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Development and validation of the sickle cell stress scale-adult

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Abstract

Disease-specific stress can partly explain Sickle Cell Disease (SCD) healthcare utilization. We developed and validated two measures of adult SCD-specific stress for research and clinical care. A large cohort of adults with SCD completed both the 3-item Likert-scale adapted from a previous disease stress measure and a 10-item Likert-scale questionnaire drafted specifically to measure SCD stress. They concurrently completed a psychosocial and health-related quality of life scale battery, then subsequently daily pain diaries. Diaires measured: daily intensity, distress and interference of pain; self-defined vaso-occlusive crises (VOC), opioid use, and types of healthcare utilization for up to 24 weeks. Analyses tested Cronbach's alpha, correlation of the three-item and 10-item stress scales with the concurrent battery, with percentages of pain days, VOC days, opioid use days, and healthcare utilization days, and correlation of baseline stress and 6-month stress for the 10-item scale. Cronbach's alpha was high for both the 3-item (0.73) and 10-item (0.83) SCD stress scales, test–retest correlation of 0.55, expected correlation with the concurrent battery, and correlation with diary-measured healthcare utilization over 6 months. The correlations with the 3-item scale were stronger, but only statistically significant for depression-anxiety. The correlation between the two stress scales was 0.59. Both the 3-item and the 10-item stress scales exhibited good face, construct, concurrent, and predictive validity as well as moderate test–retest reliability. Further scale validation should determine population norms and response to interventions.

KEYWORDS
assessment, coping, healthcare utilization, pain, sickle cell disease, stress

Novelty Statement

- We validated relationships between stress and utilization as well as stress and other psychosocial variables in SCD, leading toward validation of New 3-item and 10-item sickle cell-specific stress scales.
- Further validation should determine population norms and response to interventions.
- The 3-item scale could assess a general level of stress in SCD while the 10-item would measure more detailed and more SCD-specific stressors pre- and post-intervention.

1 | INTRODUCTION

1.1 | Sickle cell disease and stress

Sickle cell disease (SCD), a set of autosomal recessive hemoglobinopathies[1] primarily affecting patients of African and Mediterranean descent,[2] including approximately 100 000 Americans[3] is highly stressful. It is associated with a diminished immune response,[4] and diminished immune responses have long been associated with stress in other diseases.[5] It is characterized by exacerbations and fluctuations in pain,[6,7] and pain also has been associated with stress in other chronic diseases.[8,9] Most adult patients with SCD are in pain over half their days,[10] and use opioid analgesics for three-fourths of their days.[11]

SCD is well-known for vaso-occlusive crises (VOCs) resulting from deformed, very adherent red blood cells containing deoxyhemoglobin S polymers, as well as an inflammatory "soup" of very adherent white blood cells, platelets, and vascular endothelium.[12] Vaso-occlusion causes hypoxia, hypercoagulopathy, and other pathological dysfuntion.[13,14] This cacophony of vaso-occlusion, inflammation, hypercoagulopahty, and hypoxia may result in organ damage and early death.[15]

Stress may be evoked not only by pain, but also by increased healthcare utilization due to pain, and by the uncertainty of whether hospital care will be required for a given SCD VOC. VOCs are even more frequent in patients with chronic SCD pain,[16] and SCD-related ED utilization rises dramatically after childhood,[17] as do readmission rates for acute care.[6]

Along with pain, anemia is a significant stressor in SCD. Severe destructive anemia results from the above pathophysiological cacophony.[4] The stress of fatigue and health related quality of life are correlated with the degree of anemia.[18,19] A meta-analysis of 41 SCD studies showed that chronic anemia is associated with worse SCD outcomes including death.[20]

In childhood, stress may be evoked by the fear of death from infections, preventable only with prophylactic antibiotics and vaccines,[21] or from stroke, preventable only with prophylactic transfusions.[22] Even in adults, stress may be evoked by the fear of early death. People with SCD die on average 20 years earlier than those without SCD, mostly from organ failure.[15,23–25]

For males with SCD, stress may be evoked by priapism—recurrent, unwanted, painful erections often requiring emergency surgical drainage procedures and often leading to erectile dysfunction.[26]

Accompanying the stressors of the disease are the stress of poverty, fear of loss of work, low educational attainment, and poor social support. Each are more common in SCD, each are correlated with disease severity, and each help to explain depressive symptoms in SCD.[27] Patients also may worry about insurance coverage and healthcare financing. Compared to US blacks, SCD patients are less often from two-parent families (40 vs. 54%), more often from single female heads-of-household (53 vs. 42%), and more often unemployed and disabled.[28]

Not unexpectedly, SCD stress may accompany and may correlate with depression and a sense of impending doom. More VOCs predict shorter survival.[24] The mortality rate is worsening among adults[29] and may rise along with utilization and complications during the third decade and beyond.[6,30,31]

SCD stress may vary with functional status, and with pain perceptions and interpretations. SCD organ failure may include brain disease[22] and may be associated with catastrophizing,[32] somatization,[33] and other psychological responses likely diminishing activities of daily living and recreation.[34]

1.2 | Sickle cell disease and healthcare utilization

SCD results in increased hospital costs[35] from SCD VOCs.[36,37,38,39] Understanding stress in SCD may lead to better management of healthcare utilization in SCD.[40,41]

Figure 1 represents a refined version of a published conceptual model of emergency and hospital utilization due to pain and VOC in SCD[42]-based on the literature published on various biopsychosocial and other behavioral models.[43–51] We posit static factors (demographics, genotype) that influence utilization. As well, we posit a combination of both static and variable enabling forces[16,32,33,37,52–55] that may promote utilization. Similarly, we posit an opposing set of static and variable forces[56,57,57–63,64–66,67–69,70]; that may impede utilization. We posit that these forces oppose one another, and together govern whether utilization occurs in response to a given SCD VOC or pain state.

1.3 | Purpose of study

Based on the above model, we took a different view than Gil and others who focused on daily stress, and hypothesized that, as has been found in other diseases,[71] disease-specific stress as a latent trait variable, is positively associated with SCD utilization, and that stress reduction may in turn curb utilization. We developed and tested a measure of disease-specific stress experienced by adults with SCD to help understand how stress fits into a model of SCD health care utilization. We hoped that measurement of disease-specific stress would allow testing and demonstration of stress reduction tools for SCD utilization management. Herein, we describe the development and validation of the measure.

2 | METHOD

2.1 | Development of the questionnaire

Based on the then-available literature which strongly suggested important content topics and items of SCD stress, the authors constructed a pilot questionnaire. To further develop drafted items, we conducted one informal set of patient interviews in our adult SCD clinic. We then conducted a pilot study where we fielded the items for feasibility and face validity. Our initial three-item, less SCD-specific
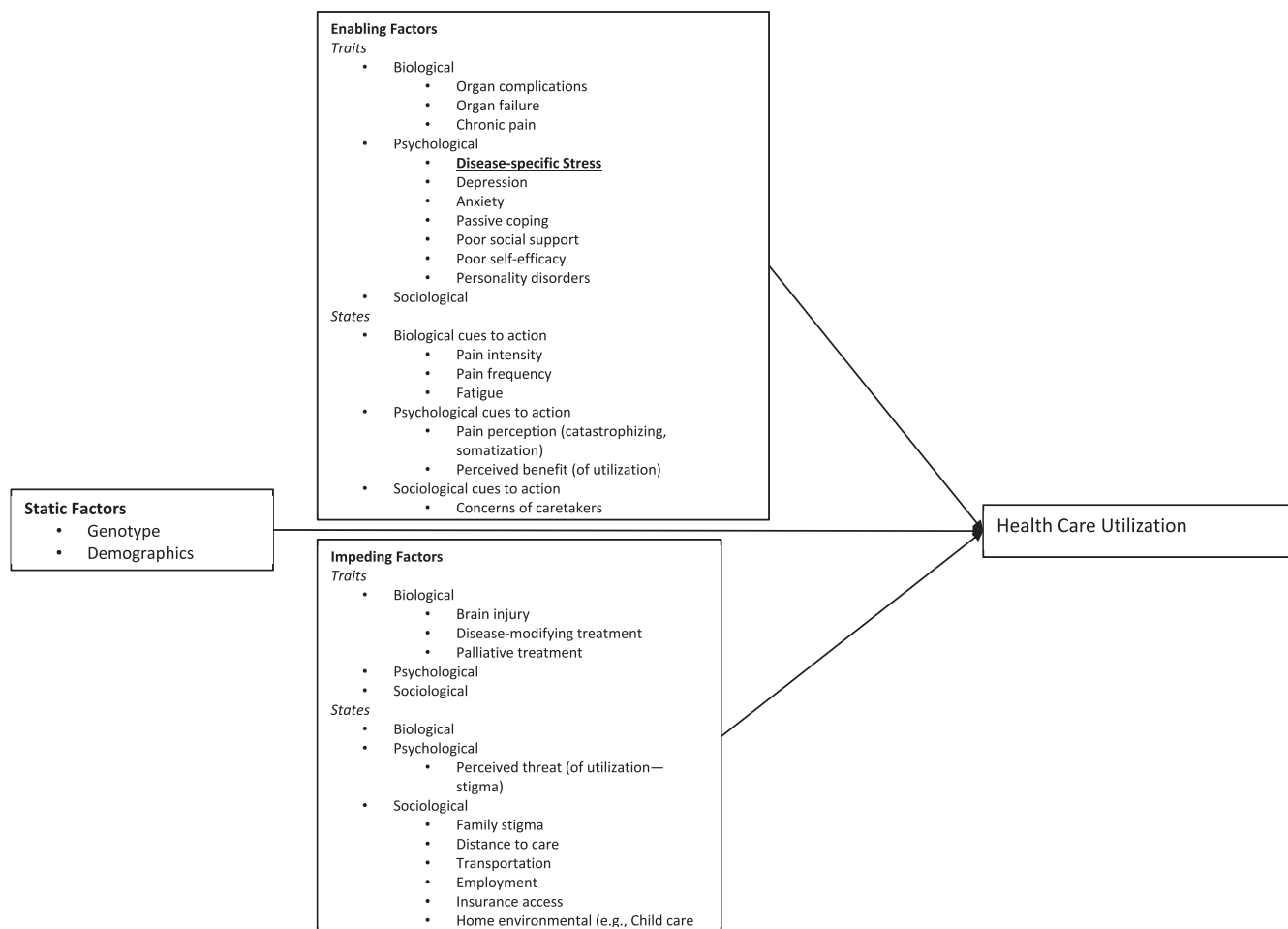
FIGURE 1 Biopsychosocial model of health care utilization in Sickle Cell Disease. Adapted from Adapted from Reese and Smith[42]

questionnaire was an adaptation of an existing battery meant to measure SCD stress as a latent variable. Patients were asked to rate three specific stressful situations on a Likert scale ranging from 1 (not at all stressful) to 5 (very stressful). The items were "dealing with medical problems," "maintaining emotional well-being", and "preparing for the future." The content of these three items was based on a list of seven adaptive tasks used in dealing with serious physical illness,[72] first applied to SCD by Thompson et al.[73] We fielded this survey as part of a pilot study of pain and healthcare utilization in SCD designed to test our theoretical utilization model. The summary stress score was obtained by adding the numerical totals from responses to each item (range 3–15). This initial three-item survey was piloted among 55 participants recruited from the adult SCD clinic at an academic Medical Center in Virginia, and from two community-based organizations serving patients with SCD in Virginia from March 1994 through 1996.

2.2 | Refinement of the questionnaire

Subsequent to analyzing results of the 3-item scale from the pilot study, we expanded the stress questionnaire to better assess SCD-specific stressors reported in the then-expanding literature and anecdotally but

repeatedly reported by patients in our SCD clinic in clinical encounters and in response to open-ended questions about SCD-specific stressors. Stressors noted anecdotally from these patients mirrored those found in the literature: worries/concerns about SCD-related financial difficulties, death and disability, family, employment, interpersonal relationships, pain control, and hospitalization. Ten items were thus constructed by the authors to comprise a new, more SCD-specific measure that asked patients to rate their level of agreement concerning these stressors. Higher item scores on a Likert scale ranging from 0 (strongly disagree) to 4 (strongly agree) indicated worse stress. The total score was obtained by summing the numerical responses 0–4 on each of 10 items (possible range = 0–40). If up to 2 values were missing, the missing values were imputed as the mean of the other values. If more than 2 values were missing, the entire stress score was left as missing.

2.3 | Sample, procedures

Both the original three-item as well as this revised 10-item questionnaire were administered as part of a longitudinal study of pain in SCD that was also a methodological study of the relationship among measures of pain, crises, and healthcare utilization in SCD. Detailed

methods of the study have been published.[10,74] Briefly, the study enrolled 308 patients aged 16 years and older between July 2002 through August 2004 from Virginia. The study was approved by the Institutional Review Board of the authors' medical center.

2.4 | Measures

At baseline and again at 6 months, patients completed a paper questionnaire querying their self-reported demographic characteristics (baseline only) and medical history, as well as the following battery of validated psychosocial surveys meant to help validate the new measure as well as better describe our sample.

The Test of Negative Social Exchange, or TENSE (18 items, 4 subscales, Cronbach alpha = 0.70–0.83,[75]) assesses social interactions and is weakly correlated with depression and anxiety.[75]

The Multidimensional Scale of Perceived Social Support or MPSS (12 items, Cronbach alpha = 0.88,[76]) is a subjective assessment of the adequacy of social support from family, friends and significant others and has been inversely associated with depression scores.[77]

The Patient Health Questionnaire (PHQ) of the PRIME-MD[78,79] measured depression, anxiety, alcohol abuse, and somatic symptoms (# items = 9, 7, 5, 11 and Cronbach alpha = 0.86–0.89, 0.92, unavailable, 0.75 respectively). We combined the two depression diagnoses generated by the PHQ into a single category of depression.[80] The designation of alcohol abuse was also derived from the PHQ.[81] Compared to a gold standard of alcohol abuse, the sensitivity/specificity of the alcohol measure was 62%/99% and the overall accuracy was 98%.[79] Our 11-item SCD adaptation of the *PHQ-15*,[82] the PHQscd,[33] avoids mislabeling the pain of SCD as somatization by excluding four common pain sites of SCD subjects.

The *Medical Outcome Study 36 item Short Form* (MOS SF-36, 36 items, Cronbach alpha = 0.79–0.93) is a well-known and accepted generic measure of functional status and well-being.[83,84] It has good reliability and validity in subjects with chronic pain.[85]

SCD Comorbidities and organ failure presence was noted by patient self-report, including 17 variables: kidney failure, transient ischemic attack/stroke, urinary tract infection, sarcoidosis, degenerative joint disease, lupus, aseptic necrosis, osteomyelitis, meningitis, sepsis, priapism, gout, gallstones/ cholesystitis, hypertension, asthma, pulmonary disease, and congestive heart failure.

Pain intensity and frequency were captured using 6 months of daily diaries.[74] Patients reported: their worst sickle cell pain intensity (0–9); daily distress due to their SCD pain (0–9); the amount interference pain caused in their daily activities (0–9); whether or not they used opioids; whether or not they made a scheduled office, unscheduled office, ED, or hospital visit overnight (each reported independently); and whether they were in a "crisis", the latter self-defined by each patient. We calculated mean daily pain, stress, and interference for these patients as well as the percent of days for which the patient reported any pain (pain > 0), the percent of days on which patients reported crisis, use of opioids, or an unplanned visit (either an unscheduled office visit, ED visit, or hospital visit overnight). While

not all patients completed the same number of diaries, leading to possible bias if a pain measure varied by number of diary days completed, the correlation between diary measures and number of diaries completed in this sample was low – moderate (0.14–0.32).

The Coping Strategies Questionnaire or CSQ,[86] as adapted for SCD[87] assesses psychological strategies to cope with stress. The 80 item questionnaire is broken into 13 subscales, which are then used according to the 3 factor solution from Anie[53,54]: Affective Negative Coping [Catastrophizing, Fear self statements, Anger self statements, Isolation], Active Coping [Praying and Hoping, Diverting Attention, Ignoring Pain Sensations, Reinterpreting Pain Sensations, Calming self statements, Increased Behavioral Activities] and Passive Coping [Taking Fluids, Resting, and Heat/Cold Massage]. Cronbach alpha for these three factors = 0.80-0.93.

2.5 | Analysis, validity assessment of the questionnaire

The frequency of responses for each item in the 3-item and 10-item scales were noted. Face validity was suggested by anecdotal

TABLE 1 Characteristics of study population (*n* = 164), taken from original study sample

Characteristic	
Demographics	Mean (SD)
Age, years	34.1 (11.5)
Gender	N, (Frequency)
Male	63 (38.4%)
Female	101 (61.6%)
Education	
<High school	17 (10.4%)
High school	72 (43.9%)
Some college	51 (31.1%)
Completed college	24 (14.6%)
Marital status	
Currently married	41 (25.0%)
Divorced/separated/widowed	15 (9.2%)
Never married	108 (65.8%)
Income	
<$10 000	69 (43.4%)
$10–20 000	34 (21.4%)
$20–30 000	20 (12.6%)
>$30 000	36 (22.6%)
Genotype	
SS/SBeta^{0}thal	119 (73.0%)
SC/SBeta$^+$thal	44 (27.0%)
	Mean (SD)
SCD comorbidities	1.6 (1.6)

Note: Missing 5 for income, 1 for genotype.

identification of the stressors captured by our items by patients with SCD during the initial pilot, and by identification of these and additional stressors by patients during clinical encounters. Internal consistency of the 3- and 10-item scales was assessed using Cronbach alpha.[88] To explore whether the 10-item scale had empirically derived sub-scales, we conducted varimax rotation factor analyses, varying the constraints on the model (e.g., specified number of factors). None of the resulting factor structures were conceptually interpretable, and low levels of internal consistency made it preferable not to treat them as subscales, and not to drop items. Concurrent validity was evaluated by examining expected correlations with known measures, including depression and alcohol abuse, diary variables, quality of life metrics, and social support, social interaction, and coping, among others. Hypothesized positive correlations were with: TENSE (interference, hostility, insensitivity and ridicule); PHQ depression, alcohol abuse, and somatic symptoms; CSQ Active Coping, Affective Coping, and

Passive Adherence; mean pain, mean daily distress, and mean interference on diaries, and; percent days with pain, crisis, opioid use, or healthcare utilization on diaries. Hypothesized negative correlations were with MSPSS and the MOS SF-36. Spearman correlations of the 3-item and 10-item scales with these variables were calculated. Values of each of these correlations were compared in order to see if the 10-item scale provided higher correlation/better validation than the 3-item scale. Due to both lack of normality of Spearman correlations, as well as the dependency between the two sets, comparisons of the correlations employed bootstrap percentile confidence intervals. Bootstrap methods are resampling methods, where observations are sampled (with replacement) many times from the original data to create a set of similar samples. One thousand such bootstrap samples were created for this analysis, and correlations were estimated from each of these bootstrap samples. The distribution of the difference between these correlations over the 1000 bootstrap samples allowed

TABLE 2 Distribution of responses to the items on the 3-item stress scale ($n = 164$) at 6 months?

	(1) Not at all stressful	(2)	(3) Moderately stressful	(4)	(5) Very stressful
Dealing with medical problems	27 (16.5)	17 (10.4)	59 (36.0)	11 (6.7)	50 (30.5)
Maintaining your emotional well-being	44 (26.8)	28 (17.1)	49 (29.9)	14 (8.5)	29 (17.7)
Preparing for the future	36 (21.9)	21 (12.8)	40 (24.4)	18 (11.0)	49 (29.9)

Note: Patients were asked: we are interested in learning your views on the types of situations that you must face due to sickle cell disease. Please indicate how stressful each of the following situations has been for you.

TABLE 3 Distribution of responses (n, %) to the items on the 10-item stress scale ($n = 164$) at 6 months?

	(0) Strongly disagree	(1) Somewhat disagree	(2) Neither agree nor disagree	(3) Somewhat agree	(4) Strongly agree
I worry that my pain medication will not control my pain	39 (23.9)	20 (12.3)	25 (15.3)	47 (28.8)	32 (19.6)
I worry about being hospitalized for long periods of time	44 (27.0)	12 (7.4)	15 (19.2)	36 (22.1)	56 (34.4)
I worry I will have limited work opportunities because of my illness	28 (17.2)	12 (7.4)	13 (8.0)	37 (22.7)	73 (44.8)
Death is always on the back of my mind	57 (35.0)	11 (6.7)	26 (16.0)	33 (20.2)	36 (22.1)
I worry that my sickle cell disease will keep me from doing the things I enjoy	31(19.0)	18 (11.0)	11 (6.7)	46 (28.2)	57 (35.0)
I worry that some doctors do not trust me with pain narcotics	92 (56.1)	11 (6.7)	19 (11.6)	16 (9.8)	26 (15.8)
I worry about who will take care of my family or children if I am disabled because of my sickle cell disease	70 (42.9)	9 (5.5)	16 (9.8)	26 (15.9)	42 (25.8)
I worry about decreased sexual performance due to my sickle cell disease	70 (43.2)	13 (8.0)	21 (13.0)	32 (19.7)	26 (16.0)
I worry about not having enough pain medication or running out of my pain medications	61 (37.2)	13 (7.9)	18 (11.0)	41 (25.0)	31 (18.9)
I worry that I will not be able to get insurance because of my sickle cell disease	64 (39.3)	12 (7.4)	15 (9.2)	25 (15.3.)	47 (18.8)

Note: Patients were asked: We are interested in learning if your sickle cell disease causes you to have stress. Please rate the extent to which you agree or disagree with the following statements using the scale.

for confidence intervals to be created without assuming normality. Correlations were considered significantly different if zero was not included in the interval between the 2.5th and 97.5th percentiles of the bootstrap distribution (95% bootstrap percentile confidence interval). Predictive validity was tested by correlating baseline stress values with subsequent pain, opioid utilization, and healthcare utilization. Test–retest reliability for the 10-item scale was assessed by correlating baseline versus 6-month repeat questionnaire results. The 3-item scale was not assessed at 6 months.

3 | RESULTS

3.1 | Study population

About half of the original study's cohort ($N = 164$) completed both the 3-item and 10-item stress scales at baseline. Table 1 provides a description of the cohort. The mean age was 34.1 years, 61.6% were female, 73% had the more severe sickle cell genotypes of SS or S-betaº thal;

75% had completed high school, and 14.6% had graduated college. Table S1 shows a sample description for the entire Pain in Sickle Cell Epidemiology Study.

3.2 | Final 3 and 10 item questionnaires

Table 2 shows the distribution of responses to each of the three items in the shorter, less SCD-specific stress scale. Fully 73.2% found dealing with medical problems at least moderately stressful, 65.3% found planning for the future at least moderately stressful, and 56.1% reported that maintaining their emotional well-being was at least moderately stressful. Thirty percent of subjects found dealing with medical problems and planning for the future to be very stressful.

Table 3 shows the responses for each of the items in the longer, more SCD-specific 10-item scale. Based on combined percentages of patients endorsing the categories "agree" and "strongly agree", more than 50% of subjects reported worrying about work opportunities (67.5%), being able to do what they enjoy (63.2%), or being

TABLE 4 Concurrent and predictive validity of 3-item and 10-item Sickle Cell Stress Scales-Adult, Pain in Sickle Cell Epidemiology Study sample ($n = 164$). Spearman correlations

Variable, expected relationship with sickle cell disease stress	10-item stress scale	3-item stress scale	95% bootstrap percentile CI for correlation differences
Expected positive correlations			
Hostility/impatience subscale, TENSE	0.1967*	0.2407*	(−0.1823, 0.0802)
Insensitivity subscale, TENSE	0.2154*	0.1972*	(−0.1357, 0.0935)
Interference subscale, TENSE	0.2058*	0.2395*	(−0.1415, 0.0621)
Ridicule subscale, TENSE	0.0332	0.0134	(−0.1319, 0.1116)
Depression/anxiety, PHQ15	0.2252*	0.4039*	(−0.2710, −0.0702)
Alcohol abuse PHQ15	−0.0009	0.0166	(−0.1212, 0.1120)
Total number of SCD comorbidities	0.1220	0.0906	(−0.0810, 0.1805)
Somatic symptom score (PHQscd)	0.3328*	0.3868*	(−0.1949, 0.0335)
Active coping, CSQ	0.2049*	0.2631*	(−0.2025, 0.0138)
Affective/Negative coping, CSQ	0.6173*	0.6371*	(−0.1570, 0.0811)
Passive coping, CSQ	0.1948*	0.2673*	(−0.2394, 0.0049)
Mean daily pain, PiSCES diaries	0.2557*	0.3374*	(−0.1812, 0.0349)
Mean daily interference, PiSCES diaries	0.3268*	0.3644*	(−0.1219, 0.0517)
Mean daily distress, PiSCES diaries	0.3020*	0.3419*	(−0.1271, 0.0523)
% pain days, PiSCES diaries	0.2681*	0.3081*	(−0.1728, 0.0654)
% crisis days, PiSCES diaries	0.2284*	0.1998*	(−0.0457, 0.1462)
% days taking opiates, PiSCES diaries	0.2578*	0.3237*	(−0.1775, 0.0705)
% days health care utilization, PiSCES diaries	0.1099	0.1020	(−0.0723, 0.1016)
Expected negative correlations			
MOS SF-36 Physical function	−0.4011*	−0.4471*	(−0.0695, 0.1771)
MOS SF-36 Mental function	−0.5050*	−0.5239*	(−0.0533, 0.1172)
Social support, MSPSS	−0.0699	−0.0021	(−0.2128, 0.0887)

Abbreviations: CSQ, Coping Strategies Questionnaire, adapted for SCD, 3-factor solution; MOS SF-36, Medical Outcomes Study Short Form-36; MSPSS, Multidimensional Scale of Perceived Social Support; PHQscd, 11-item SCD adaptation of the Patient Health Questionnaire-15 of the PRIME-MD; PHQ15, Patient Health Questionnaire-15 of the PRIME-MD; TENSE, Test of Negative Social Exchange.
*$p < .05$.

hospitalized for a long period of time (56.5). The plurality of patients (42.3%) agreed or strongly agreed that "death is always on the back of my mind." A smaller percentage of subjects worried about decreased sexual performance (35.7%), getting insurance (34.1%), or doctors not trusting them with narcotics (opioids, 25.6%).

3.3 | Internal consistency and reliability

Measured at baseline, the mean value of the three-item scale was 9.1 (range 3–15) and the mean value of the 10-item scale was 19.7 (range 0–40). Correlation between the two scales was 0.59 ($p < .0001$). At baseline, Cronbach's alpha (raw) was 0.73 for the three-item scale and 0.83 for the 10-item scale, indicating good evidence of scale internal consistency/reliability. Subsequently, 102 subjects also completed the 10-item scale at 6 months. For them, Cronbach's alpha was 0.85 at 6 months, and the test–retest reliability indicated correlation between the two time periods of 0.53 ($p < .0001$).

3.4 | Questionnaire validation

Table 4 shows concurrent and predictive validity of both the 3-item and the 10-item scales for the primary subjects. Correlations were in the expected direction for all variables, except for the near-zero correlation ($r = 0.001$) of the 10-item scale with alcohol abuse. Four of the variables—TENSE ridicule, alcohol abuse, number of SCD comorbidities, and social support had nonsignificant correlations. The strongest correlations were with affective coping, both mental and physical SF-36 quality of life composite scores, mean diary interference and distress, and somatic symptoms. While the correlations with the 3-item scales were numerically higher than for the 10 item scale for almost all but a few non-significant correlations, only the correlation with depression-anxiety was significantly different between the two. Table S2 shows similar results for the entire Pain in Sickle Cell Epidemiology Study sample. Table S3 shows the correlations with pain variables, controlling for the number of diaries. Results of the latter are very similar to that of Table 4 in the main text.

4 | DISCUSSION

Our results indicate that both the 3-item and 10-item Sickle Cell Stress Scale-Adult exhibited good construct validity, concurrent validity, predictive validity, internal consistency, and test–retest reliability. Results also further support the validity of our refined model of SCD utilization.

Our results show that viewing SCD and stress as a trait variable, rather than a state variable as hypothesized by Gil and others, has validity. Early research in SCD found that stress measured at baseline using the Daily Hassles questionnaire was positively associated with average pain and negatively associated with the level of daily activity.[89] To assess SCD stress as part of daily diaries, Porter

and Gil asked participants to describe 'the most bothersome event or issue of the day'.[90–92] Patients then rated the perceived stress of the situation on a 100 mm VAS, and check one of five categories that best described the situation, including SCD. The category for SCD related stress was added specifically. Daily stress measured this way using diaries was positively associated with measures of daily pain and interference with activities.[93] Furthermore, daily increases in diary-measured stress was associated with increases in same-day pain, healthcare utilization and absences from work.[94] Stress remained a significant predictor of pain even after omitting stressors related to SCD (2000).

In contrast, our utilization model conceived of disease-specific stress as a more long-term trait, as part of a set of psychosocial variables that were enabling or impeding forces toward healthcare utilization. We hypothesized that stress was mostly enabling, that is, that it would be associated with greater perceived pain, greater utilization, and more impaired functional status.

Our results support these hypotheses, that the concept of stress, both generic stress as well as a new SCD-specific stress measure, is associated with pain, opioid utilization, and healthcare utilization in SCD, as a result of painful VOCs. They extend Gil's earlier findings by showing that stress, measured as a trait rather than a state, predicts subsequent pain, subsequent opioid use, and subsequent healthcare utilization for pain.

Our results support use of either the 3-item, less SCD-specific, or the 10-item more SCD-specific scale, depending on the circumstance. The use of the 10-item scale yields more disease-specific information and more detail, we find. But some researchers may want a brief SCD stress measure with lower respondent burden, or a measure to be used as part of a larger battery of tests, and may be willing to sacrifice detail in favor of the 3-item summary scale, which performs with equally high, sometimes better predictive validity. We prefer the ability to assess more detailed and more SCD-specific stressors, for example to measure the response of a specific stressor to a utilization reduction intervention. Once norms have been established for this 10-item scale, the subset of patients requiring intervention, and the type and specificity of interventions they require, may become clearer, making the 10-item scale more suitable for certain uses.

There are several limitations to our findings. The two administrations of the 10-item stress scale used to assess test–retest reliability were 6 months apart. The test–retest reliability value of 0.55 may have reflected not only reliability but also real changes taking place over time. SCD-specific stress may not be as stable a trait as the model hypothesizes. Furthermore, since our sample is from Virginia, our results may not be generalizable to other SCD populations. Also, there have been no norms or cutoffs established for an abnormal total Sickle Cell Stress Scale-Adult score. Data to establish validity and norms outside of Virginia, are needed.[95,96] We encourage further use of the Sickle Cell Disease Stress Scale-Adult toward those ends.

4.1 | Future directions

Our results associating SCD stress and pain, SCD stress and crisis days, and SCD stress and heath care utilization, raise hope for studies

that demonstrate the measures' sensitivity to change. For example, stress reduction interventions in adults with SCD could focus on lessening pain or improving self-care for pain, to lower utilization. Investigators began these types of interventions decades ago in chronic pain patients,[97] as well as patients with SCD.[98] Further study of cognitive behavioral therapy,[99–101] mindfulness meditation,[102,103] and biopsychological techniques[104,105] may show reduced stress among adults with SCD, with corresponding reduced utilization, or, our measure may demonstrate sensitivity to change from stress interventions designed to make specific changes to the social, physical, and economic contexts associated with SCD that are described above.

CONFLICTS OF INTEREST

During the time of this work, none of the co-authors had any relevant conflicts of interest or appearances of conflict of interest.

DATA AVAILABILITY STATEMENT

The Pain in sickle cell epidemiology study dataset has been used by several other authors. It is not currenty archived publicly, but we have sent a request to BioLincc, an NIH archive, to send our data and samples. Meanwhile, upon request, the authors will make the data used in this publication available by sending a link and a codebook.

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