Longitudinal predictors of stigma in first-episode psychosis (FEP): Mediating effects of depression

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Abstract

Aim: Stigma is commonly experienced among individuals with schizophrenia spectrum disorders and has been shown to be a barrier to help-seeking and behavioral service utilization. Given the established relationships between stigma, barriers to treatment, and poorer psychiatric outcomes including depression and psychotic symptoms, we examined the relationships between symptoms of depression, positive and negative symptoms, and the emergence of stigma longitudinally among a sample of first-episode of psychosis (FEP) participants in the United States.

Methods: Data were obtained from the Recovery After an Initial Schizophrenia Episode project of National Institute of Mental Health's Early Treatment Program. Participants (n=404) included adults between ages 15 and 40 with schizophrenia or other psychotic disorders based upon the DSM-IV. Data were analyzed using structural equation modeling (SEM).

Results: Findings indicated that increased positive and negative symptoms independently related to greater symptoms of depression at baseline. Further, increased positive symptoms and symptoms of depression at baseline independently related to the emergence of greater stigma being experienced over time.

Conclusion: Considering the role that symptoms of depression played as a factor explaining the relationships between positive and negative symptoms and emergence of stigma over time among individuals in FEP, symptoms of depression is important predictor of stigma and may furthermore present as a viable and less stigmatizing initial treatment target in the early course of a psychotic disorder.

Keywords: first episode psychosis, stigma, depression, positive symptoms, negative symptoms, structural equation modeling**,** early intervention

Introduction

Historically, mental illness has been associated with negative attributions and discrimination with individuals depicted as dangerous, unpredictable, and devalued in society (González-Torres et al., 2007; Dickerson et al., 2002; Kleim et al., 2008). These perceptions lead to the experience of stigma, involving the experience of negative stereotypes and discrimination for individuals with mental illness (Penn and Wykes, 2003). Common among individuals with schizophrenia spectrum disorders, stigma is a predominant barrier to the treatment of depression and other mental disorders (Goffman, 1963), having been shown to negatively impact help-seeking behaviors (Griffiths et al., 2014; Latalova et al., 2014), mental health service utilization (Grant et al., 2017; Harrigan et al., 2003), adherence to psychological and pharmacological treatments (Corcoran et al., 2007; Corrigan and Watson, 2002; Fung et al., 2008), and overall quality of life (Ho et al., 2018; Staring et al., 2009).

For individuals experiencing psychosis, literature suggests poor treatment adherence relates with greater likelihood of relapse, poorer clinical outcomes, and lesser degrees of

recovery (Marshall et al., 2005; Franz et al., 2010; Perkins et al., 2005). Aside from its impact on service use and engagement, stigma also relates to hope, social and vocational functioning, self-esteem, self-efficacy, quality of life, depression, and symptoms of psychosis (Lysaker et al., 2007; Yanos et al., 2008; Young and Ng, 2016). The prevalence of depression in schizophrenia is estimated to be 40% (Upthegrove, Marwaha, & Birchwood, 2017), with a range of 22%-75% (Birchwood, 2011) depending on phase of illness (e.g. chronic versus first-episode), state (i.e. acute versus post-psychotic), and study characteristics (definitions of depression, study setting, and duration of observation). Rates of depression in an acute state of illness is estimated to be 60% with growing support for the role that positive symptoms of psychosis play in increased risk for depression (Bornheimer, 2016; Bornheimer & Jaccard, 2017; Siris, 2001). Positive symptoms are furthermore shown to weaken social skills, increase avoidance of social contact, and impair development and maintenance of support systems, which are all known to be important protective factors in risk for depression (Tarrier et al., 2013). Negative symptoms (diminished emotional expression, avolition, alogia, anhedonia, and asociality; American Psychiatric Association, 2013) are also prevalent and may be confused with symptoms of depression in clinical practice (Krynicki et al., 2018). While there are commonalities, such as anhedonia, avolition, and anergia, there are also differences (e.g. diminished emotional expression) which highlight the importance of distinguishing these symptoms in practice as they relate to treatment, particularly so in schizophrenia (Krynicki et al., 2018). Furthermore, and pertinent to the current study, the experience of stigma has also been associated with greater positive (e.g. hallucinations

and delusions) and negative symptoms (e.g. blunted affect and apathy; Lysaker et al., 2007; Schrank et al., 2014; Kane et al., 2016; Mueser et al., 2015). It is theorized that an experience of feeling alienated or being viewed as a lesser valued member of society both strongly relate to worsening positive and negative symptoms (Lysaker et al., 2007).

Of importance, much research to date on stigma and psychosis focuses on chronic mental illness, thus, there are limited understandings of the experience of stigma particularly within first-episode psychosis (FEP; Grant et al., 2017; Franz et al., 2010). One of few studies found societal and familial beliefs about mental illness and the fear of being labeled with a mental illness to be prominent themes within the experience of stigma in FEP (Franz et al., 2010). A greater understanding of stigma and its contributing factors in FEP is warranted as a foundation to better target behavioral interventions with the goal of buffering the experience of stigma**,** remediating barriers to help-seeking behaviors, and increasing engagement. Accordingly, this study aims to: (1) examine the independent relationships between stigma and symptoms of depression, and positive and negative symptoms over time; and, (2) examine the mediation of symptoms of depression as a potential factor explaining the relationships between stigma and positive and negative symptoms over time among a sample of early-treatment-phase participants in the United States. It is hypothesized in the proposed model that: (1) positive and negative symptoms and symptoms of depression will directly relate to the emergence of stigma over time, and (2) positive and negative symptoms will also indirectly relate to the emergence of stigma

over time through symptoms of depression (mediator). Thus, positive and negative symptoms are predicted to also directly relate to symptoms of depression within the mediational chain.

Methods

Participants

Data were obtained from the Recovery After an Initial Schizophrenia Episode (RAISE) project of National Institute of Mental Health's Early Treatment Program (ETP); publicly available via the National Institute of Mental Health Data Archive (NDA; # 2249). ETP aimed to change the trajectory and prognosis of first-episode psychosis (FEP) and compared two early treatment programs to improve functional outcomes and quality of life between 2010 and 2012 (Kane et al., 2016). Seventy-nine sites in the United States initially responded to the national advertisement of the project and participants were ultimately recruited from 34 sites who completed the following requirements: a detailed questionnaire, site visits, and evaluation to support the study treatment. Community mental health clinics (n=34) across 21 states were randomized using a cluster randomized design to one of two programs: 1) early treatment intervention (n=223) or, 2) standard community care (n=181). The early treatment program, entitled NAVIGATE, included medication management, psychoeducation, resilience-focused 1:1 therapy, and supported employment and education (Mueser et al., 2015). Standard care involved clinical care for psychosis as determined by providers and clinic capacities (Kane et al., 2016).

Participants (n=404) between the ages of 15 and 40 with a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder, brief psychotic disorder, or psychotic

disorder not otherwise specified based upon the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) were included in the study. All of whom experienced a first episode of psychosis, spoke English, and had been on antipsychotic medications for 6 or less months across the lifespan. Centralized independent raters from MedAvante followed a strict and systematic protocol to administer clinical assessments for outcome measures in the RAISE project, including measurement of depression and positive and negative symptoms in the current study. Non-clinical assessments, including stigma, were administered by research assistants at each study site. Greater detail can be found in Mueser et al. (2015) and Kane et al. (2015) of the RAISE project including more information regarding the NAVIGATE early treatment program.

Measurement

Symptoms of depression were measured at baseline using The Calgary Depression Scale for Schizophrenia (CDSS; Addington et al., 1990). The CDSS is a widely used well-validated scale to assess severity of depressive symptoms in individuals diagnosed with schizophrenia (Addington et al., 1993). Items pertain to the following constructs within symptoms of depression: depression, hopelessness, self-depreciation, guilty ideas of reference, pathological guilt, morning depression, early wakening, suicidal ideation and attempt, and observed depression. Item ratings are coded as 0 *absent*, 1 *mild*, 2 *moderate*, or 3 *severe* with a total score representing the sum of item scores. CDSS demonstrated a Cronbach's alpha of .81 at baseline.

Positive and negative symptoms were measured at baseline with the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987). Widely used in clinical studies of

psychosis with strong reliability and validity, the PANSS contains 30 items assessing symptoms including positive (e.g. hallucinations and delusions), negative (e.g. blunted affect and apathy), and general psychopathology (e.g. guilt and judgment). Of focus in the current study are the positive and negative subscales. The positive symptom subscale includes 7 items related to organization, hallucinations, excitement, grandiosity, and suspiciousness/persecution. The negative symptom subscale includes 7 items related to blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation, and stereotyped thinking. Item rating anchors range from 1 *absent* to 7 *extreme* and items are summed to obtain a total score. Both subscale total scores range from 7 to 49 with higher scores indicating greater presence and severity of positive and negative symptoms, independently. The positive and negative symptom subscales both demonstrated Cronbach's alphas of .70 at baseline.

Stigma was measured at 12-month assessment using a Self-Rating Stigma Scale (SRSS; King et al., 2007). The RAISE project included 7 of the original SRSS 42-items examining the experience of self-reported stigma. The scale included 3 specific subscales of stigma: 4 discrimination items (e.g. people have avoided me because of my mental health problems, 2 disclosure items (e.g. I find it hard telling people I have mental health problems), and 1 positive aspect item reverse coded as negative for scoring purposes (e.g. some people with mental health problems are dangerous). All item ratings range from 1 *strongly disagree* to 7 *strongly agree* and higher scores indicating greater experience and perception of stigma related to mental

illness. The SRSS demonstrated a Cronbach's alpha of .71 at 12-month assessment. Additionally, Confirmatory Factor Analysis (CFA) was performed within the structural equation model and all stigma items loaded significantly onto their respective factor, with loadings ranging from 0.61 to 0.84.

Quantitative Modeling and Analysis

Data were analyzed using SPSS 24 and Mplus 8. Structural equation modeling (SEM) was preformed to examine study aims using a robust Huber-White maximum likelihood algorithm to deal with non-normality and variance heterogeneity. Endogenous variables included a latent stigma variable (dependent variable) represented by the 7 stigma factors at 12-month assessment and symptoms of depression at baseline (mediator) while exogenous variables included positive and negative symptoms (independent variables), both at baseline. The multi-level model was run with clustering effects by site, given participants were recruited from 34 sites in the U.S. The model unadjusted and adjusted with clustering effects by study site is presented in Supplemental Table 1. Randomized treatment condition, medication, stigma at baseline, participant age, gender, and diagnosis (schizophrenia, schizoaffective bipolar, schizoaffective depressive, schizophreniform provisional or definite, brief psychotic disorder, or psychotic disorder NOS) were included as covariates for the endogenous variables. Stigma at baseline (Cronbach's alpha of .80) was included as a covariate to control for past stigma since the endogenous stigma outcome variable is measured at 12-month assessment and both stigma at baseline and 12-months were moderately correlated; $r = .415$, $p < .001$). Missing data, though

minimal, were treated using Full Information Maximum Likelihood (FIML) methods. The fit of the model was evaluated using both global (chi square, CFI, standardized RMR, RMSEA) and focused (standardized residuals and modification indices) fit indices (Muthén and Muthén, 1998-2012).

Results

Demographic characteristics of participants at baseline are presented in Table 1. Participants were on average 23.6 years of age (SD=5.06) and identified as male (73%), White (54%), and non-Hispanic/Latino (82%). The majority endorsed being single/unmarried (89%), attending some high school or less (36%), not working/employed (86%), living with family (71%), and being uninsured (48%). Participants most often had a diagnosis of schizophrenia (53%) and reported the experience of untreated psychosis for on average 6 months (SD=.72). At the time of consent, 83% of participants reported current use of one or more antipsychotic medications and differing types are presented in Table 1.

[INSERT TABLE 1]

Figure 1 presents the unstandardized parameter estimates for the structural model with margins of error in parentheses. Global fit indices all pointed to good model fit ($\chi 2 = 69.94$, df = 64, p-value = 0.285; CFI = 0.990, RMSEA = 0.015, p-value for close fit = 0.935, standardized RMR = 0.033) and focused fit indices (standardized residuals and modification indices) revealed no theoretically meaningful points of stress. Symptoms of depression, positive and negative symptoms, and all covariates (randomized treatment condition, medication, stigma at baseline,

participant age, gender, and diagnosis) accounted for 24% of the variance in stigma. Positive and negative symptoms and all covariates accounted for 10% of the variance in symptoms of depression.

[INSERT FIGURE 1]

Positive symptoms at baseline related to stigma at 12-month assessment both directly and indirectly through symptoms of depression at baseline, thus serving as a partial explaining factor (formally termed a partial mediator) of the relationship between positive symptoms and stigma over time, as indicated by the joint significance test (MacKinnon et al., 2002). As positive symptoms increased, on average, there was an associated increase in stigma holding covariates, symptoms of depression, and negative symptoms constant ($b = .042$, standard error (SE)$= .02$, $p < .05$). Additionally, as positive symptoms increased, on average, there was an associated increase in symptoms of depression holding all other variables constant ($b = .172$, $SE = .03$, $p < .001$). Lastly, as symptoms of depression increased, on average, there was an associated increase in stigma holding all other variables constant ($b = .112$, $SE = .02$, $p < .001$). Taken together, the total effect indicated that for every one-unit increase in positive symptoms, there was an average associated .061 unit increase in stigma holding all other variables constant. This means that as positive symptoms increasd at baseline, there was an associated increase in symptoms of depression at baseline, and in turn, related to greater stigma 12-months later.

Negative symptoms at baseline related to stigma at 12-month assessment indirectly through symptoms of depression at baseline, thus serving as a full explaining factor (formally

termed a full mediator) of the relationship between negative symptoms and stigma over time, as indicated by the joint significance test (MacKinnon et al., 2002). As negative symptoms increased, on average, there was an associated increase in symptoms of depression holding all other variables constant (b= .114, SE= .04, $p < .01$). Furthermore, as noted above, there was an associated increase in stigma holding all other variables constant (b= .112, SE= .02, $p < .001$) as symptoms of depression increased. This finding indicates that as negative symptoms increased at baseline, on average symptoms of depression also increased at baseline, and in turn, those increases related to greater stigma 12-months later.

Discussion

Given the empirical support for the relationships between stigma, barriers to treatment, and poor psychiatric outcomes including depression and symptoms of psychosis for individuals with schizophrenia spectrum disorders (Link, 1987; Sirey et al., 2001; Corcoran et al., 2007; Harrigan et al., 2003; Young & Ng, 2016), a greater understanding of stigma and contributing factors in FEP is needed as a foundation to better target behavioral interventions. Much research to date on the experience of stigma focuses on individuals with chronic mental illness. Therefore, developing a better understanding of the emergence of stigma being experienced over time and its contributing factors in FEP will lead to better targeting of interventions to buffer stigma, remediate barriers to help-seeking behaviors, and increase treatment engagement.

Findings of this study emphasize the direct relationship between positive symptoms of psychosis and emergence of stigma being experienced over time, and its indirect relationship

through depression. This means that while positive symptoms related to stigma over time on its own, depression functioned as an explaining factor in the relationship between positive symptoms and stigma over time. Negative symptoms of psychosis did not directly relate to stigma over time; however, it did indirectly relate to stigma over time through depression. Thus, there was no relationship between negative symptoms and stigma over time when depression was not considered as a potential factor explaining the way in which the two variables related. This is consistent with prior research in which stigma is found to relate to increased depression and positive symptoms, yet not with increased negative symptoms (van Zelst, 2009; Ertugrul & Ulug, 2004; Schrank et al., 2014). One potential reason for negative symptoms not directly relating to stigma may be the way in which symptoms are experienced. The overall experience of having positive symptoms may be interpreted as odd, uncomfortable, or catastrophic; potentially leading to anxiety or fearful thoughts as one considers the impact of mental illness, and psychosis specifically, on an individual's life (i.e. experiencing stigma). Whereas, negative symptoms could be experienced more subtly in which an individual may develop an attribution about personal failure, and further impacting self-esteem (Grant & Beck, 2008). This raises implications for future research to examine the relationships between psychosis and internalized stigma, otherwise known as self-stigma.

The positive relationship found between negative symptoms and symptoms of depression is also an interesting finding. As mentioned in the introduction, negative symptoms in practice may be confused with symptoms of depression (Krynicki et al., 2018) due to several

commonalities: anhedonia, avolition, and anergia. However, there are also differences (e.g. diminished emotional expression) which highlight the importance of distinguishing these symptoms in practice as they relate to treatment, particularly so in psychosis. The positive relationship between negative symptoms and depression, if negative symptoms aren't mistaken for depression, may be unique to FEP and future research is needed to further examine those relationships. Also, beyond symptoms and diagnostics, it is possible that insight plays a role in the relationship between negative symptoms and depression. The current study did not involve measurement for insight, thus future research is needed in this area.

These findings have several important clinical implications. First, considering the role of depression in explaining the relationships between positive and negative symptoms and stigma, symptoms of depression are an important treatment target in practice among individuals in FEP and clinicians should routinely assess for them. Second, within the vein of depression and aiming to improve treatment adherence and engagement, greater focus on depressive symptoms may present as a viable and less stigmatizing initial target (i.e., self-deprecation, hopelessness, guilty ideas of reference, pathological guilt) for intervention in the early course of a psychotic disorder. Individuals in FEP may be more easily engaged to relieve the specific distress of depression as opposed to discussing the impact of stigma or processing the meanings of positive or negative symptoms. Especially considering the unremarkable impact of pharmacology on negative symptoms, a medial target of depression may be more productive and lead to varying behavioral treatment options (e.g. psychosocial) in reducing stigma. For example, a systematic,

recovery-oriented treatment could inoculate against stigma by reducing depression. As research consistently describes schizophrenia as a degenerative condition with a wide range of recovery experiences, recovery-oriented treatments and services can foster hope, self-efficacy, interpersonal interactions, and quality of life through mobilization of strengths and resources to work towards goals (Davidson et al., 2005; Lysaker & Buck, 2008; Davidson et al., 2009).

The current study must be considered in light of several potential limitations. First, the RAISE project was not conducted to address the aims of the current study, thus, measurement of stigma was constrained. The RAISE project included only 7 of the 42-item SRSS scale and future research examining stigma should utilize the full scale. Second, self-report and social desirability are common concerns in mental health research and should be considered in the current study, particularly so when considering the construct of stigma. Third, while antipsychotic medication was available in the dataset and we did control for it statistically in our model, we were unable to obtain additional medications (e.g. mood stabilizers) that participants may have been taking. There could be a potential impact of medication on the study variables and future research should examine potential differences, particularly related to mood stabilizers and antipsychotic medications which may have antidepressant effects. Fourth, while diagnostic categories within psychosis were available in the dataset, we did not have additional comorbid mental health information. Major depressive disorder, for example, could potentially impact the model and findings, thus future research should measure this information and make decisions regarding exclusion and/or subgroup analyses to handle potential confounding variables. Fifth, it

is important to note the sample was homogenous with participants mostly being in their early twenties (M=23.6, SD=5.06) with a small range overall (23.62 – 28.68), and most often identifying as male (73%), White (54%), and non-Hispanic/Latino (82%). As a result, findings may not necessarily be generalizable to other ages and groups. Lastly, it is important to consider the findings in light of the comorbid diagnostic limitation since the presence of major depressive disorder could impact the degree of focus on depression as an initial treatment target. Since the current study did not examine differing severities of positive and negative symptoms, in addition to the potential presence of a major depressive disorder, the delivery of treatment with an initial focus on symptoms of depression as a potentially less stigmatizing target will likely vary based upon clinical presentation.

In sum, these results support the relationships between positive and negative symptoms, depression, and the emergence of stigma being experienced in FEP. To gain a better understanding of depression as a factor explaining the relationships between positive and negative symptoms and stigma, differing symptoms of depression within the CDSS (i.e. items) should be examined to ultimately inform intervention focus. Further investigation should also examine the relationships between psychosis and internalized stigma given the potential role of self-esteem.

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Conflict of Interest Statement

The authors have declared that there are no conflicts of interest.

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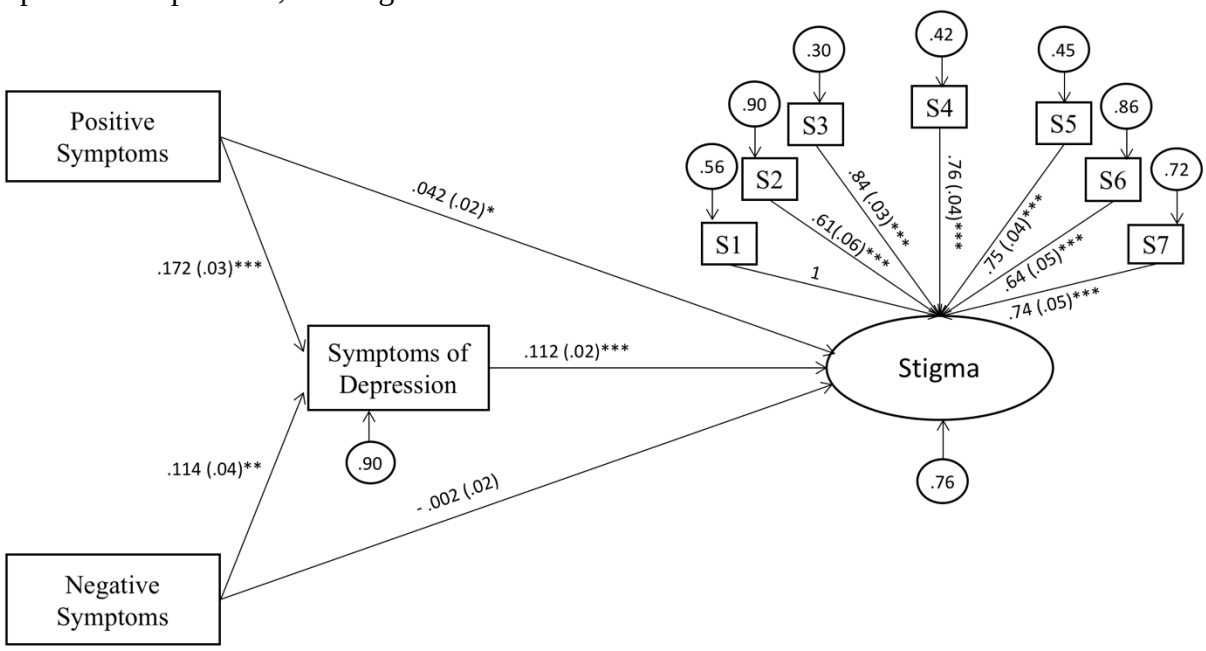
Table 1: Demographic characteristics of the RAISE sample at baseline

Characteristic	n	%
Age (M ± SD)	404	23.62 ± 5.06
Gender		
Male	293	72.5
Female	111	27.5
Race		
African American	152	37.6
White	218	54.0
American Indian or Alaska Native	31	5.2
Asian	12	3.0
Hawaiian or Pacific Islander	1	0.2
Ethnicity		
Hispanic	73	18.1
Not Hispanic	331	81.9
Marital Status		
Married	24	5.9
Single/unmarried	358	88.6
Divorced, widowed, or separated	22	5.4
Education		
Some high school or less	145	36.0
Completed high school	133	33.0
Some college or higher	125	31.0
Employment		
Currently working	58	14.4
Not currently working	346	85.6
Insurance Type		
Private	82	20.4
Public	127	31.7
Uninsured	192	47.9
Residence		
Independent living	72	17.8
Lives with family	287	71.0
Supported or structured housing	14	3.5
homeless, shelter, other	31	7.7
Medication Status		
Using antipsychotic(s)	337	83.4
Not using antipsychotic(s)	67	16.6
Medication Type		
Aripiprazole	43	10.6
Asenapine	2	0.5
Clozapine	3	0.7
Haloperidol	18	4.5

Loxapine	1	0.2
Lurasidone	7	1.7
Olanzapine	52	12.9
Paliperidone	20	5.0
Perphenazine	4	1.0
Quetiapine	30	7.4
Risperidone	122	30.2
Thiothixene	2	0.5
Ziprasidone	16	4.0
Months of untreated psychosis (M ± SD)	355	6.36 ± 8.62
Age of first psychiatric illness (M ± SD)	398	16.52 ± 6.32
Age of first psychotic symptoms (M ± SD)	392	19.15 ± 6.12
Number of psychiatric hospitalizations (M ± SD)	314	1.94 ± 1.98
Diagnosis		
Schizophrenia	214	53.0
Schizoaffective bipolar	24	5.9
Schizoaffective depressive	57	14.1
Schizophreniform provisional or definite	67	16.6
Brief psychotic disorder	2	0.5
Psychotic disorder NOS	40	9.9

N=404

Figure 1. Model findings of the relationships between positive and negative symptoms, symptoms of depression, and stigma over time



Notes: Unstandardized parameter estimates are presented for the structural model and standardized parameter estimates are presented for the measurement model; Stigma measured at 12-month assessment, all other variables measured at baseline; * p< .05, ** p < .01, *** p < .001
Stigma items: sometimes I feel I am being talked down to because of my mental heath problems (S1); some people with mental health problems are dangerous (S2); very often I feel alone because of my mental health problems (S3); I keep to myself because of peoples' reactions to my mental health problems (S4); people have avoided me because of my mental health problems (S5); I feel embarrassed because of my mental health problems (S6); I feel the need to hide my mental health problems from my friends (S7).

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