



A stress-coping model of mental illness stigma: II. Emotional stress responses, coping behavior and outcome

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ABSTRACT

Stigma can be a major stressor for people with schizophrenia and other mental illnesses, leading to emotional stress reactions and cognitive coping responses. Stigma is appraised as a stressor if perceived stigma-related harm exceeds an individual's perceived coping resources. It is unclear, however, how people with mental illness react to stigma stress and how that affects outcomes such as self-esteem, hopelessness and social performance. The cognitive appraisal of stigma stress as well as emotional stress reactions (social anxiety, shame) and cognitive coping responses were assessed by self-report among 85 people with schizophrenia, schizoaffective or affective disorders. In addition to self-directed outcomes (self-esteem, hopelessness), social interaction with majority outgroup members was assessed by a standardized role-play test and a seating distance measure. High stigma stress was associated with increased social anxiety and shame, but not with cognitive coping responses. Social anxiety and shame predicted lower self-esteem and more hopelessness, but not social performance or seating distance. Hopelessness was associated with the coping mechanisms of devaluing work/education and of blaming discrimination for failures. The coping mechanism of ingroup comparisons predicted poorer social performance and increased seating distance. The cognitive appraisal of stigma-related stress, emotional stress reactions and coping responses may add to our understanding of how stigma affects people with mental illness. Trade-offs between different stress reactions can explain why stress reactions predicted largely negative outcomes. Emotional stress reactions and dysfunctional coping could be useful targets for interventions aiming to reduce the negative impact of stigma on people with mental illness.

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1. Introduction

Stigma is a stressor for many people with schizophrenia and other mental illnesses and therefore a major clinical and public health issue (Corrigan, 2005; Hinshaw, 2007; Thornicroft, 2006). Yet some individuals with mental illness are

demoralized by stigma while others remain relatively unaffected (Corrigan and Watson, 2002; Rüsch et al., 2006b). In part 1 of this two-part paper, we discussed public and personal predictors of stigma stress, that is whether stigmatized individuals feel that the potential harm of stigma exceeds their resources to cope with this threat (Rüsch et al., 2009-this issue). In part 2, we apply the same social-psychological stress-coping model of stigma (Major and O'Brien, 2005) to examine emotional and cognitive reactions to stigma stress appraisal and how these reactions affect broader outcomes for stigmatized individuals (Fig. 1). While

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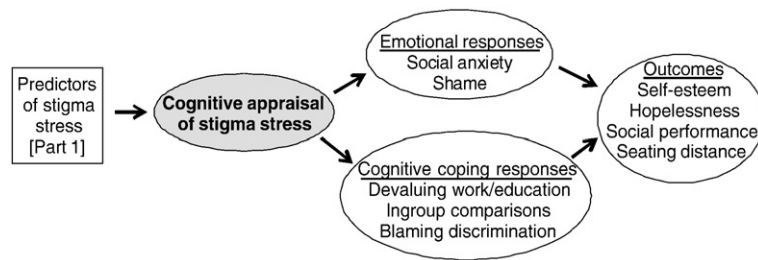


Fig. 1. Cognitive appraisal of stigma-related stress, stress reactions and outcomes (part 2, adapted from Major and O'Brien, 2005).

previous work investigated other stressors and coping in schizophrenia (Betensky et al., 2008; Cooke et al., 2007; Myin-Germeys and van Os, 2007; Roe et al., 2006), we focus here on stigma-related stress and its consequences. This can provide a better understanding of how stigma affects people with mental illness and help to identify targets for interventions that aim to reduce stigma's negative impact (Knight et al., 2006; Lysaker et al., 2007a; MacInnes and Lewis, 2008).

Reactions to stigma stress can explain why individuals cope more or less successfully with stigma. Stress appraisal leads to two sets of responses (Fig. 1), involuntary emotional reactions and deliberate cognitive coping responses. Two key emotions in the context of stigma are social anxiety and shame (Lazarus, 1993). Social anxiety is a reaction to stigma as a threat in social interactions (Spencer et al., 1999). Likewise, shame is prominent in mental illness (Rüsch et al., 2007b), an emotional correlate of internalized stigma (Rüsch et al., 2006a) and a reaction to being socially exposed and humiliated as a devalued person (Lewis, 1998). This is consistent with findings that shame and social anxiety are consequences of social devaluation among members of the public (Gilbert and Miles, 2000) and of stigmatizing experiences in persons with psychosis (Birchwood et al., 2007).

Coping responses, on the other hand, are conscious and volitional regulation efforts in response to stressors (Miller, 2006). In their classic paper, Crocker and Major (1989) explored three coping mechanisms that can help preserve the self-esteem of stigmatized individuals. First, group members can devalue domains in which their group stereotypically performs poorly, such as work and education in the case of people with mental illness. Negative feedback or failures such as unemployment are then less likely to have a negative impact on the person because these domains become peripheral in the person's self-concept. The second coping mechanism is to compare oneself primarily with ingroup members, i.e. with other people with mental illness; because other ingroup members are likely to be similarly disadvantaged, ingroup comparisons are usually less painful and self-esteem threatening than comparisons with more advantaged majority outgroup members (i.e., members of the public). Third, a person may choose to attribute negative feedback to discrimination rather than to internal causes such as lack of ability, blaming discrimination instead of blaming the self (Major et al., 2003).

Emotional or cognitive stress responses influence global outcomes. No reaction to stigma is universally beneficial or detrimental (Major and O'Brien, 2005) because one coping response may be helpful in one domain but harmful in another. For example, a person with mental illness may use the coping

mechanism of ingroup comparisons to stabilize self-esteem. However, lack of outgroup comparisons may undermine motivation and learning opportunities, resulting in lower academic, vocational or social performance in the long run. Therefore we measured four outcomes, two of which are related to a person's self-image and two to social performance. First we studied self-esteem and hopelessness as a pair of self-directed outcomes. Self-esteem is of interest because the above-mentioned cognitive coping responses can protect self-esteem (Crocker and Major, 1989; Major et al., 2003) and experiencing stigma is often associated with lower self-esteem (Corrigan et al., 2006; Link et al., 2001; Lysaker et al., 2007b, 2008b; Rüsch et al., 2006a; Wright et al., 2000; Yanos et al., 2008). Hopelessness, as a negative self-directed outcome, is a proxy for demoralization as a consequence of stigma, its relevance being underlined by its association with suicidality (Brezo et al., 2006). Although not assessing stigma stress appraisal, previous studies found aspects of internalized stigma, such as feeling devalued or agreeing with negative stereotypes, and impaired self-experience as reflected by illness narratives to be associated with reduced hope in schizophrenia (Lysaker et al., 2006, 2008a; Yanos et al., 2008). A second pair of outcomes referred to social behavior in the interaction with "normal" majority outgroup members, who are often the source of stigma. Social behavior was measured by a standardized role-play test and a seating distance measure. We examined the hypotheses that first, higher stigma-induced stress appraisal predicts higher levels of emotional stress reactions and cognitive coping responses; and second, that emotional and cognitive stress responses predict broader outcomes.

2. Materials and methods

2.1. Participants

In part 1 (Rüsch et al., 2009-this issue) we reported details of study participants. Briefly, 85 persons with mental illness participated. Twenty-three (27%) participants had schizophrenia, 22 (26%) schizoaffective, 30 (35%) bipolar I or II, and the remaining 10 (12%) recurrent unipolar major depressive disorders. Overall, 33 subjects (39%) suffered from a comorbid current alcohol- or substance-related abuse or dependence.

2.2. Emotional and cognitive responses to stigma stress

Social anxiety and shame were measured as involuntary emotional responses to stigma. Social anxiety was assessed by the fear score of the Liebowitz Social Anxiety scale (Liebowitz,

1987), with a sum score across 24 situations (Cronbach's $\alpha = .92$). Shame-proneness in social situations was measured by Tangney's Test of Self-Conscious Affect (TOSCA-3; Tangney et al., 2000), a scenario-based self-report questionnaire. We used a short version, validated by Tangney and colleagues, that consists of 11 negative instead of 16 scenarios (Cronbach's $\alpha = .75$; Rüsch et al., 2007a).

Three voluntary, cognitive coping responses to mental illness stigma were measured following Crocker and Major (1989). First, devaluing domains in which the stigmatized group stereotypically performs poorly, such as work and education in the case of people with mental illness ('I care a lot if I am successful in terms of work, training or education'); second, ingroup comparisons ('When I think about my successes or failures and how I compare to others, I primarily compare myself to other people who also have a mental illness, not so much to "normals"'); and third attributing negative outcomes to discrimination ('When I suffer a setback and don't achieve something I wanted, for example looking for a job or an apartment, I usually think: "I did not get what I wanted because other people discriminated against me because of my mental illness"'). After reverse-coding the first, higher scores from 1 to 9 indicated stronger endorsement of the respective coping mechanisms.

2.3. Outcomes

General self-esteem was measured using Rosenberg's ten-item Self-Esteem Scale with an average score between 0 and 3 (Cronbach's $\alpha = .88$; Rosenberg, 1965). Hopelessness, a proxy for demoralization as a possible consequence of stigma, was assessed by Beck's 20-item Hopelessness Scale (Beck et al., 1974; Steed, 2001) with higher sum scores between 20 and 100 indicating more hopelessness (Cronbach's $\alpha = .92$). We used a standardized and widely used role-play test, the Maryland Assessment of Social Competence (Bellack et al., 2006; Sayers et al., 1995), as a measure of social performance in the pursuit of social, treatment- and employment-related goals and of the ability and motivation to interact with outgroup members in order to achieve goals in domains that are threatened by stigma. Following a short practice scene, three social scenes, 3 min each, were administered by a trained confederate. We adapted three scenes that were provided by Dr. Bellack. The first involved speaking with a new neighbor; the second scene required talking to a psychiatrist about difficulties with new medication and symptom monitoring; in the last scene the participant had to negotiate with a supervisor of a job training program. Role-plays were videotaped and rated in terms of conversational and non-verbal content and effectiveness from 1, very poor, to 5, very good. Interrater reliability between three raters that rated all subjects was high with intra-class correlation coefficients 0.85 for verbal content, 0.84 for non-verbal content and 0.90 for effectiveness, respectively. To derive an index of overall social performance, we calculated a mean score across the three scenes and evaluated domains.

To measure social distance from "normal" majority group members (Penn and Corrigan, 2002), participants were asked to go to another room in which they found a table with a single seat at the head and four chairs along the length. It was explained that a "healthy and talkative" man/woman (always

the gender of the participant) would arrive in a minute, sit down in the single seat at the head of the table and talk to the participant. The participant was then asked to sit down in one of the four chairs on the side of the table. Once the participant sat down, the seat number was recorded (between 1 and 4, with higher numbers indicating increased distance from the talkative healthy person).

3. Results

3.1. Stress appraisal, reactions and outcomes across diagnostic groups

We examined possible differences in levels of cognitive stress appraisal, emotional stress reactions, coping responses and outcomes between the four groups of subjects with schizophrenia, schizoaffective disorder, bipolar disorder or unipolar depression. Analyses of variance did not indicate significant group effects, except for the coping mechanism of ingroup comparisons ($F = 2.84$, $p = .04$) and hopelessness ($F = 3.01$, $p = .04$). Post-hoc Scheffé tests showed significantly higher use of ingroup comparisons in the schizophrenia ($M = 4.7$, $SD = 2.5$) than in the bipolar group ($M = 2.9$, $SD = 1.8$; $p = .049$); and a trend for less hopelessness in the schizophrenia ($M = 40.9$, $SD = 12.5$) than in the unipolar depression group ($M = 55.5$, $SD = 17.5$, $p = .10$). Other group differences were non-significant. Subjects with versus without substance- or alcohol-related disorders did not differ with respect to stress appraisal, stress reactions or outcomes (all p -values $> .20$).

3.2. Stress appraisal and emotional and cognitive responses

As far as our first hypothesis was concerned, higher cognitive appraisal of stigma stress was associated with more social anxiety ($r = .24$, $p = .02$) and shame ($r = .25$, $p = .02$). Examining the association of primary and secondary appraisals, that underlie stress appraisal, with emotional stress reactions, we found that more perceived resources to cope with stigma were related to decreased social anxiety ($r = -.23$, $p = .03$);

Table 1

Correlations of emotional and cognitive stress responses (left column) with outcome variables (top row).

	Self-esteem ^a	Hopelessness ^b	Social performance ^c	Seating distance ^d
Social anxiety ^e	-.50 **	.55 **	.01	.23 *
Shame ^f	-.45 **	.41 **	.07	.16
Devaluing work/education	-.04	.22 *	-.15	.26 *
Ingroup comparisons	-.00	.06	-.50 **	.27 *
Blaming discrimination	-.09	.22 *	-.13	.27 *

* $p < .05$ ** $p < .01$ (two-tailed).

Correlations with self-esteem, hopelessness and social performance are bivariate Pearson correlations; because of its skewed distribution, correlations with seating distance are Spearman rank correlations.

(a) Rosenberg's Self-Esteem Scale (Rosenberg, 1965).

(b) Beck's Hopelessness Scale (Beck et al., 1974).

(c) Maryland Assessment of Social Competence (Bellack et al., 2006).

(d) Seating distance from a talkative "normal" person.

(e) Liebowitz Social Anxiety Scale (Liebowitz, 1987).

(f) Test of Self-Conscious Affect-3 (Tangney et al., 2000).

Table 2

Regressions on outcome variables.

Dependent variable	Independent variables	Beta / B ^a	T / Wald ^a	p	R ² /Nagel-Kerke R ^{2 a}
Self-esteem ^b	Social anxiety ^(c)	−0.40	−3.50	.001	.32
	Shame ^(d)	−0.27	−2.52	.014	
	Devaluing work/education	−0.03	−0.34	.73	
	Ingroup comparisons	0.13	1.27	.21	
	Blaming discrimination	0.04	.38	.71	
Hopelessness ^e	Social anxiety ^c	0.44	3.97	<.001	.37
	Shame ^d	0.21	2.03	.046	
	Devaluing work/education	0.19	2.06	.043	
	Ingroup comparisons	−0.10	−1.05	.30	
	Blaming discrimination	0.05	0.48	.64	
Social Performance ^f	Social anxiety ^c	0.09	0.76	.45	.30
	Shame ^d	0.10	0.92	.36	
	Devaluing work/education	−0.14	−1.45	.15	
	Ingroup comparisons	−0.54	−5.39	<.001	
	Blaming discrimination	0.03	0.31	.76	
Seating Distance ^g	Social anxiety ^c	0.01	0.29	.59	.12
	Shame ^d	−0.01	0.04	.85	
	Devaluing work/education	−0.06	0.14	.71	
	Ingroup comparisons	0.24	4.02	.045	
	Blaming discrimination	0.09	0.51	.48	

(a) Linear regressions on self-esteem, hopelessness and social performance; and logistic regression on seating distance (close versus far).

(b) Rosenberg's Self-Esteem Scale (Rosenberg, 1965).

(c) Liebowitz Social Anxiety Scale (Liebowitz, 1987).

(d) Test of Self-Conscious Affect-3 (Tangney et al., 2000).

(e) Beck's Hopelessness Scale (Beck et al., 1974).

(f) Maryland Assessment of Social Competence (Bellack et al., 2006).

(g) Seating distance from a talkative "normal" person.

perceiving stigma as more harmful was linked to higher levels of shame ($r = .26$, $p = .02$). Cognitive stress appraisal, on the other hand, was not significantly related to any of the three cognitive coping responses (p -values $> .40$).

3.3. Correlations between stress responses and outcomes

With regard to our second hypothesis, higher levels of both social anxiety and shame were associated with low self-esteem and more hopelessness, but not with behavioral measures, except for a link between more social anxiety and increased seating distance from outgroup members (Table 1). On the other hand, stronger endorsement of all three cognitive coping responses was associated with increased seating distance; and proneness to ingroup comparisons was strongly linked to poorer social performance. None of the cognitive coping responses were related to self-esteem, but two coping mechanisms, devaluing work/education and blaming discrimination, were significantly associated with more hopelessness.

3.4. Regressions on outcomes

Regressions on each of the four outcome variables examined the five emotional and cognitive stress response variables as predictors of outcome to investigate whether univariately

Table 3

Regressions on outcome variables, controlling for depressive symptoms and diagnosis.

Dependent variable	Independent variables	Beta / B ^a	T / Wald ^a	p	R ² / Nagel-Kerke R ^{2 a}
Self-esteem ^b	Social anxiety ^c	−0.22	−1.99	.050	.48
	Shame ^d	−0.12	−1.18	.24	
	Devaluing work/education ^e	−0.02	−0.25	.81	
	Ingroup comparisons ^e	−0.00	−0.01	.99	
	Blaming discrimination ^e	0.12	1.21	.23	
Hopelessness ^g	Depressive symptoms ^f	−0.59	−4.75	<.001	
	Schizophrenia or schizoaffective disorder	0.03	0.28	.78	
	Social anxiety ^c	0.31	2.75	.007	.44
	Shame ^d	0.13	1.25	.22	
	Devaluing work/education ^e	0.18	2.00	.049	
Social Performance ^h	Ingroup comparisons ^e	−0.01	−0.06	.95	
	Blaming discrimination ^e	0.03	0.27	0.79	
	Depressive symptoms ^f	0.26	2.34	.02	
	Schizophrenia or schizoaffective disorder	0.11	1.24	.22	
	Social anxiety ^c	0.12	0.94	.35	.30
Seating Distance ⁽ⁱ⁾	Shame ^d	0.13	1.08	.29	
	Devaluing work/education ^e	−0.14	−1.41	.16	
	Ingroup comparisons ^e	−0.57	−5.23	<.001	
	Blaming discrimination ^e	0.05	0.41	.68	
	Depressive symptoms ^f	−0.08	−0.68	.50	
Social Performance ^h	Schizophrenia or schizoaffective disorder	0.01	0.06	.96	
	Social anxiety ^c	−0.02	0.56	.45	.14
	Shame ^d	0.01	0.01	.91	
	Devaluing work/education ^e	0.06	0.13	.72	
	Ingroup comparisons ^e	−0.21	2.84	.09	
Seating Distance ⁽ⁱ⁾	Blaming discrimination ^e	−0.08	0.36	.55	
	Depressive symptoms ^f	0.01	0.04	.84	
	Schizophrenia or schizoaffective disorder	0.50	0.61	.43	

^a Linear regressions on self-esteem, hopelessness and social performance; and logistic regression on seating distance (close versus far).

^b Rosenberg's Self-Esteem Scale (Rosenberg, 1965).

^c Liebowitz Social Anxiety Scale (Liebowitz, 1987).

^d Test of Self-Conscious Affect-3 (Tangney et al., 2000).

^e Cognitive coping response to stigma-related stress (Crocker and Major, 1989).

^f Center for Epidemiologic Studies Depression Scale (Radloff, 1977).

^g Beck's Hopelessness Scale (Beck et al., 1974).

^h Maryland Assessment of Social Competence (Bellack et al., 2006).

ⁱ Seating distance from a talkative "normal" person.

significant predictors acted independently (Table 2). Because of its skewed distribution, seating distance was coded as a binary dependent variable (close, score 1 or 2, versus distant, score 3 or 4) in a logistic regression (Table 2). The five independent variables in these regressions were only moderately interrelated (all correlation coefficients $< .50$). Reduced self-esteem and increased hopelessness were independently predicted by the emotional stress reactions of social anxiety and shame. The cognitive coping response of devaluing work/education predicted more hopelessness beyond the variance explained by shame and social anxiety. Regarding behavioral outcome measures, endorsement of ingroup comparisons as a coping mechanism predicted both poorer social performance and increased seating distance from outgroup members. Social anxiety or shame did not predict behavioral measures beyond the variance explained by coping responses.

We then repeated the four regression analyses to control for two possible confounding variables (Table 3), depressive symptoms and diagnosis of schizophrenia or schizoaffective disorder (versus bipolar disorder or unipolar depression). Because the subgroup comparisons had not shown any significant group differences between the schizophrenia and schizoaffective group, both were collapsed into one diagnostic category and contrasted with affective disorders as an independent dummy variable. Diagnosis did not predict any of the outcomes, while depressive symptoms predicted self-directed outcomes but not behavior (Table 3). After controlling for depression, social anxiety remained a significant predictor of self-esteem and hopelessness, but shame did not. Devaluing work and education remained a significant predictor of hopelessness; and ingroup comparisons still predicted social performance, but predicted seating distance only at a trend level.

Since correlations and regressions supported the link between stress appraisal, emotional responses (social anxiety and shame) and two outcome variables (self-esteem and hopelessness), additional regression analyses examined whether the effect of stress appraisal on self-esteem and hopelessness was mediated by emotional responses. Stress appraisal was regressed on self-esteem and hopelessness first by itself and then together with social anxiety and shame. According to Baron and Kenny (1986) a mediational model is supported if the independent variable (stress appraisal) predicts the dependent variable (self-esteem or hopelessness), but is no longer significant in the full model that includes the mediator variables (shame and social anxiety). While stress appraisal, when regressed on self-esteem or hopelessness alone, was significant ($p = .005$ and $p = .015$, respectively), it turned non-significant ($p = .10$ and $p = .23$, respectively) after adding shame and social anxiety as independent variables to the equation.

4. Discussion

We tested a model of cognitive appraisal of stigma-induced stress and its consequences, emotional stress reactions and coping responses, that in turn shape broader outcomes (Major and O'Brien, 2005) among people with schizophrenia and other mental illnesses. Part 1 of this study discussed predictors of stigma-related stress appraisal and here in part 2 we investigated the consequences of stigma stress. Our first hypothesis on the link between stress

appraisal and responses was supported for involuntary emotional responses, underlining the role of shame and social anxiety for stigmatized individuals (Birchwood et al., 2007; Lewis, 1998; Rüsch et al., 2006a; Spencer et al., 1999). However, we could not find evidence for the hypothesized impact of stress appraisal on cognitive coping mechanisms. Stigma stress as well as coping responses play out partly in threatening situations in which stigmatizing cues become salient (Kaiser et al., 2004; McCoy and Major, 2003) which may limit the sensitivity of our trait-based investigation.

Our second hypothesis regarding stress responses and outcomes was partially supported. Mediating the influence of stress appraisal on self-directed outcomes, emotional stress responses predicted self-esteem and hopelessness but, unlike cognitive coping responses, were largely unrelated to social performance. Emotional stress responses, particularly social anxiety, predicted a negative self-concept as indicated by hopelessness and low self-esteem even after controlling for depressive symptoms and diagnosis. Cognitive coping mechanisms, on the other hand, were more predictive of social performance than of self-directed outcomes. Devaluing work and education, which predicted hopelessness beyond the variance explained by shame and social anxiety, seems a particularly problematic coping style. Distancing oneself from this domain may have short-term benefits for self-esteem in case of professional failures, but reduces long-term hope to compete professionally even after taking depressive symptoms and diagnosis into account. All cognitive coping responses were associated with increased seating distance from "normal" majority outgroup members which is plausible because these coping responses imply cognitive distancing from outgroup standards.

Crocker and Major (1989) pointed out potential negative consequences of the self-protective coping strategies which was underlined by our finding of a strong association between the coping style of ingroup comparisons and poor social performance. Ingroup comparisons may buffer self-esteem, but they can undermine motivation and achievement in various domains. Upward comparisons with advantaged outgroups, on the contrary, increase performance even if lowering self-esteem (Seaton et al., 2008). This highlights the unfortunate fact that for stigmatized individuals there is no easy way out. The coping strategy of ingroup comparisons, facilitated by social segregation typical for many people with serious mental illness, may come at the price of decreased social performance.

Before drawing conclusions, limitations of our study have to be considered. First, our data are cross-sectional and therefore cannot determine causality. While this stress-coping model of stigma (Major and O'Brien, 2005) plausibly suggests that stress leads to stress reactions which in turn influence outcomes, reverse causality or feedback loops are possible and longitudinal studies need to investigate the direction of causal relationships. Second, stigma stress and responses are often related to threatening situations which were not assessed by the trait-measures in our study. Third, involuntary stress responses like decreased test performance (Quinn et al., 2004) or physiological reactions (Blascovich et al., 2001), other coping mechanisms beyond those examined in our study (Roe et al., 2006) and additional outcomes such as health or educational achievement should be investigated in future research. Nevertheless, our findings highlight the role of

cognitive appraisal of stigma-related stress as well as emotional and cognitive reactions that in turn shape broader outcomes. Our results were mostly independent of psychiatric diagnosis which is consistent with stigma as a stressor across different mental illnesses.

In part 1 we had identified factors that predict the perception of mental illness stigma as stressful and therefore may render stigmatized individuals more vulnerable to stigma stress. In part 2 we found evidence that stigma stress leads to both involuntary emotional reactions and cognitive coping responses which in turn shape broader outcomes. Both parts support the stress-coping model of stigma (Major and O'Brien, 2005) when applied to people with schizophrenia and other mental illnesses. Our findings have implications for interventions that aim to reduce stigma-related stress and thus the negative impact of public stigma on stigmatized individuals, whether in group programs (Knight et al., 2006; MacInnes and Lewis, 2008) or in individual settings using narrative approaches (Lysaker et al., 2007a). These interventions could address emotional stress reactions such as social anxiety and shame as well as coping responses that offer a short-term relief, but may undermine long-term outcomes.

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Contributors

N.R. and P.W.C. designed the study. N.R., K.P., A.R., S.W. and K.B. organized recruitment and collected data. N.R., P.W.C. and M.O. analyzed, and all authors interpreted the data. N.R. wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

All authors declare that they have no conflict of interest.

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