



Published in final edited form as:

*Fatigue*. 2013 ; 1(4): . doi:10.1080/21641846.2013.843255.

## Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) Symptom Severity: Stress Management Skills are Related to Lower Illness Burden

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### Abstract

**Background**—The onset of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) typically involves reductions in *activities of daily living* and *social interactions* (jointly referred to as “illness burden”). Emotional distress has been linked to increased reported symptoms, and stress management skills have been related to lower fatigue severity in CFS patients. Symptom severity and illness burden are highly correlated. The ability to manage stress may attenuate this relationship, allowing individuals to feel less burdened by the illness independent of the severity of their symptoms.

**Purpose**—This study aimed to evaluate if perceived stress management skills affect illness burden via emotional distress, independent of ME/CFS symptom severity.

**Methods**—A total of 117 adults with ME/CFS completed measures of perceived stress management skills, emotional distress, ME/CFS symptom severity and illness burden.

**Results**—Regression analyses revealed that greater perceived stress management skills related to less social and fatigue-related illness burden, via lower emotional distress. This relationship existed independent of the association of symptom severity on illness burden, and was stronger among those not currently employed.

**Conclusions**—Ability to manage stress is associated with a lower illness burden for individuals with ME/CFS. Future studies should evaluate the efficacy of psychosocial interventions in lowering illness burden by targeting stress management skills.

### Keywords

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome; stress management; emotional distress; illness burden

## Introduction

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a prevalent disabling disorder (estimated at 400,000 to 800,000; 1, 2) with a substantial physical, emotional and economic burden (estimated at \$9.1 billion annually in lost productivity; 3). Symptoms of this disorder include profound fatigue, post-exertional malaise, sleep dysfunction, pain, and cognitive impairments. The onset of ME/CFS, typically involves a number of substantive decrements in an individual's day-to-day functioning (4, 5). These changes can include limitations on general activities of daily living, such as bathing and dressing oneself, as well as limitations on social interactions, such as visiting with others. These perceived limitations can be conceptualized as an individual's *illness burden*.

In the context of ME/CFS, one's illness burden can be further delineated into: a) *fatigue-related illness burden*, which encompasses general interference in activities of daily living due to fatigue, a cardinal symptom of the syndrome, and b) *social illness burden*, which encompasses limitations in social interactions. Across a variety of health conditions, there is a positive correlation between illness symptom severity and illness burden (6-8). Due to the multi-systemic and unpredictable nature of ME/CFS and because effective treatments are lacking, there is a need to identify factors that can reduce the burden of illness and improve daily functioning among ME/CFS patients who must deal with ongoing symptoms. The discovery of these factors capable of reducing the burden of illness in afflicted individuals is of utmost importance to clinical researchers as these factors can then be utilized as targets of interventions.

Psychosocial factors, such as coping skills, may impact the relationship between the severity of illness and the overall burden of the illness because such skills may mitigate the emotional distress associated with managing the illness. In the case of ME/CFS, individuals lacking the skills to manage the challenges of the illness may have low self-efficacy and underestimate their abilities to engage in activities, leading to withdrawal, greater distress, and a higher illness burden. In contrast, those with more adequate coping skills to manage such challenges may show better adaptation to illness, less distress, and a lower illness burden (9, 10).

It has been repeatedly observed that stressors and emotional distress may exacerbate ME/CFS symptoms (10-13) and we have formulated a model to explain this association (14). The hypothesized model follows the Folkman and Lazarus (15) definition of stress, which states that stress occurs when a situation is appraised by the individual as exceeding his or her personal resources. Therefore, emotional distress (decreases) would occur after the initial utilization of personal stress management resources. This model has been used in other cross-sectional studies involving clinical populations dealing with physical symptoms (16, 17).

Our research group previously found that greater perceived stress management skills were associated with lower levels of fatigue severity via lowered levels of emotional distress suggesting that fluctuations in emotional distress may mediate symptom severity (18). Other work demonstrated that teaching stress management skills (such as the effective use of relaxation techniques and cognitive restructuring) may reduce emotional distress and mitigate ME/CFS symptoms (19). Thus, increasing levels of perceived stress management skills may work on symptoms by reducing distress. It is also plausible that stress management skills are applied by CFS patients to reinterpret the impact of symptoms on their day-to-day illness burden as they reduce their emotional distress.

This study examined whether greater perceived stress management skills are associated with lower reports of both general and social illness burden, independent of ME/CFS symptom

severity. Based on our theoretical model, we hypothesized that having greater perceived stress management skills relates to less fatigue-related and social illness burden via lower emotional distress (see Figure 1). Because individuals experiencing significant emotional distress may disengage from their social environment (20, 21), we hypothesized that these relationships would be greatest for social illness burden, which includes willing participation in social activities. Because coping skills and emotional distress processes have been found to differ across the lifespan (22, 23), among men and women (24-26), and among employed compared to unemployed persons, such that employed individuals may demonstrate more positive coping strategies (27, 28), age, gender and employment status were examined as moderators of the effects of perceived stress management skills on markers of illness burden via emotional distress.

## Methods

### Participants and Procedures

Participants in the present study were recruited primarily through physician referral for a larger telephone-delivered intervention study. Initial eligibility was determined by the presence of a physician-determined ME/CFS diagnosis according to the Centers for Disease Control (CDC) criteria (29). Participants were required to be fluent in English, live within the study area, have an active home telephone line, and be between the ages of 21 and 75 years. A telephone screening interview was used to determine eligibility. The Short Portable Mental Status Questionnaire (30) was used to determine cognitive impairment. Participants were excluded if they made four or more errors on this measure, as four or more errors indicate cognitive impairment. Potential participants were also excluded if they had a medical condition (e.g., AIDS, lupus, rheumatoid arthritis) that would influence biological processes associated with CFS symptomology, or if they had a past psychiatric hospitalization, met criteria for schizophrenia, bipolar disorder, or substance abuse, or were actively suicidal. Potential psychiatric exclusions were assessed using a brief screening adapted from the Structured Clinical Interview for the DSM-IV (31).

Interested participants who were deemed eligible for the study signed an informed consent form approved by a University-based Institutional Review Board. Following enrollment, participants received a home visit by a member of the study staff. During this visit, a battery of measures examining ME/CFS symptoms and participants' psychosocial status was administered. Participants were each compensated \$50 for their time and effort.

### Measures

**Perceived stress management skills**—The Measure of Current Status (MOCS;32) was used to assess perceived stress management skills. Participants were asked to rate their perceived ability to appropriately respond to challenges and demands of daily life on a 5 point scale which ranged from “1 - I cannot do this at all” to “5 – I can do this extremely well.” Items on the MOCS are based on tendencies and behaviors that are associated with efficient stress management, such as “I am able to use mental imagery to reduce any tension I experience” and “I can clearly express my needs to other people who are important to me.” Higher scores on the MOCS indicate better perceived stress management skills. Consistent with past research using the MOCS for men with localized prostate cancer (33), the items on the MOCS were summed to create an overall stress management measure. In the present study, the MOCS demonstrated adequate psychometric properties and had a high degree of internal consistency (Cronbach's  $\alpha = .85$ ).

**Emotional distress**—The Perceived Stress Scale (PSS; 34), the Center for Epidemiologic Studies Depression Scale (CES-D; 35), and the Profile of Mood States (POMS) Depression-

Dejection and Anxiety-Tension subscales (36) were administered to assess the degree of emotional distress during the prior week. Consistent with past research suggesting that feelings of perceived stress, depression and anxiety contribute to the total experience of emotional distress (37, 38), an emotional distress composite score was created by summing the z-scores of the PSS, CES-D, POMS Depression-Dejection and POMS Anxiety-Tension subscales. This composite score demonstrated a high degree of internal consistency in the present sample (Cronbach's  $\alpha = .89$ ).

**ME/CFS symptom severity**—The total score from the CDC Symptom Inventory (39) was used to measure ME/CFS symptom severity over the past month. Participants were asked to separately rate the frequency and intensity of 20 ME/CFS-related symptoms on 5 point scales. The frequency and intensity scales were then summed and multiplied to create the total symptom severity score. These 20 symptoms include the 8 case definition symptoms (29) as well as other common ME/CFS-related symptoms, such as sleeping problems, stomach or abdominal pain, and sensitivity to light. This measure has been shown to be a reliable measure of ME/CFS symptoms (39) and demonstrated a high degree of internal consistency in the present sample (Cronbach's  $\alpha = .83$ ).

**Fatigue-related illness burden**—The degree to which participants were generally burdened by their fatigue was measured using the Interference subscale of the Fatigue Symptom Inventory (FSI; 40). This scale consists of 7 items which are answered on an 11-point scale ranging from “0 – no interference” to “10 – extreme interference.” Items on this measure ask participants to rate how much, in the past week, fatigue interfered with various activities including their “ability to bathe and dress” independently, and their “ability to concentrate.” In the current study, the general illness burden measure demonstrated a high degree of internal consistency (Cronbach's  $\alpha = .85$ ).

**Social illness burden**—The degree to which participants experienced declines in social activities as a result of their illness was measured using the Social Interaction subscale from the Sickness Impact Profile (SIP; 41). Participants were asked whether or not they engaged in a range of socially-relevant behaviors as a result of their illness and provided dichotomous responses of “yes” or “no.” Sample items from this scale include “I isolate myself as much as I can from the rest of the family” and “I am doing fewer social activities with groups of people.” This measure demonstrated adequate internal consistency in the present sample (Cronbach's  $\alpha = .74$ ).

## Statistical Analyses

Statistical analyses were performed using SPSS version 18.0. Linear regressions and Pearson correlations were conducted to examine the relationships between socio-demographic factors, perceived stress management skills, emotional distress and measures of illness burden. In order to examine the proposed indirect relationships between perceived stress management skills and illness burden via emotional distress, an SPSS macro developed by Preacher and Hayes (42) was used. This macro allows for the estimation of indirect effects with covariates included in the model, and calculates the bias-corrected bootstrapped confidence intervals for the indirect effect. Bootstrapped confidence intervals were used to assess for indirect effect because this method does not assume normality of the distribution of the indirect effect, which provides increased sensitivity to detecting effects compared to more traditional methods, such as Baron and Kenny (43) or the Sobel test (44). Further, this method is recommended for small to medium sample sizes (42). In the present study, perceived stress management skills served as the independent variable, emotional distress served as the mediator, and fatigue-related illness burden and social illness burden served as the dependent variables in two separate models. In order to examine these

relationships independent of ME/CFS symptom severity, the total score from the CDC Symptom Inventory (39) was included as a covariate in both models. To examine potential sociodemographic (age, gender and employment status) moderators of the indirect effects models (see figure 1), another SPSS macro developed by Preacher and colleagues (45) was used. This macro generates an omnibus interaction effect and provides a method for examining the significance of the indirect effect at different levels the proposed moderator. The total score from the CDC Symptom Inventory (39) was again included as a covariate in the moderated mediation model.

## Results

### Study Sample

Of the 161 men and women approached to participate in the study, 134 individuals were eligible and 17 declined participation in the study, primarily due to time constraints, resulting in a final sample of 117. Major reasons for ineligibility included living outside the study area (40%), not having a ME/CFS diagnosis (22%), and having an exclusionary medical condition (19%). None of the potential participants were excluded for cognitive impairment. The majority of participants in the sample were women (72%) and non-Hispanic White (79.5%). The average age was 50.7 years ( $SD = 11.5$ ) and participants were highly educated, with 87.2% of the sample having had attended at least some college. At the time of assessment, approximately 42.7% of the sample was married. The majority of participants (66.2%) were not working, with 40.2% of participants on disability, 13.7% unemployed, and 10.3% retired.

Although official eligibility criteria for the study stated that participants needed to have a ME/CFS diagnosis based on the Fukuda (29) case definition, 109 participants were recruited from a clinic that also utilizes the Carruthers (2003) case definition for ME/CFS (46). Therefore, in addition to meeting the Fukuda criteria (fatigue of > 6 months duration and 4 of 8 symptom criteria including fatigue, myalgia, arthralgia, headache of a new and different type, nonrestorative sleep, cognitive complaints, sore throat and tender lymph nodes), these participants also met the Carruthers criteria—exercise-induced relapse and symptoms from at least of 3 categories (immune, autonomic, endocrine). The other 8 participants enrolled in the study had their ME/CFS diagnosis confirmed using solely the Fukuda (1994) definition. There were no differences on main study variables between those participants meeting both the Carruthers and the Fukuda case definitions, versus those meeting the Fukuda (29) case definition alone (all  $p$ 's > .20).

### Preliminary Analyses

Results of correlations examining the relationships between the study variables are presented in Table 1. As hypothesized, total ME/CFS symptom severity was positively associated with both fatigue-related illness burden and social illness burden ( $p$ 's < .05). Significant relationships were found between employment status and age, symptom severity, and social illness burden such that unemployed participants were older, reported a greater symptom severity, and reported higher levels of social illness burden compared to currently employed participants ( $p$ 's < .05).

### Stress Management Skills, Emotional Distress and Indicators of Illness Burden

**Fatigue-related illness burden**—Perceived stress management skills were not directly related to fatigue-related illness burden ( $r = -.157, p = .099$ ) while emotional distress was significantly related to fatigue-related illness burden ( $r = .456, p < .001$ ). However, as seen in figure 2, greater perceived stress management skills were related to less emotional distress ( $r = -.460, p < .001$ ). Using bootstrapping, statistical support was found for an

indirect effect model. The 95% confidence interval for emotional distress as a mediator was  $-.412$  to  $-.089$ . Mediation was indicated by the fact that this confidence interval did not contain zero, providing support that the indirect effect is significantly different than zero. These findings support the hypothesis that greater perceived stress management skills relate to lower fatigue-related illness burden reports via lower emotional distress. These paths existed independent of the effect of ME/CFS symptom severity, which remained a significant predictor in the model ( $\beta = .349, p < .001$ ).

**Social illness burden**—Results of linear regression analyses indicated that perceived stress management skills were negatively correlated with social illness burden ( $\beta = -.340, p < .001$ ). Conversely, emotional distress was positively related to social illness burden ( $\beta = .439, p < .001$ ). As noted previously, greater perceived stress management skills related to less emotional distress. As seen in figure 3, the addition of emotional distress to the model in which perceived stress management skills predicted social illness burden created a non-significant relationship between perceived stress management skills and social illness burden ( $\beta = -.167, p = .084$ ). Further, based on 1000 bootstrap resamples, the 95% confidence interval for emotional distress as a mediator was  $-.082$  to  $-.014$ . Mediation was indicated by the fact that this confidence interval did not contain zero. These findings support the hypothesis that greater perceived stress management skills relate to lower social illness burden reports via lower emotional distress. These paths existed independent of the effect of ME/CFS symptom severity, which did not remain significant in this model ( $\beta = .160, p = .072$ ).

**Sociodemographic Moderator Analyses**—Age, employment status and gender were examined as possible moderators of the indirect effect of perceived stress management skills on illness burden via emotional distress. Due to the finding that older participants were less likely to be employed at time of assessment, age was included as an additional covariate when examining employment status as a moderator of the indirect effect model. Neither age, employment status nor gender served as a moderator in the indirect effect model predicting fatigue-related illness burden ( $p$ 's  $> .05$ ).

When examining the indirect effect model predicting social illness burden, employment status was a significant moderator ( $p < .01$ ), such that the relationship between perceived stress management skills and social illness burden via lowered emotional distress was stronger for individuals who were not working at the time of assessment ( $p = .015$ ) than for individuals who were employed ( $p = .051$ ). Based on 1000 bootstrap resamples, the 95% confidence interval for emotional distress as a mediator was  $-.097$  to  $-.015$  for those who were not working, and was  $-.082$  to  $-.016$  for those who were employed, indicating that the indirect effect of perceived stress management skills on social illness burden was significantly different from zero in both groups. Gender and age did not serve as moderators in the indirect effect model predicting social illness burden ( $p$ 's  $> .05$ ).

## Discussion

The present study examined relationships between perceived stress management skills, emotional distress, and illness burden among adults with ME/CFS. Our past work has demonstrated that having greater perceived stress management skills relates to a lower fatigue symptom severity via the influence of greater perceived stress management skills on emotional distress levels (18). These past findings were consistent with research on individuals with cancer diagnoses showing that greater perceived stress management skills relate to less distress and greater physical and emotional health-related quality of life (17, 37). Here, we demonstrate that having greater perceived stress management skills are associated with a lower illness burden, via lowered emotional distress, and that these

relationships exist independent of total symptom severity. We also demonstrated that the relation between perceived stress management skills and one's social illness burden was stronger than the relation between perceived stress management skills and one's general fatigue-related illness burden.

Results of the present study indicated that the indirect effect model in which greater perceived stress management skills related to a lower fatigue-related illness burden was not moderated by age, gender or employment status. The lack of moderation in the aforementioned indirect effect model demonstrated that, regardless of age, gender or employment status, individuals with good perceived stress management skills reported a lower fatigue-related illness burden and were better able to maintain activities of daily living such as self-grooming and completing tasks in the home.

However, moderation was evident in the indirect effect model in which greater perceived stress management skills related to a lower social illness burden. Specifically, the indirect effect was found to be stronger among those who were not working at the time of assessment compared to those who were employed, although the relationship was significant for both groups. These results suggest people who are not currently employed may particularly benefit from stress management training. These are novel findings in the literature on stress management in ME/CFS, but are consistent with past research indicating differences in coping with stress and social adjustment between chronically ill individuals who are employed compared to those who are not currently working (27, 28). Contrary to our hypothesis, gender and age did not moderate the indirect effect model in which greater perceived stress management skills related to a lower social illness burden, indicating the men and women across the age continuum responded in similar patterns.

The moderation results should be interpreted with caution. Although the social interaction subscale of the SIP, used to quantify social illness burden does refer to work-related social activities, it is possible that work-related social contact, which is inherent in many work environments, influenced participants' recall of their social activities (41). More sensitive assessments, such as calendar tracking of social activities, are needed to further elucidate the potential differential impact of stress management skills on individuals' social illness burden among those who are employed and those who are not currently working. Based on commonly observed differences in stress and coping among different ethnic groups (48, 49), the indirect effect model in which greater perceived stress management skills related to a lower illness burden may be moderated by ethnicity. However, the ethnic homogeneity of the present sample did not provide us with the ability to reliably assess differences by ethnic group.

There are a few notable limitations of the present study. Information regarding the nature of participants' illness onset (sudden versus gradual) was not collected. Given past research suggesting more severe symptoms in those with a sudden onset of illness compared to a gradual illness onset (50), the observed relationships should be separately examined in these subgroups of participants in the future. Analyses were based on a cross-sectional design; therefore caution should be used in interpreting the relationships. The associations between perceived stress management skills, emotional distress, and illness burden may be bi-directional, such that individuals who experienced a high illness burden responded with increased emotional distress and deemed themselves less able to manage current stressors. These relationships should be further examined longitudinally to more clearly delineate if greater stress management skills lead to lower emotional distress, or if less distressed individuals perceive themselves as more capable of managing stressors.

Additionally, the present study relied on self-report measures. Although the self-report measures of emotional distress, perceived stress management skills, and illness burden have been well validated, the reliance on self-report measures alone may have introduced a common methods bias that may account for some of the observed relationships between variables (51). The use of a dichotomous measure of social illness burden (SIP; 41) compared to the likert-type measure for fatigue-related illness burden (FSI; 40) may partially account for the observed differences in relation strength between perceived stress management skills and the illness burden variables. While the CDC Symptom Inventory (39) is a validated self-report measure of ME/CFS symptoms, there are more commonly used measures, such as the Chalder Fatigue Scale (52). The use of the CDC Symptom Inventory may be considered a limitation of this study as it is not directly comparable to research using the Chalder Fatigue Scale. Further, while fatigue is a central symptom of ME/CFS, fatigue-related illness burden may not encompass the full extent to which one's symptoms burden general life activities, since other symptoms (such as pain) may have separate and significant impacts. There is a definite need to develop more comprehensive and consistent measures of illness burden to further elucidate our understanding of various aspects of living with a chronic illness.

Despite these limitations, results of the present study contribute to the limited literature on modifiable psychological constructs that contribute to the illness burden of both men and women with ME/CFS. This is the first study to demonstrate the potential health benefits of stress management skills on day-to-day functioning with an illness, while accounting for the impact of illness symptom severity. Considering the long, continued search for appropriate medical treatments for individuals with ME/CFS, these findings offer hope that interventions which enhance stress management skills may reduce the burden of illness among individuals with ME/CFS. Previously, a small pilot study demonstrated cognitive-behavioral stress management (CBSM) group intervention's ability to decrease both symptom severity and perceived stress, while improving self-reported quality of life (19). However, the small sample size in the pilot study limited the investigators' ability to adequately examine the mechanisms by which these benefits were attained. The present study offers a model to tailor psychosocial interventions to improve day-to-day functioning of individuals with ME/CFS.

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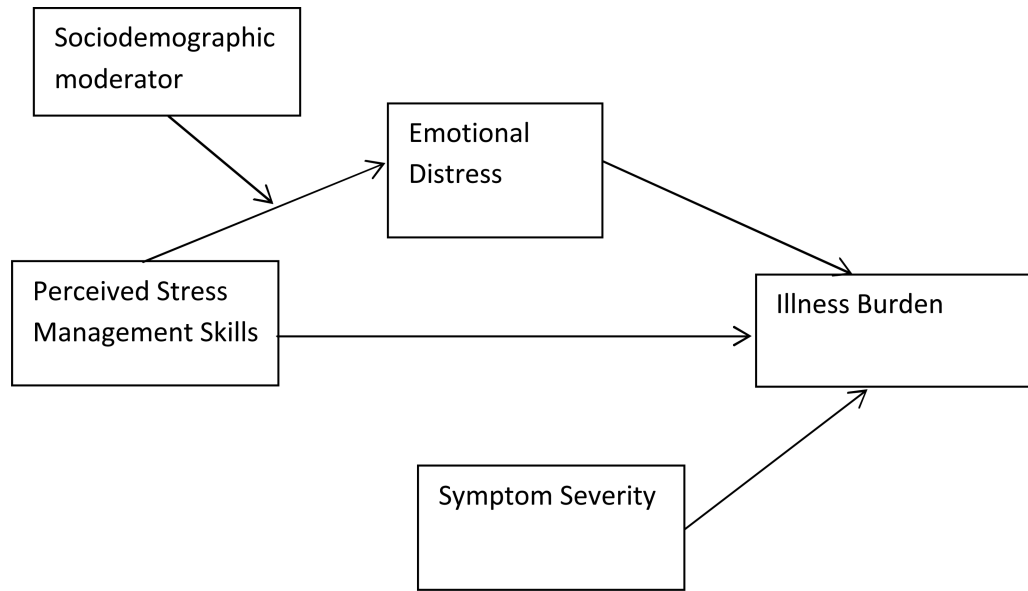
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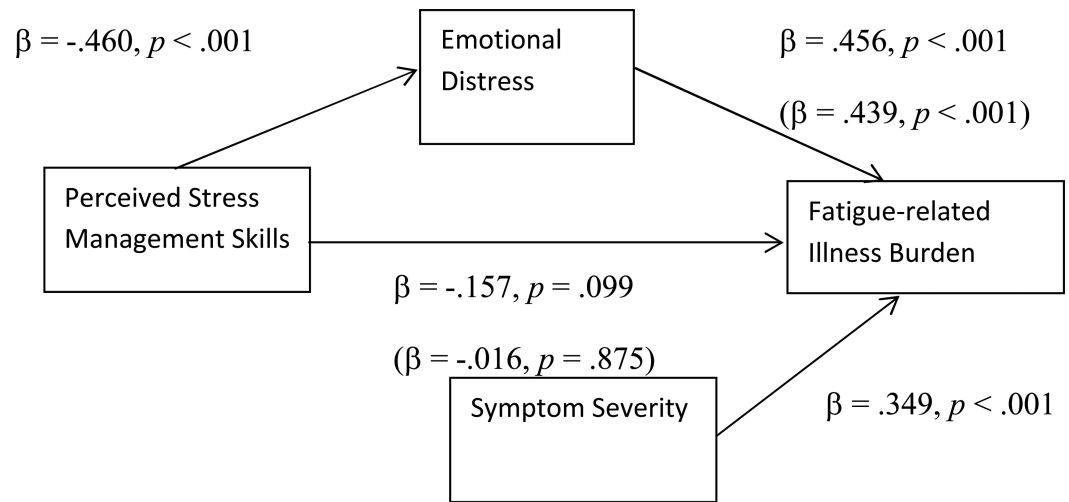
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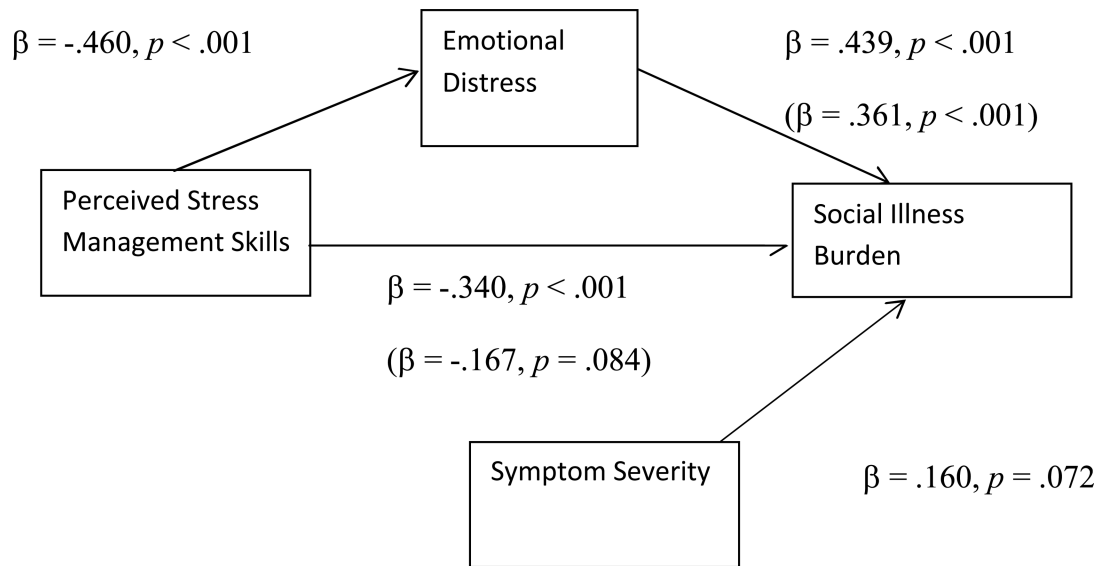
**Figure 1.**  
Theoretical model



Note: 95% C.I. for full model -.412, -.089

**Figure 2.**

The indirect effect of perceived stress management skills on fatigue-related illness burden



Note: 95% C.I. for full model  $-.082, -.014$

**Figure 3.**

The indirect effect of perceived stress management skills on social illness burden

**Table 1**

Pearson correlations between study variables

	1	2	3	4	5	6	7	8
1 Age	-							
2 Gender	.09	-						
3 Partner Status	.04	-.04	-					
4 Employment Status	-.29**	-.17	-.08	-				
5 Total Symptom Severity	-.11	.17	-.00	-.20*	-			
6 Social Illness Burden	-.02	-.03	.02	-.19*	.253**	-		
7 General Illness Burden	-.01	.02	.01	-.14	.41**	.46**	-	
8 Stress Management Skills	-.13	-.13	.05	-.02	-.06	-.34**	-.16	-
9 Emotional Distress	-.07	.15	-.06	-.13	.25*	.44**	.46**	-.46**

\* significant at 0.05 level

\*\* significant at 0.01 level