreased Spontaneous Movements

The patient shows few or no spontaneous movements, does not shift position, move extremities, etc.

- 0 =Not at all. Patient moves normally or is overactive.
- 1 = Questionable decrease.
- 2 = Mild. Some decrease in spontaneous movements.
- 3 = Moderate. Significant decrease in spontaneous movements.
- 4 = Marked. Movements are markedly decreased.
- 5 = Severe. Patients sits immobile throughout the interview.
- 3. _____ Paucity of Expressive Gestures

The patient does not use his/her body as an aid in expressing his/her ideas through such means as hand gestures, sitting forward in his/her chair when intent on a subject, leaning back when relaxed, etc. This may occur in addition to decreased spontaneous movements.

- 0 = Not at all. Patient uses expressive gestures normally or excessively.
- 1 =Questionable decrease.
- 2 = Mild. Uses expressive gestures but is less animated than appropriate for interview situation.
- 3 = Moderate. Uses expressive gestures sometimes but is noticeably less animated than appropriate for the interview situation.
- 4 = Marked. Patient very infrequently uses his/her body as an aid in expression.
- 5 = Severe. Patient never uses his/her body as an aid in expression.

4. ____ Poor Eye Contact

When speaking or listening, the patient avoids looking at the interviewer. He/she does not use eye contact to facilitate communication with the interviewer. Do not rate for periods when the patient looks away to compose his/her thoughts.

0 = Not at all. Good eye contact and expression.

- 1 = Questionable decrease.
- 2 = Mild. When speaking or listening, the patient overall maintains eye contact with the interviewer but does look away during
 - the interview for brief periods of time.
- 3 = Moderate. Patient fails to make eye contact with the interviewer to the extent that communication between the patient and interviewer seems reduced.
- 4 = Marked. Patient does not make eye contact with the interviewer for most of the interview.
- 5 = Severe. Patient orients himself/herself away from the interviewer for most or all of the interview.
- 5. _____ Affective Non-Responsivity

The patient fails to smile or laugh when prompted.

- 0 = Not at all.
- 1 =Questionable lack of responsivity.
- 2 = Mild. Slight but definite lack in responsivity.
- 3 = Moderate. Moderate decrease in responsivity.
- 4 = Marked. Marked decrease in responsivity.
- 5 = Severe. Patient essentially unresponsive, even on prompting.

6. Lack of Vocal Inflections

While speaking the patient fails to show normal vocal emphasis patterns. Speech has a monotonous quality, and important words are not emphasized through changes in pitch or volume. Patient also may fail to change volume with changes of subject so that he does not drop his voice when discussing private topics or raise it as he discusses things which are exciting or for which louder speech might be appropriate.

- 0 = Not at all. Normal vocal inflections.
- 1 = Questionable decrease.
- 2 = Mild. Slight decrease in range of vocal inflections.
- 3 = Moderate. Definite decrease in range of vocal inflections although subject has some spontaneous change in inflection.
- 4 = Marked. Most of speech during interview is in a monotone.
- 5 = Severe. Virtually all speech during interview is in a monotone.
- 7. _____ Global Rating of Affective Flattening

The global rating should focus on overall severity of affective flattening or blunting. Special emphasis should be given to such core features as lack of expression and overall decrease in emotional intensity.

- 0 = No flattening. Normal affect.
- 1 = Questionable affective flattening.
- 2 = Mild affective flattening.
- 3 = Moderate affective flattening.
- 4 = Marked affective flattening.
- 5 = Severe affective flattening.

ALOGIA

Alogia is a general term coined to refer to the impoverished thinking and cognition that often occur in patients with schizophrenia (Greek a = no, non; logos = mind, thought). Patients with alogia have thinking processes that seem empty, turgid, or slow. Since thinking cannot be observed directly, it is inferred from the patient's speech. The two major manifestations of alogia are nonfluent empty speech (poverty of speech) and fluent empty speech (poverty of content of speech). Blocking and increased latency of response may also reflect alogia.

8. _____ Poverty of Speech

Restriction in the amount of spontaneous speech, so that replies to questions tend to be brief, concrete, and unelaborated. Unprompted additional information is rarely provided. For example, in answer to the question, "How many children to you have", the patient replies, "Two. A girl and a boy. The girl is 13 and the boy is 10." "Two" is all that is required to answer the question, and the rest of the reply is additional information. Replies may be monosyllabic, and some of the questions may be left unanswered altogether. When confronted with this speech pattern, the interviewer may find himself/herself frequently prompting the patient in order to encourage elaboration of replies. To elicit this finding, the examiner must allow the patient adequate time to answer and to elaborate his answer.

- 0 = No poverty of speech. A substantial and appropriate number of replies to questions include additional information.
- 1 = Questionable poverty of speech.
- 2 = Slight poverty of speech. Occasional replies do not include elaborated information even though this is appropriate.
- 3 = Moderate poverty of speech. Some replies do not include appropriately elaborated information, and many replies are monosyllabic or very brief ("Yes." "No." "Maybe." "Don't know." "Last week.").
- 4 = Marked poverty of speech. Answers are rarely more than a few words in length.
- 5 = Severe poverty of speech. Patient says very little and occasionally fails to answer questions.
- 9. <u>NA</u> Poverty of Content of Speech (Do not use)

<u>Although the subject's replies are long enough, they convey little information.</u> Speech may be nebulous, overabstract, overconcrete or repetitive. The interviewer may find that the patient has spoken at some length but has not given adequate information to answer the question. Alternatively, the patient may provide enough information, but require many words to do so, so that a lengthy reply can be summarized in a sentence or two. Sometimes the interviewer may characterize the speech as "empty philosophizing."

Exclusions: This finding differs from circumstantiality in that the circumstantial patient tends to

provide a wealth of detail.

- 0 = No poverty of content of speech.
- 1 = Questionable poverty of content of speech.
- 2 = Mild poverty of content of speech. Occasional replies are too vague to be comprehensible or can be markedly condensed.
- 3 = Moderate poverty of content of speech. Replies which are vague or can be markedly condensed make up at least a 1/4 of the interview.
- 4 = Marked poverty of content of speech. At least half of the patient's speech is composed of vague or incomprehensible replies.
- 5 = Severe poverty of contact of speech. Nearly all the patient's speech is vague, incomprehensible, or can be markedly condensed.
- 10. Blocking

Interruption of a train of speech before a thought or idea has completed. After a period of silence which may last from a few seconds to minutes, the person indicates that he/she cannot recall what he had been saying or meant to say. Blocking should only be judged to be present if a person voluntarily describes losing his/her thought or if upon questioning by the interviewer the person indicates that that was hi/her reason for pausing.

0 = No blocking.

- 1 =Questionable decrease.
- 2 = Mild blocking. A single instance noted during a 15 minute period.
- 3 = Moderate blocking. Occurs twice during 15 minutes.
- 4 = Marked blocking. Occurs three times during 15 minutes.
- 5 = Severe blocking. Occurs more than three times.
- 11. Increased Latency of Response

The patient takes a longer time to reply to questions than is usually considered normal. He/she may seem "distant" and sometimes the examiner may wonder if he/she has even heard the question. Upon questioning by the interviewer, the patient should indicate that he/she is aware of the question but is having difficulty in developing his/her thoughts.

- 0 = Not at all. Patient typically replies promptly.
- 1 =Questionable increase.
- 2 = Mild. Occasional brief pauses before replying.

3 = Moderate. Frequent brief pauses before replying or long pauses before replying to a third of questions.

4 = Marked. Long pauses before replying to half of questions.

5 = Severe. Long pauses prior to nearly all replies.

12. <u>Global Rating of Alogia</u>

Since the core features of alogia are poverty of speech and poverty of content, the global rating should place particular emphasis on these.

- 0 = No alogia.
- 1 =Questionable alogia.
- 2 = Mild. Mild but definite impoverishment in thinking.
- 3 = Moderate. Significant evidence for impoverished thinking.
- 4 = Marked. Patient's thinking seems impoverished much of the time.
- 5 = Severe. Patient's thinking seems impoverished nearly all the time.

AVOLITION-APATHY

Avolition manifests itself as a characteristic lack of energy, drive and interest. Patients are unable to mobilize themselves to initiate or persist in completing many different kinds of tasks. Unlike the diminished energy or interest of depression, the avolitional symptom complex in schizophrenia is usually not accompanied by saddened or expressed effect.

13. <u>Grooming and Hygiene</u>

The patient displays less attention to grooming and hygiene than normal. Clothing may appear sloppy, outdated, or soiled. Patient may bathe infrequently and not care for hair, nails, or teeth, leading to such manifestations as greasy or uncombed hair, dirty hands, body odor, or unclean teeth and bad breath. Overall, the appearance is dilapidated and disheveled. In extreme cases, the patient may even have poor toilet habits with soiling.

- 0 = No evidence of poor grooming and hygiene.
- 1 =Questionable decrease.

2 = Mild. Some slight but definite indication of inattention to appearance (e.g. hair not combed, rumpled clothing).

- 3 = Moderate. Appearance is somewhat disheveled (e.g. as above but more severe or clothes inappropriate or mismatched).
- 4 = Marked. Appearance is significantly disheveled (e.g. bathes infrequently, clothes soiled).
- 5 = Severe. Appearance is extremely disheveled (e.g. refused to bathe, clothes filthy, unfastened, or refuses to wear clothes).

ROLE FUNCTION

The patient may have difficulty fulfilling social role expectations (employment, school, homemaking) as appropriate for his or her age and cultural background.

In rating role functioning, one must consider both 1) the difficulty of the role that the patient is attempting to fulfill and 2) how well the patient is functioning within that role. Therefore, this item is rated in two parts. First, the degree to which the patient's current role is appropriate to his/her age and social and cultural background is rated. Next, the degree to which the patient fulfills that role is rated separately.

14. _____ Current Role Function - Level

Patient's current social/vocational level (Code 5 for inpatients)

0 = Age and socially appropriate role (full-time paid employment, matriculated in full-time school program NOT including psychiatric rehabilitation affiliated work or school programs, fulfills expectations of full-time homemaker, etc.).

1 = Questionable decrease.

- 2 = As above not full-time (part-time student, part-time paid employment, etc.)
- 3 = High-level psychiatric setting (high-level day program, vocational programs, etc.)
- 4 = Low-expectation psychiatric setting (e.g. social/recreational programs or undemanding training programs).

5 = Does not engage in any appropriate activities (no job, training program or therapeutic program) or is an inpatient.

15a. _____ Current Role Function – Quality – For Outpatients Only

Degree to which patient fulfills role noted above in item #14.

- 0 = Fulfills expectations of current role (as rated in previous item).
- 1 =Questionable decrease.
- 2 = Fulfills expectations of current role but with some difficulty (e.g. occasionally misses work, school or program without justifiable reason, occasionally fails to fulfill responsibilities.
- 3 = Has definite difficulty fulfilling role responsibilities (e.g. consistently fails to attend and/or participate appropriately in current role.
- 4 = Functioning at current role is seriously compromised and/or in danger of being dropped from current activity.
- 5 = Not functioning in role (Note: Patients given this rating should have been rated 5 on the item above).

15b. _____ Participation in Unit-Appropriate Activities – For Inpatients Only

Patients may have difficulty in attending and/or participating in assigned activities and general unit activities such as groups on the unit. Patients with mild impairment may attend activities but do not participate fully or do not complete assigned tasks. Patients with more severe impairment attend activities only with staff encouragement or not at all.

- 0 = Participates appropriately in unit activities.
- 1 = Questionable decrement in participation.
- 2 = Mild. Patient requires some encouragement to attend or maintain participation in activities.

4 = Marked. Patient needs activities less than half the time and/or participates minimally.

5 = Severe. Patient consistently fails to attend activities.

16. _____ Physical Anergia

The core concept is the extent to which the patient tests to be physically inactive given age-appropriate expectations of the general population. He/she may spend large amounts of time in physically inactive and mentally undemanding tasks such as watching TV. The family may report that he/she spends most of his/her time "doing nothing except sitting around." The patient may report an increased need to rest beyond that appropriate for his/her level of physical exertion. In sever cases, he/she may spend most or all of his/her time in bed.

0 = No evidence of physical anergia.

- 1 = Questionable physical anergia.
- 2 =Mild anergia. Spends slightly more time resting or in physically undemanding activities than expected given the patient's age.
- 3 = Moderate anergia. Spends a significant amount of time resting or in physically undemanding tasks.
- 4 = Marked anergia. Spends most of his/her time resting or in physically undemanding tasks.
- 5 = Severe anergia. Spends almost al of his/her time resting or in physically undemanding tasks.

17. _____ Global Rating of Avolition

The global rating should reflect the overall severity of the avolition symptoms, given expectations of outpatients.

0 = No avolition.

- 1 =Questionable avolition.
- 2 = Mild but definitely present.
- 3 = Moderate avolition.
- 4 = Marked avolition.
- 5 = Severe avolition.

ASOCIALITY-ANHEDONIA

18. _____ Asociality

The core features of asociality is a decrease in social interactions with others. Rate primarily on the basis of patient report. Patients with mild asociality may not initiate social contact with others but do respond to overtures by others. In more severe cases, patients avoid social contact with others.

- 0 = No evidence of lack of sociability.
- 1 =Questionable decrease.
- 2 = Mild. Reports some difficulty initiating social interactions but usually welcomes overtures by others.
- 3 = Moderate. Rarely initiates social activities but sometimes responds to overtures by others.

4 = Marked. Rarely initiates social activities; avoids being with others unless prodded by others.

5 = Severe. Avoids being with others whenever possible.

19. _____ Anhedonia

Patients with anhedonia have loss of interest in initiating pleasurable activities or, in more severe cases, lose the ability to experience pleasure when participating in activities normally considered pleasurable.

Psychiatric patients frequently have significant financial restraints on the recreational activities in which they may engage. These restrictions should be taken into account in rating anhedonia.

0=No evidence of anhedonia; seeks out pleasurable opportunities available to him/her and reports enjoyment of activities he/she engages in.

- 1 = Questionable decrease.
- 2 = Mild. Does not usually initiate pleasurable activities but often participates in what is offered and enjoys it.
- 3 = Moderate. Has to be encouraged to participate in pleasurable activities and/or sometimes does not enjoy otherwise pleasurable activities.
- 4 = Marked. Usually does not participate in activities and reports little enjoyment or activities.
- 5 = Severe. Reports total inability to enjoy activities.

20. _____ Decreased Sexual Interest and Activity

The patient may show a decrement in sexual interest and/or activity. Rate upon the basis of expressed interest and activities engaged by patient given the patient's environment and social and cultural background.

- 0 = No evidence of decreased sexual interest or activity.
- 1 = Questionable decrease.
- 2 = Mild. Reports some diminished interest in sex but does pursue some sexual activity.
- 3 = Moderate. Expresses interest in sex but little or no pursuit of sexual activity.
- 4 = Marked. Reports little interest in sex and does not pursue sexual activity.
- 5 = Severe. Reports no interest in sex and no sexual activity.
- 21. _____ Ability to Feel Intimacy and Closeness

The patient may be unable to form close and emotionally intimate relationships. The core feature to be rated is the degree to which patients can confide with others their feelings, goals, problems, or other important aspects of their lives. This should be distinguished from patients who may be superficially sociable without being close to others.

- 0 = Consistently maintains a close relationship with at least one family member/spouse and at least one person outside family.
- 1 =Questionable decrease.
- 2 = Mild. Consistently maintains a close relationship with either a family member or one person outside the family.
- 3 = Moderate. Sometimes is able to be close to a family member or someone outside the family.
- 4 = Marked. Rarely is able to be close to others.
- 5 = Severe. Has no close relationships with family or people outside the family.
- 22. _____ Global Rating of Asociality-Anhedonia

The global rating should reflect the overall severity of the asocial-anhedonic symptoms.

- 0 = No asociality-anhedonia.
- 1 = Questionable asociality-anhedonia.
- 2 = Mild asociality-anhedonia.
- 3 = Moderate associality-anhedonia.
- 4 = Marked asociality-anhedonia.
- 5 = Severe asociality-anhedonia.

Appendix C

MPRC BRIEF PSYCHIATRIC RATING SCALE ANCHORS

Introduce all questions with "During the past week have you..."

*Ratings based primarily upon verbal report.

- 1. SOMATIC CONCERN: Degree of concern over present bodily health. Rate the degree to which physical health is perceived as a problem by the patient, whether complaints have a realistic basis or not. Do not rate mere reporting of somatic symptoms. Rate only concern for (or worrying about) physical problems (real or imagined). Rate on the basis of reported (i.e., subjective) information pertaining to the past week.
 - 1 Not reported
 - 2 Very Mild: occasionally is somewhat concerned about body, symptoms, or physical illness
 - 3 Mild: occasionally is moderately concerned, or often is somewhat concerned
 - 4 Moderate: occasionally is very concerned, or often is moderately concerned
 - 5 Moderately Severe: often is very concerned
 - 6 Severe: is very concerned most of the time
 - 7 Very Severe: is very concerned nearly all of the time
 - 9 Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness; or not assessed
- 2. ANXIETY: Worry, fear, or over concern for present or future. Rate solely on the basis of verbal report of patients's own subjective experience pertaining to the past week. Do not infer anxiety from physical signs or from neurotic defense mechanisms. Do not rate if restricted to somatic concern. If anxious about a delusion, rate degree of anxiety on this item.
 - 1 Not reported
 - 2 Very Mild: occasionally feels somewhat anxious
 - 3 Mild: occasionally feels moderately anxious, or often feels somewhat anxious
 - 4 Moderate: occasionally feels very anxious, or often feels moderately anxious
 - 5 Moderately Severe: often feels very anxious
 - 6 Severe: feels very anxious most of the time
 - 7 Very Severe: feels very anxious nearly all of the time
 - 9 Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness; or not assessed
- 3. EMOTIONAL WITHDRAWAL: Deficiency in relating to the interviewer and to the interview situation. Overt manifestations of this deficiency include poor/absence of eye contact, failure to orient oneself physically toward the interviewer, and a general lack of involvement or engagement in the interview. Distinguish from BLUNTED AFFECT, in which deficits in facial expression,

body gesture, and voice pattern are scored. Rate on the basis of observations made during the interview.

- 1 Not observed
- 2 Very Mild: e.g., occasionally exhibits poor eye contact
- 3 Mild: e.g., as above, but more frequent
- 4 Moderate: e.g., exhibits little eye contact, but still seems engaged in the interview and is appropriately responsive to all questions
- 5 Moderately Severe: e.g., stares at floor or orients self away from interviewer, but still seems moderately engaged
- 6 Severe: e.g., as above, but more persistent or pervasive
- 7 Very Severe: e.g., appears "spacey" or "out of it" (total absence of emotional relatedness), and is disproportionately uninvolved or unengaged in the interview. (DO NOT SCORE IF EXPLAINED BY DISORIENTATION.)
- 4. CONCEPTUAL DISORGANIZATION: Degree of speech incomprehensibility. Include any type of formal thought disorder (e.g., loose associations, incoherence, flight of ideas, neologisms). DO NOT include mere circumstantiality or pressured speech, even if marked. DO NOT rate on the basis of the patient's subjective impressions (e.g., "my thoughts are racing. I can't hold a thought," "my thinking gets all mixed up"). Rate ONLY on the basis of observations made during the interview.
 - 1 Not observed
 - 2 Very Mild: e.g., somewhat vague, but of doubtful clinical significance
 - 3 Mild: e.g., frequently vague, but the interview is able to progress smoothly; occasional loosening of associations
 - 4 Moderate: e.g., occasional irrelevant statements, infrequent use of neologisms, or moderate loosening of associations
 - 5 Moderately Severe: as above, but more frequent
 - 6 Severe: formal thought disorder is present for most of the interview, and the interview is severely strained
 - 7 Very Severe: very little coherent information can be obtained
- 5. GUILT FEELINGS: Over concern or remorse for past behavior. Rate on the basis of the patient's subjective experiences of guilt as evidenced by verbal report pertaining to the past week. Do not infer guilt feelings from depression, anxiety or neurotic defenses.
 - 1 Not reported
 - 2 Very Mild: occasionally feels somewhat guilty
 - 3 Mild: occasionally feels moderately guilty, or often feels somewhat guilty
 - 4 Moderate: occasionally feels very guilty, or often feels moderately guilty
 - 5 Moderately Severe: often feels very guilty

- 6 Severe: feels very guilty most of the time, or encapsulated delusion of guilt
- 7 Very Severe: agonizing constant feelings of guilt, or pervasive delusion(s) of guilt

9 - Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness; or Not assessed

- 6. TENSION: Rate motor restlessness (agitation) observed during the interview. DO NOT rate on the basis of subjective experiences reported by the patient. Do not rate movements of tardive dyskinesia.
 - 1 Not observed
 - 2 Very Mild: e.g., occasionally fidgets
 - 3 Mild: e.g., frequently fidgets
 - 4 Moderate: e.g., constantly fidgets, or frequently fidgets, wrings hands and pulls clothing
 - 5 Moderately Severe: e.g., constantly fidgets, wrings hand and pulls clothing
 - 6 Severe: e.g., cannot remain seated (i.e., must pace)
 - 7 Very Severe: e.g., paces in a frantic manner
- 7. MANNERISMS AND POSTURING: Unusual and unnatural motor behavior. Rate only abnormality of movements. Do not rate simple heightened motor activity here. Consider frequency, duration, and degree of bizarreness. Do not rate movements of tardive dyskinesia.
 - 1 Not observed
 - 2 Very Mild: odd behavior but of doubtful clinical significance, e.g., occasional unprompted smiling, infrequent lip movements
 - 3 Mild: strange behavior but not obviously bizarre, e.g., infrequent head-tilting (side to side) in a rhythmic fashion, intermittent abnormal finger movements
 - 4 Moderate: e.g., assumes unnatural position for a brief period of time, infrequent tongue protrusions, rocking, facial grimacing
 - 5 Moderately Severe: e.g., assumes and maintains unnatural position throughout interview, unusual movements in several body areas
 - 6 Severe: as above, but more frequent, intense, or pervasive
 - 7 Very Severe: e.g., bizarre posturing throughout most of the interview, continuous abnormal movements in several body areas
- 8. GRANDIOSITY: Inflated self-esteem (self-confidence), or inflated appraisal of one's talents, powers, abilities, accomplishments, knowledge, importance, or identity. Do not socre mere grandiose <u>quality</u> of claims (e.g., "I'm the worse sinner in the world," "The entire country is trying to kill me") unless the guilt/persecution is related to some special, exaggerated attributes of the individual. Also, <u>the patient</u> must claim exaggerated attributes: e.g., if patient denies talents, powers, etc., even if he or she states that <u>others</u> indicate that he/she has these attributes, this item should not be scored. Rate on the basis of reported (i.e., subjective) information pertaining to the past week.

- 1 Not reported
- 2 Very Mild: e.g., is more confident than most people, but of only possible clinical significance
- 3 Mild: e.g., definitely inflated self-esteem or exaggerates talents somewhat out of proportion to the circumstances
- 4 Moderate: e.g., inflated self-esteem clearly out of proportion to the circumstances, or suspected grandiose delusion(s)
- 5 Moderately Severe: e.g., a single (definite) encapsulated grandiose delusion, or multiple (definite) fragmentary grandiose delusions
- 6 Severe: e.g., a single (definite) grandiose delusion/delusional system, or multiple (definite) grandiose delusions that seem to preoccupy the patient
- 7 Very Severe: e.g., as above, but nearly all conversation is directed towards the patient's grandiose delusion(s)
- 9 Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness; or not assessed
- 9. DEPRESSIVE MOOD: Subjective report of feeling depressed, blue, "down in the dumps," etc. Rate only degree of reported depression. Do not rate on the basis of inferences concerning depression based upon general retardation and somatic complaints. Rate on the basis of reported (i.e., subjective) information pertaining to the past week.
 - 1 Not reported
 - 2 Very Mild: occasionally feels somewhat depressed
 - 3 Mild: occasionally feels moderately depressed, or often feels somewhat depressed
 - 4 Moderate: occasionally feels very depressed, or often feels moderately depressed
 - 5 Moderately Severe: often feels very depressed
 - 6 Severe: feels very depressed most of the time
 - 7 Very Severe: feels very depressed nearly all of the time
 - 9 Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness; or not assessed
- 10. HOSTILITY: Animosity, contempt, belligerence, disdain for other people outside the interview situation. Rate solely on the basis of the verbal report of feelings and actions of the patient toward others during the past week. Do not infer hostility from neurotic defenses, anxiety or somatic complaints.
 - 1 Not reported
 - 2 Very Mild: occasionally feels somewhat angry
 - 3 Mild: often feels somewhat angry, or occasionally feels moderately angry
 - 4 Moderate: occasionally feels very angry, or often feels moderately angry
 - 5 Moderately Severe: often feels very angry

- 6 Severe: has acted on his anger by becoming verbally or physically abusive on one or two occasions
- 7 Very Severe: has acted on his anger on several occasions
- 9 Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness; or not assessed
- 11. SUSPICIOUSNESS: Belief (delusional or otherwise) that others have now, or have had in the past, malicious or discriminatory intent toward the patient. On the basis of verbal report, rate only those suspicions which are currently held whether they concern past or present circumstances. Rate on the basis of reported (i.e., subjective) information pertaining to the past week.
 - 1 Not reported
 - 2 Very Mild: rare instances of distrustfulness which may or may not be warranted by the situation
 - 3 Mild: occasional instances of suspiciousness that are definitely not warranted by the situation
 - 4 Moderate: more frequent suspiciousness, or transient ideas of reference
 - 5 Moderately Severe: pervasive suspiciousness, frequent ideas of reference, or an encapsulated delusion
 - 6 Severe: definite delusion(s) of reference or persecution that is (are) not wholly pervasive (e.g., an encapsulated delusion)
 - 7 Very Severe: as above, but more widespread, frequent, or intense
 - 9 Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness; or not assessed
- 12. HALLUCINATORY BEHAVIOR: Perceptions (in any sensory modality) in the absence of an identifiable external stimulus. Rate only those experiences that have occurred during the last week. DO NOT rate "voices in my head," or visions in my mind" unless the patient can differentiate between these experiences and his or her thoughts.
 - 1 Not reported
 - 2 Very Mild: suspected hallucinations only
 - 3 Mild: definite hallucinations, but insignificant, infrequent, or transient (e.g., occasional formless visual hallucinations, a voice calling the patient's name)
 - 4 Moderate: as above, but more frequent or extensive (e.g., frequently sees the devil's face, two voices carry on lengthy conversations)
 - 5 Moderately Severe: hallucinations are experienced nearly every day, or are a source of extreme distress
 - 6 Severe: as above, and has had a moderate impact on the patient's behavior (e.g., concentration difficulties leading to impaired work functioning)
 - 7 Very Severe: as above, and has had a severe impact (e.g., attempts suicide in response to command hallucinations)

- 9 Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness; or not assessed
- 13. MOTOR RETARDATION: Reduction in energy level evidenced in slowed movements. Rate on the basis of the behavior of the patient only. Do not rate on the basis of the patient's subjective impression of his own energy level.
 - 1 Not observed
 - 2 Very Mild and of doubtful clinical significance
 - 3 Mild: e.g., conversation is somewhat retarded, movements somewhat slowed
 - 4 Moderate: e.g., conversation is noticeably retarded but not strained
 - 5 Moderately Severe: e.g., conversation is strained, moves very slowly
 - 6 Severe: e.g., conversation is difficult to maintain, hardly moves at all
 - 7 Very Severe: e.g., conversation is almost impossible, does not move at all throughout the interview
 - 14. UNCOOPERATIVENESS: Evidence of resistance, unfriendliness, resentment, and lack of readiness to cooperate with the interviewer. Rate only on the basis of the patient's attitude and responses to the interviewer and the interview situation. Do not rate on the basis of reported resentment or uncooperativeness outside the interview situation.
 - 1 Not observed
 - 2 Very Mild: e.g., does not seem motivated
 - 3 Mild: e.g., seems evasive in certain areas
 - 4 Moderate: e.g., monosyllabic, fails to elaborate sponeaneously, somewhat unfriendly
 - 5 Moderately Severe: e.g., expresses resentment and is unfriendly throughout the interview
 - 6 Severe: e.g., refuses to answer a number of questions
 - 7 Very Severe: e.g., refuses to answer most questions
- 15. UNUSUAL THOUGHT CONTENT: Severity of delusions of any type. Consider conviction and effect on actions. Assume full conviction if patient has acted on his or her beliefs. Rate on the basis of reported (i.e., subjective) information pertaining to past week.
 - 1 Not reported
 - 2 Very Mild: delusion(s) suspected or likely
 - 3 Mild: at times, patient questions his or her belief(s) (partial delusion)
 - 4 Moderate: full delusional conviction, but delusion(s) has little or no influence on behavior
 - 5 Moderately Severe: full delusional conviction, but delusion(s) has only occasional impact on behavior
 - 6 Severe: delusion(s) has significant effect, e.g., neglects responsibilities because of preoccupation with belief that he/she is God

- 7 Very Severe: delusion(s) has major impact, e.g., stops eating because believes food is poisoned
- 9 Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness; or not assessed
- 16. BLUNTED AFFECT: Diminished affective responsivity, as characterized by deficits in facial expression, body gestures and voice pattern. Distinguish from EMOTIONAL WITHDRAWAL, in which the focus is on interpersonal impairment rather than affect. Consider degree and consistency of impairment. Rate based on observations made during interview.
 - 1 Not observed
 - 2 Very Mild: e.g., occasionally seems indifferent to material that is usually accompanied by some show of emotion
 - 3 Mild: e.g., somewhat diminished facial expression, or somewhat monotonous voice or somewhat restricted gestures
 - 4 Moderate: e.g., as above, but more intense, prolonged, or frequent
 - 5 Moderately Severe: including at least <u>two</u> of the three features: severe lack of facial expression, monotonous voice, or restricted body gestures
 - 6 Severe: e.g., profound blunting of affect
 - 7 Very Severe: e.g., totally monotonous voice, <u>and</u> total lack of expressive gestures throughout the evaluation
- 17. EXCITEMENT: Heightened emotional tone, including irritability and expansiveness (hypomanic affect). Do not infer affect from statements of grandiose delusions. Rate based on observations made during interview.
 - 1 Not observed
 - 2 Very Mild and of doubtful clinical significance
 - 3 Mild: e.g., irritable or expansive at times
 - 4 Moderate: e.g., frequently irritable or expansive
 - 5 Moderately Severe: e.g., constantly irritable or expansive; or, at times, enraged or euphoric
 - 6 Severe: e.g., enraged or euphoric throughout most of the interview
 - 7 Very Severe: e.g., as above, but to such a degree that the interview must be terminated prematurely
- 18. DISORIENTATION: Confusion or lack of proper association for person, place or time. Rate based on observations made during interview.
 - 1 Not observed
 - 2 Very Mild: e.g., seems somewhat confused
 - 3 Mild: e.g., indicated 1982 when, in fact, it is 1983

- 4 Moderate: e.g., indicates 1978
- 5 Moderately Severe: e.g., is unsure where he/she is
- 6 Severe: e.g., has no idea where he/she is
- 7 Very Severe: e.g., does not know who he/she is
- 9 Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness; or not assessed
- POVERTY OF SPEECH: A restriction in the amount of spontaneous speech, i.e., conversation and answers to questions are either brief or unelaborated. Meaningful information is rarely provided.
 - 1 Not observed
 - 2 Very Mild: Questionable
 - 3 Mild: Occasional replies do not include elaborated information even when this is appropriate
 - 4 Moderate: As above, but more frequently replies do not include elaborated information or occasional replies are monosyllabic or brief
 - 5 Moderately Severe: At least half of the patients' replies are monosyllabic or brief
 - 6 Severe: Most answers are rarely more than a few words in length, and occasionally questions may be left unanswered
 - 7 Very Severe: Patients' answers are either monosyllabic or she/he fails to answer questions
 - 9 Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness; or not assessed
- 20. INAPPROPRIATE AFFECT: Affect expressed is inappropriate or incongruous with the context of the situation. Most typically, this manifestation of affective disturbance takes the form of smiling or assuming a silly facial expression while talking about a serious or sad subject.
 - 1 Not observed
 - 2 Very Mild: Questionable
 - 3 Mild: At least one clear instance of inappropriate smiling or other inappropriate affect
 - 4 Moderate: At least two instances of inappropriate affect
 - 5 Moderately Severe: Occasional to frequent instances of inappropriate affect
 - 6 Severe: Frequent instances of inappropriate affect
 - 7 Very Severe: Affect is inappropriate most of the time
 - 9 Cannot be assessed adequately because of severe formal thought disorder, uncooperativeness, or marked evasiveness/guardedness; or not assessed

References

- Addington, J., Heinssen, R. K., Robinson, D. G., Schooler, N. R., Marcy, P., Brunette,
 M. F., ... Kane, J. M. (2015). Duration of untreated psychosis in community
 treatment settings in the United States. *Psychiatric Services*, 66(7), 753-756.
 doi:10.1176/appi.ps.201400124
- Addington, J., Van Mastrigt, S., & Addington, D. (2004). Duration of untreated psychosis: Impact on 2-year outcome. *Acta Psychiatrica Scandinavica*, *106*, 69-106. doi:10.1034/j.1600-0447.106.s413.1_14.x
- Altamura, A. C., Buoli, M., Caldiroli, A., Caron, L., Cumerlato Melter, C., Dobrea, C.,
 ... Zanelli Quarantini, F. (2015). Misdiagnosis, duration of untreated illness
 (DUI) and outcome in bipolar patients with psychotic symptoms: A naturalistic study. *Journal of Affective Disorders*, *182*, 70-75. doi:10.1016/j.jad.2015.04.024
- Altamura, A. C., Buoli, M., & Serati, M. (2011). Duration of illness and duration of untreated illness in relation to drug response in psychiatric disorders. *Neuropsychiatry*, 1(1), 81-90. doi:10.2217/npy.10.2
- Alvarez-Jimenez, M., Gleeson, J., Henry, L., Harrigan, S., Harris, M., Amminger, G., ...
 McGorry, P. (2012). Prediction of a single psychotic episode: A 7.5-year,
 prospective study in first-episode psychosis. *Schizophrenia Research*, *125*(2-3),
 236-246. doi:10.1016/j.schres.2010.10.020
- American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders (DSM-5®)*. Arlington, VA: American Psychiatric Pub.
- Amminger, G. (2002). Duration of untreated psychosis and cognitive deterioration in first-episode schizophrenia. *Schizophrenia Research*, *54*(3), 223-230. doi:10.1016/s0920-9964(01)00278-x

- Anderson, K. K., Voineskos, A., Mulsant, B. H., George, T. P., & McKenzie, K. J. (2014). The role of untreated psychosis in Neurodegeneration: A review of hypothesized mechanisms of neurotoxicity in first-episode psychosis. *The Canadian Journal of Psychiatry*, *59*(10), 513-517. doi:10.1177/070674371405901003
- Andreasen, N. C. (1989). The Scale for the Assessment of Negative Symptoms (SANS):
 Conceptual and theoretical foundations. *British Journal of Psychiatry*, 155(7),
 49-52. doi:10.1192/s0007125000291496
- Andreasen, N. C. (1992). The Comprehensive Assessment of Symptoms and History (CASH). Archives of General Psychiatry, 49(8), 615. doi:10.1001/archpsyc.1992.01820080023004
- Andreasen, N. C. (2008). Scale for the Assessment of Positive Symptoms (SAPS); Scale for the assessment of Negative Symptoms (SANS). In A. J. Rush Jr., M. B. First, & D. B. Blacker (Eds), Handbook of psychiatric measures (2nd ed.), (pp. 483 487). Arlington, VA: APA.
- Anglin, D. M., Ereshefsky, S., Klaunig, M. J., Bridgwater, M. A., Niendam, T. A.,
 Ellman, L. M., ... Van der Ven, E. (2021). From womb to neighborhood: A racial analysis of social determinants of psychosis in the United States. *American Journal of Psychiatry*, *178*(7), 599-610.
 doi:10.1176/appi.ajp.2020.20071091
- Asarnow, R. F., Nuechterlein, K. H., Asamen, J., Fogelson, D., Subotnik, K. L., Zaucha, K., & Guthrie, D. (2002). Neurocognitive functioning and schizophrenia spectrum disorders can be independent expressions of familial liability for schizophrenia in community control children: The UCLA family

study. *Schizophrenia Research*, *54*(1-2), 111-120. doi:10.1016/s0920-9964(01)00358-9

- Austin, S. F., Mors, O., Budtz-Jørgensen, E., Secher, R. G., Hjorthøj, C. R., Bertelsen, M., ... Nordentoft, M. (2015). Long-term trajectories of positive and negative symptoms in first episode psychosis: A 10 year follow-up study in the OPUS cohort. *Schizophrenia Research*, *168*(1-2), 84-91. doi:10.1016/j.schres.2015.07.021
- Barnes, T. R., Leeson, V. C., Mutsatsa, S. H., Watt, H. C., Hutton, S. B., & Joyce, E. M. (2008). Duration of untreated psychosis and social function: 1-year follow-up study of first-episode schizophrenia. *British Journal of Psychiatry*, *193*(3), 203-209. doi:10.1192/bjp.bp.108.049718
- Bearden, C. E., Rosso, I. M., Hollister, J. M., Sanchez, L. E., Hadley, T., &
 Cannon, T. D. (2000). A prospective cohort study of childhood behavioral deviance and language abnormalities as predictors of adult schizophrenia. *Schizophrenia Bulletin*, 26(2), 395-410.
 doi:10.1093/oxfordjournals.schbul.a033461
- Beiser, M., & Erickson, D. (1993). Establishing the onset of psychotic illness. *American Journal of Psychiatry*, 150(9), 1349-1354.
 doi:10.1176/ajp.150.9.1349
- Bell, V., Halligan, P. W., & Ellis, H. D. (2006). Cardiff Anomalous Perceptions Scale. *PsycTESTS Dataset*. doi:10.1037/t29560-000
- Birchwood, M., Todd, P., & Jackson, C. (1998). Early intervention in psychosis. *International Clinical Psychopharmacology*, *13*, S31-S40.
 doi:10.1097/00004850-199801001-00006

Birnbaum, M. L., Wan, C. R., Broussard, B., & Compton, M. T. (2015). Associations between duration of untreated psychosis and domains of positive and negative symptoms. *Early Intervention in Psychiatry*, *11*(5), 375-382. doi:10.1111/eip.12256

Black, K., Peters, L., Rui, Q., Milliken, H., Whitehorn, D., & Kopala, L. (2001).
Duration of untreated psychosis predicts treatment outcome in an early psychosis program. *Schizophrenia Research*, 47(2-3), 215-222. doi:10.1016/s0920-9964(00)00144-4

- Boonstra, N., Klaassen, R., Sytema, S., Marshall, M., De Haan, L., Wunderink, L., &
 Wiersma, D. (2012). Duration of untreated psychosis and negative symptoms —
 A systematic review and meta-analysis of individual patient data. *Schizophrenia Research*, *142*(1-3), 12-19. doi:10.1016/j.schres.2012.08.017
- Bottlender, R., Sato, T., Jäger, M., Wegener, U., Wittmann, J., Strauß, A., & Möller, H. (2003). The impact of the duration of untreated psychosis prior to first psychiatric admission on the 15-year outcome in schizophrenia. *Schizophrenia Research*, 62(1-2), 37-44. doi:10.1016/s0920-9964(02)00348-1
- Bourgou, S., Halayem, A., & Hayalem, M. B. (2012). Tunisian mothers' beliefs about their child's first psychotic episode. *L'encephale*, *38*(6), 473-479. doi:10.1016/j.encep.2012.01.012

Brohan, E., Elgie, R., Sartorius, N., & Thornicroft, G. (2010). Self-stigma,
empowerment and perceived discrimination among people with schizophrenia in
14 European countries: The GAMIAN-Europe study. *Schizophrenia Research*, *122*(1-3), 232-238. doi:10.1016/j.schres.2010.02.1065

- Buckley, P. F., Miller, B. J., Lehrer, D. S., & Castle, D. J. (2009). Psychiatric comorbidities and schizophrenia. *Schizophrenia Bulletin*, 35(2), 383-402. doi:10.1093/schbul/sbn135
- Cechnicki, A., Hanuszkiewicz, I., Polczyk, R., & Bielanska, A. (2011). How DUP predicts the dynamic of outcome in the long-term course of schizophrenia -20year follow-up study. *Psychiatrische Praxis*, *38*(S 01). doi:10.1055/s-0031-1277873
- Chilale, H. K., Silungwe, N. D., Gondwe, S., & Masulani-Mwale, C. (2017). Clients and carers perception of mental illness and factors that influence help-seeking: Where they go first and why. *International Journal of Social Psychiatry*, 63(5), 418-425. doi:10.1177/0020764017709848
- Clarke, M., Whitty, P., Browne, S., Mc Tigue, O., Kinsella, A., Waddington, J. L., ...
 O'Callaghan, E. (2006). Suicidality in first episode psychosis. *Schizophrenia Research*, 86(1-3), 221-225. doi:10.1016/j.schres.2006.05.026
- Cohen, J. (1988). *Statistical power analysis for the behavioral sciences*. Hillsdale, NJ: L. Erlbaum Associates.
- Compton, M. T., Bakeman, R., Alolayan, Y., Balducci, P. M., Bernardini, F., Broussard,
 B., ... Wan, C. R. (2015). Personality domains, duration of untreated psychosis,
 functioning, and symptom severity in first-episode psychosis. *Schizophrenia Research*, *168*(1-2), 113-119. doi:10.1016/j.schres.2015.06.028
- Compton, M. T., Gordon, T. L., Goulding, S. M., Esterberg, M. L., Carter, T., Leiner, A. S., ... Kaslow, N. J. (2011). Patient-level predictors and clinical correlates of duration of untreated psychosis among hospitalized first-episode patients. *The Journal of Clinical Psychiatry*, 72(02), 225-232. doi:10.4088/jcp.09m05704yel

Compton, M. T., Goulding, S. M., Gordon, T. L., Weiss, P. S., & Kaslow, N. J. (2009).
Family-level predictors and correlates of the duration of untreated psychosis in
African American first-episode patients. *Schizophrenia Research*, *115*(2-3), 338-345. doi:10.1016/j.schres.2009.09.029

Craig, T. J., Bromet, E. J., Fennig, S., Tanenberg-Karant, M., Lavelle, J., & Galambos,
N. (2000). Is there an association between duration of untreated psychosis and
24-month clinical outcome in a first-admission series? *American Journal of Psychiatry*, 157(1), 60-66. doi:10.1176/ajp.157.1.60

- Craig, T. J., Richardson, M. A., Pass, R., & Bregman, Z. (1985). Measurement of mood and affect in schizophrenic inpatients. *American Journal of Psychiatry*, 142(11), 1272-1277. doi:10.1176/ajp.142.11.1272
- Crow, T. J., MacMillan, J. F., Johnson, A. L., & Johnstone, E. C. (1986). A randomised controlled trial of prophylactic neuroleptic treatment. *British Journal of Psychiatry*, 148(2), 120-127. doi:10.1192/bjp.148.2.120
- Cuesta, M. J., García de Jalón, E., Campos, M. S., Ibáñez, B., Sánchez-Torres, A. M., & Peralta, V. (2012). Duration of untreated negative and positive symptoms of psychosis and cognitive impairment in first episode psychosis. *Schizophrenia Research*, 141(2-3), 222-227. doi:10.1016/j.schres.2012.08.019
- Cuesta, M. J., Peralta, V., Campos, M. S., & Garcia-Jalon, E. (2011). Can insight be predicted in first-episode psychosis patients? A longitudinal and hierarchical analysis of predictors in a drug-naïve sample. *Schizophrenia Research*, *130*(1-3), 148-156. doi:10.1016/j.schres.2011.04.032

Curran, P. J., West, S. G., & Finch, J. F. (1996). The robustness of test statistics to nonnormality and specification error in confirmatory factor analysis. *Psychological Methods*, 1(1), 16-29. doi:10.1037/1082-989x.1.1.16

de Haan, L., Linszen, D. H., Lenior, M. E., De Win, E. D., & Gorsira, R. (2003).
Duration of untreated psychosis and outcome of schizophrenia: Delay in intensive psychosocial treatment versus delay in treatment with antipsychotic medication. *Schizophrenia Bulletin*, 29(2), 341-348.
doi:10.1093/oxfordjournals.schbul.a007009

- de Haan, L., Van der Gaag, M., & Wolthaus, J. (2000). Duration of untreated psychosis and the long-term course of schizophrenia. *European Psychiatry*, *15*(4), 264-267. doi:10.1016/s0924-9338(00)00234-0
- Dixon, L. B., Goldman, H. H., Srihari, V. H., & Kane, J. M. (2018). Transforming the treatment of schizophrenia in the United States: The RAISE initiative. *Annual Review of Clinical Psychology*, 14(1), 237-258. doi:10.1146/annurev-clinpsy-050817-084934
- Drake, R. J., Haley, C. J., Akhtar, S., & Lewis, S. W. (2000). Causes and consequences of duration of untreated psychosis in schizophrenia. *British Journal of Psychiatry*, 177(6), 511-515. doi:10.1192/bjp.177.6.511

Elsheshtawy, E., & Hussein, R. A. (2015). Determinants of long duration of untreated psychosis and medication adherence in Egyptian schizophrenic patients : The role of social support. *The Arab Journal of Psychiatry*, *26*(1), 84-93. doi:10.12816/0010509

Esterberg, M., & Compton, M. (2012). Family history of psychosis negatively impacts age at onset, negative symptoms, and duration of untreated illness and psychosis

in first-episode psychosis patients. *Psychiatry Research*, *197*(1-2), 23-28. doi:10.1016/j.psychres.2012.03.001

- Faay, M. D., & Van Os, J. (2020). Aggressive behavior, hostility, and associated care needs in patients with psychotic disorders: A 6-Year follow-up study. *Frontiers in Psychiatry*, 10. doi:10.3389/fpsyt.2019.00934
- Faustman, W. O., & Overall, J. E. (1999). Brief Psychiatric Rating Scale. In M. E.
 Maruish (Ed.), *The use of psychological testing for treatment planning and outcomes assessment* (p. 791–830). Lawrence Erlbaum Associates Publishers.
- First, M. B., Williams, J. B. W., Karg, R. S., & Spitzer, R. L. (2015). Structured Clinical Interview for DSM-5: Research Version. Arlington, VA: American Psychiatric Association.
- Flanagan, P., & Compton, M. T. (2012). A comparison of correlates of suicidal ideation prior to initial hospitalization for first-episode psychosis with prior research on correlates of suicide attempts prior to initial treatment seeking. *Early Intervention in Psychiatry*, 6(2), 138-144. doi:10.1111/j.1751-7893.2011.00320.x
- Foley, S. R., Browne, S., Clarke, M., Kinsella, A., Larkin, C., & O'Callaghan, E. (2007).
 Is violence at presentation by patients with first-episode psychosis associated with duration of untreated psychosis? *Social Psychiatry and Psychiatric Epidemiology*, *42*(8), 606-610. doi:10.1007/s00127-007-0217-9
- Fusar-Poli, P., Cappucciati, M., Rutigliano, G., Schultze-Lutter, F., Bonoldi, I.,
 Borgwardt, S., ... McGuire, P. (2015). At risk or not at risk? A meta-analysis of
 the prognostic accuracy of psychometric interviews for psychosis prediction. *World Psychiatry*, 14(3), 322-332. doi:10.1002/wps.20250

- Gayer-Anderson, C., & Morgan, C. (2013). Social networks, support and early psychosis: a systematic review. *Epidemiology and Psychiatric Sciences*, 22(2), 131-146. doi:10.1017/s2045796012000406
- Goff, D. C., Zeng, B., Ardekani, B. A., Diminich, E. D., Tang, Y., Fan, X., Galatzer-Levy, I., Li, C., Troxel, A. B., & Wang, J. (2018). Association of hippocampal atrophy with duration of untreated psychosis and molecular biomarkers during initial antipsychotic treatment of first-episode psychosis. *JAMA Psychiatry*, 75(4), 370. doi:10.1001/jamapsychiatry.2017.4595
- Gottesman, I. I. (1991). Schizophrenia genesis: The origins of madness. New York: Freeman.
- Goulding, S. M., Holtzman, C. W., Trotman, H. D., Ryan, A. T., MacDonald, A. N., Shapiro, D. I., ... Walker, E. F. (2013). The prodrome and clinical risk for psychotic disorders. *Child and Adolescent Psychiatric Clinics of North America*, 22(4), 557-567. doi:10.1016/j.chc.2013.04.002
- Gumley, A. I., Schwannauer, M., Macbeth, A., Fisher, R., Clark, S., Rattrie, L., ...
 Birchwood, M. (2014). Insight, duration of untreated psychosis and attachment in first-episode psychosis: prospective study of psychiatric recovery over 12-month follow-up. *British Journal of Psychiatry*, 205(1), 60-67.
 doi:10.1192/bjp.bp.113.126722
- Gur, R. E., Reznick, P. D., Levick, S. M., Erwin, R., Saykin, A. J., & Gur, R. C. (1991).
 Relations among clinical scales in schizophrenia. *American Journal of Psychiatry*, 148(4), 472-478. doi:10.1176/ajp.148.4.472

- Haas, G. L., & Sweeney, J. A. (1992). Premorbid and onset features of first-episode schizophrenia. *Schizophrenia Bulletin*, *18*(3), 373-386.
 doi:10.1093/schbul/18.3.373
- Häfner, H., Riecher-Rössler, A., Hambrecht, M., Maurer, K., Meissner, S., Schmidtke,
 A., ... Van der Heiden, W. (1992). IRAOS: An instrument for the assessment of
 onset and early course of schizophrenia. *Schizophrenia Research*, 6(3), 209-223.
 doi:10.1016/0920-9964(92)90004-0
- Harrington, E., Neffgen, M., Sasalu, P., Sehgal, T., & Woolley, J. (2013). Initial predictors of outcome in an early intervention in psychosis service. *Early Intervention in Psychiatry*, 7(3), 311-314. doi:10.1111/eip.12028
- Hill, M., Crumlish, N., Whitty, P., Clarke, M., Browne, S., Kamali, M., ... O'Callaghan,
 E. (2010). Nonadherence to medication four years after a first episode of psychosis and associated risk factors. *Psychiatric Services*, *61*(2), 189-192. doi:10.1176/ps.2010.61.2.189
- Ho, B., Alicata, D., Ward, J., Moser, D. J., O'Leary, D. S., Arndt, S., & Andreasen, N.
 C. (2003). Untreated initial psychosis: Relation to cognitive deficits and brain morphology in first-episode schizophrenia. *American Journal of Psychiatry*, *160*(1), 142-148. doi:10.1176/appi.ajp.160.1.142
- Howes, O. D., & Murray, R. M. (2014). Schizophrenia: An integrated sociodevelopmental-cognitive model. *The Lancet*, 383(9929), 1677-1687. doi:10.1016/s0140-6736(13)62036-x
- Howes, O. D., Whitehurst, T., Shatalina, E., Townsend, L., Onwordi, E. C., Mak, T. L.,Arumuham, A., O'Brien, O., Lobo, M., Vano, L., Zahid, U., Butler, E., & Osugo,M. (2021). The clinical significance of duration of untreated psychosis: An

umbrella review and random-effects meta-analysis. *World Psychiatry*, 20(1), 75-95. doi:10.1002/wps.20822

- Jablensky, A., Sartorius, N., Ernberg, G., Anker, M., Korten, A., Cooper, J. E., ...
 Bertelsen, A. (1992). Schizophrenia: Manifestations, incidence and course in different cultures. A World Health Organization Ten-Country Study. *Psychological Medicine. Monograph Supplement*, 20, 1-97.
 doi:10.1017/s0264180100000904
- Jackson, H. J., McGorry, P. D., & Dudgeon, P. (1995). Prodromal symptoms of schizophrenia in first-episode psychosis: Prevalence and specificity.
 Comprehensive Psychiatry, 36(4), 241-250. doi:10.1016/s0010-440x(95)90068-3
- Jeppesen, P., Petersen, L., Thorup, A., Abel, M., Øhlenschlæger, J., Christensen, T., ... Nordentoft, M. (2008). The association between pre-morbid adjustment, duration of untreated psychosis and outcome in first-episode psychosis. *Psychological Medicine*, 38(8), 1157-1166. doi:10.1017/s0033291708003449
- Jonas, K. G., Fochtmann, L. J., Perlman, G., Tian, Y., Kane, J. M., Bromet, E. J., & Kotov, R. (2020). Lead-time bias confounds association between duration of untreated psychosis and illness course in schizophrenia. *American Journal of Psychiatry*, 177(4), 327-334. doi:10.1176/appi.ajp.2019.19030324
- Jones, S. R., & Fernyhough, C. (2007). A new look at the neural diathesis stress model of schizophrenia: The primacy of social-evaluative and uncontrollable situations. *Schizophrenia Bulletin*, 33(5), 1171-1177. doi:10.1093/schbul/sbl058
- Kane, J. M., Robinson, D. G., Schooler, N. R., Mueser, K. T., Penn, D. L., Rosenheck,R. A., ... Heinssen, R. K. (2016). Comprehensive versus usual community carefor first-episode psychosis: 2-year outcomes from the NIMH RAISE early

treatment program. *American Journal of Psychiatry*, *173*(4), 362-372. doi:10.1176/appi.ajp.2015.15050632

- Kane, J. M., Schooler, N. R., Marcy, P., Correll, C. U., Brunette, M. F., Mueser, K. T., ... Robinson, D. G. (2015). The RAISE early treatment program for first-episode psychosis. *The Journal of Clinical Psychiatry*, 76(03), 240-246. doi:10.4088/jcp.14m09289
- Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). The Positive and Negative Syndrome Scale (PANSS) for Schizophrenia. *Schizophrenia Bulletin*, *13*(2), 261-276. doi:10.1093/schbul/13.2.26
- Lally, J., & MacCabe, J. H. (2015). Antipsychotic medication in schizophrenia: A review. *British Medical Bulletin*, *114*(1), 169-179. doi:10.1093/bmb/ldv017
- Lappin, J. M., Morgan, K., Morgan, C., Hutchison, G., Chitnis, X., Suckling, J., ...
 Dazzan, P. (2006). Gray matter abnormalities associated with duration of untreated psychosis. *Schizophrenia Research*, 83(2-3), 145-153. doi:10.1016/j.schres.2005.11.018
- Large, M., Nielssen, O., Slade, T., & Harris, A. (2008). Measurement and reporting of the duration of untreated psychosis. *Early Intervention in Psychiatry*, 2(4), 201-211. doi:10.1111/j.1751-7893.2008.00080.x
- Larsen, T. K., Johannessen, J. O., & Opjordsmoen, S. (1998). First-episode schizophrenia with long duration of untreated psychosis: Pathways to care. *British Journal of Psychiatry*, 172(S33), 45-52. doi:10.1192/s0007125000297651
- Larsen, T. K., Moe, L. C., Vibe-Hansen, L., & Johannessen, J. O. (2000). Premorbid functioning versus duration of untreated psychosis in 1 year outcome in first-

episode psychosis. *Schizophrenia Research*, *45*(1-2), 1-9. doi:10.1016/s0920-9964(99)00169-3

- Lucksted, A., Essock, S. M., Stevenson, J., Mendon, S. J., Nossel, I. R., Goldman, H.
 H., ... Dixon, L. B. (2015). Client views of engagement in the RAISE
 Connection Program for early psychosis recovery. *Psychiatric Services*, 66(7), 699-704. doi:10.1176/appi.ps.201400475
- Malla, A. K., Bodnar, M., Joober, R., & Lepage, M. (2011). Duration of untreated psychosis is associated with orbital–frontal grey matter volume reductions in first episode psychosis. *Schizophrenia Research*, *125*(1), 13-20. doi:10.1016/j.schres.2010.09.021
- Marshall, M., Lewis, S., Lockwood, A., Drake, R., Jones, P., & Croudace, T. (2005).
 Association between duration of untreated psychosis and outcome in cohorts of first-episode patients. *Archives of General Psychiatry*, 62(9), 975.
 doi:10.1001/archpsyc.62.9.975

McAusland, L., Buchy, L., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A.,
Heinssen, R., McGlashan, T. H., Perkins, D. O., Seidman, L. J., Tsuang, M. T.,
Walker, E. F., Woods, S. W., Bearden, C. E., Mathalon, D. H., & Addington, J.
(2015). Anxiety in youth at clinical high risk for psychosis. *Early Intervention in Psychiatry*, *11*(6), 480-487. doi:10.1111/eip.12274

McGlashan, T. H. (1999). Duration of untreated psychosis in first-episode schizophrenia: marker or determinant of course? *Biological Psychiatry*, 46(7), 899-907. doi:10.1016/s0006-3223(99)00084-0

- McGorry, P. D., Copolov, D. L., & Singh, B. S. (1990). Royal Park Multidiagnostic Instrument for Psychosis: Part I. Rationale and review. *Schizophrenia Bulletin*, 16(3), 501-515. doi:10.1093/schbul/16.3.501
- McGorry, P. D., Killackey, E., & Yung, A. (2008). Early intervention in psychosis: concepts, evidence and future directions. *World Psychiatry*, 7(3), 148-156. doi:10.1002/j.2051-5545.2008.tb00182.x
- McGorry, P. D., Yung, A. R., & Phillips, L. J. (2003). The "close-in" or ultra high-risk model: A safe and effective strategy for research and clinical intervention in prepsychotic mental disorder. *Schizophrenia Bulletin*, 29(4), 771-790. doi:10.1093/oxfordjournals.schbul.a007046
- Miller, T. J., McGlashan, T. H., Rosen, J. L., Cadenhead, K., Ventura, J., McFarlane,
 W., ... Woods, S. W. (2003). Prodromal assessment with the Structured
 Interview for Prodromal Syndromes and the Scale of Prodromal Symptoms:
 Predictive validity, interrater reliability, and training to reliability. *Schizophrenia Bulletin*, 29(4), 703-715. doi:10.1093/oxfordjournals.schbul.a007040
- Millman, Z. B., Gold, J. M., Mittal, V. A., & Schiffman, J. (2019). The critical need for help-seeking controls in clinical high-risk research. *Clinical Psychological Science*, 7(6), 1171-1189. doi:10.1177/2167702619855660
- Millman, Z. B., Rakhshan Rouhakhtar, P. J., DeVylder, J. E., Smith, M. E.,
 Phalen, P. L., Woods, S. W., ... Schiffman, J. (2019). Evidence for
 differential predictive performance of the prime screen between black and
 white help-seeking youths. *Psychiatric Services*, *70*(10), 907-914.
 doi:10.1176/appi.ps.201800536

- Morlan, K. K., & Tan, S. (1998). Comparison of the brief psychiatric rating scale and the brief symptom inventory. *Journal of Clinical Psychology*, 54(7), 885-894. doi:10.1002/(sici)1097-4679(199811)54:7<885::aid-jclp3>3.0.co;2-e
- Mouridsen, S. E., & Hauschild, K. (2008). A longitudinal study of schizophrenia- and affective spectrum disorders in individuals diagnosed with a developmental language disorder as children. *Journal of Neural Transmission*, *115*(11), 1591-1597. doi:10.1007/s00702-008-0110-z
- Nagai, T., Tada, M., Kirihara, K., Yahata, N., Hashimoto, R., Araki, T., & Kasai, K. (2013). Auditory mismatch negativity and P3a in response to duration and frequency changes in the early stages of psychosis. *Schizophrenia Research*, *150*(2-3), 547-554. doi:10.1016/j.schres.2013.08.005
- National Institute for Health and Care Excellence. (2014). Psychosis and schizophrenia in adults. Retrieved from https://www.nice.org.uk/guidance/cg178/evidence/fullguideline-490503565
- National Institute of Mental Health. (2015). NIMH fact sheet: First episode psychosis. Retrieved from https://www.nimh.nih.gov/health/topics/schizophrenia/raise/fact-sheet-first-episode-psychosis.shtml
- Norman, R. M., & Malla, A. K. (1993). Stressful life events and schizophrenia. *British Journal of Psychiatry*, *162*(2), 161-166. doi:10.1192/bjp.162.2.161
- Norman, R. M., Malla, A. K., Verdi, M. B., Hassall, L. D., & Fazekas, C. (2004). Understanding delay in treatment for first-episode psychosis. *Psychological Medicine*, 34(2), 255-266. doi:10.1017/s0033291703001119
- Opjordsmoen, S., Friis, S., Melle, I., Haahr, U., Johannessen, J. O., Larsen, T. K., ... McGlashan, T. H. (2010). A 2-year follow-up of involuntary admission's

influence upon adherence and outcome in first-episode psychosis. *Acta Psychiatrica Scandinavica*, *121*(5), 371-376. doi:10.1111/j.1600-0447.2009.01536.x

Overall, J. E., & Gorham, D. R. (1962). The Brief Psychiatric Rating Scale. *Psychological Reports*, *10*(3), 799-812. doi:10.2466/pr0.1962.10.3.799

Penttilä, M., Jääskeläinen, E., Hirvonen, N., Isohanni, M., & Miettunen, J. (2014).
Duration of untreated psychosis as predictor of long-term outcome in schizophrenia: systematic review and meta-analysis. *British Journal of Psychiatry*, 205(2), 88-94. doi:10.1192/bjp.bp.113.127753

- Perkins, D. O. (2005). Evaluating and treating the prodromal stage of schizophrenia. *Current Psychosis & Therapeutics Reports*, 3(2), 79-85. doi:10.1007/bf02629426
- Perkins, D. O., Leserman, J., Graham, K., Kazmer, J., Jarskog Jeffrey, F., & Lieberman,
 A. (2000). The symptom onset in schizophrenia (SOS) scale: Test-retest
 reliability. *Schizophrenia Research*, *41*(1), 179. doi:10.1016/s09209964(00)90734-5
- Register-Brown, K., & Hong, L. E. (2014). Reliability and validity of methods for measuring the duration of untreated psychosis: A quantitative review and metaanalysis. *Schizophrenia Research*, *160*(1-3), 20-26. doi:10.1016/j.schres.2014.10.025
- Skeate, A., Jackson, C., Wood, M. B., & Jones, C. (2002). Duration of untreated psychosis and pathways to care in first-episode psychosis. *British Journal of Psychiatry*, 181(S43), s73-s77. doi:10.1192/bjp.181.43.s73

- Spear, L. (2000). The adolescent brain and age-related behavioral manifestations. *Neuroscience & Biobehavioral Reviews*, 24(4), 417-463. doi:10.1016/s0149-7634(00)00014-2
- Spencer, T. J., Thompson, B., Oliver, D., Diederen, K., Demjaha, A., Weinstein, S., ... McGuire, P. (2021). Lower speech connectedness linked to incidence of psychosis in people at clinical high risk. *Schizophrenia Research*, 228, 493-501. doi:10.1016/j.schres.2020.09.002
- Stowkowy, J., Colijn, M. A., & Addington, J. (2012). Pathways to care for those at clinical high risk of developing psychosis. *Early Intervention in Psychiatry*, 7(1), 80-83. doi:10.1111/j.1751-7893.2012.00368.x
- Strkalj Ivezić, S., Sesar, M. A., & Mužinić, L. (2017). Effects of a group psychoeducation program on self-stigma, empowerment and perceived discrimination of persons with schizophrenia. *Psychiatria Danubina*, 29(1), 66-73. doi:10.24869/psyd.2017.66
- Sullivan, S. A., Carroll, R., Peters, T. J., Amos, T., Jones, P. B., Marshall, M., ... Tilling, K. (2018). Duration of untreated psychosis and clinical outcomes of first episode psychosis: An observational and an instrumental variables analysis. *Early Intervention in Psychiatry*, *13*(4), 841-847. doi:10.1111/eip.12676

Tabo, A., Aydın, E., Yumrukçal, H., Yiğit, S., Uzun, U. E., & Karamustafalıoğlu, O.
(2017). Longer duration of untreated psychosis hinders improvement in treatment of chronic schizophrenia: Community based early intervention is an evidence based option. *Community Mental Health Journal*, *53*(8), 929-935.
doi:10.1007/s10597-017-0088-9
- Tanskanen, S., Morant, N., Hinton, M., Lloyd-Evans, B., Crosby, M., Killaspy, H., ... Johnson, S. (2011). Service user and carer experiences of seeking help for a first episode of psychosis: A UK qualitative study. *BMC Psychiatry*, 11(1). doi:10.1186/1471-244x-11-157
- Tsuang, M. T., van Os, J., Tandon, R., Barch, D. M., Bustillo, J., Gaebel, W., ... Carpenter, W. (2013). Attenuated psychosis syndrome in DSM-5. *Schizophrenia Research*, 150(1), 31-35. doi:10.1016/j.schres.2013.05.004
- Üçok, A., Polat, A., Genç, A., Çakır, S., & Turan, N. (2004). Duration of untreated psychosis may predict acute treatment response in first-episode schizophrenia. *Journal of Psychiatric Research*, *38*(2), 163-168. doi:10.1016/s0022-3956(03)00104-3
- Van Erp, T. G., Hibar, D. P., Rasmussen, J. M., Glahn, D. C., Pearlson, G. D., & Turner, J. A. (2015). Subcortical brain volume abnormalities in 2028 individuals with schizophrenia and 2540 healthy controls via the ENIGMA consortium. *Molecular Psychiatry*, 21(4), 547-553. doi:10.1038/mp.2015.63
- van Os, J., Rutten, B. P., & Poulton, R. (2008). Gene-environment interactions in schizophrenia: Review of epidemiological findings and future directions. *Schizophrenia Bulletin*, 34(6), 1066-1082. doi:10.1093/schbul/sbn117
- Ventura, J., Green, M. F., Shaner, A., & Liberman, R. P. (1993). Training and quality assurance with the Brief Psychiatric Rating Scale: "The drift busters." *International Journal of Methods in Psychiatric Research*, 3(4), 221–244.
- Verdoux, H., Liraud, F., Bergey, C., Assens, F., Abalan, F., & van Os, J. (2001). Is the association between duration of untreated psychosis and outcome confounded? A

two year follow-up study of first-admitted patients. *Schizophrenia Research*, 49(3), 231-241. doi:10.1016/s0920-9964(00)00072-4

- Welham, J., Scott, J., Williams, G. M., Najman, J. M., Bor, W., O'Callaghan, M., & McGrath, J. (2010). The antecedents of non-affective psychosis in a birth-cohort, with a focus on measures related to cognitive ability, attentional dysfunction and speech problems. *Acta Psychiatrica Scandinavica*, *121*(4), 273-279. doi:10.1111/j.1600-0447.2009.01470.x
- Winsper, C., Singh, S. P., Marwaha, S., Amos, T., Lester, H., Everard, L., ...
 Birchwood, M. (2013). Pathways to violent behavior during first-episode psychosis. *JAMA Psychiatry*, 70(12), 1287.
 doi:10.1001/jamapsychiatry.2013.2445