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A Preliminary Study of Psychiatric, Familial, and Medical Characteristics of High Utilizing Sickle Cell Disease Patients

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Abstract

Objectives—To identify demographic, medical, and psychosocial characteristics that distinguished sickle cell disease patients who were frequent utilizers of urgent or emergent care resources from low-utilizing patients.

Methods—Patients at a large urban comprehensive sickle cell disease treatment center were recruited from clinic or during urgent care visits. Participants who were high utilizers, defined as having more than 4 acute or emergency care visits in the prior 12 months, were compared to patients with more typical utilization patterns on lifetime complications of SCD, family background, psychiatric history, occupational function, coping, depressive symptoms, and personality.

Results—High utilizers were nearly a decade younger on average; despite this they had a similar lifetime history of SCD complications. High utilizing patients' parents appeared to have greater educational achievement overall. High utilizers reported a nearly three-fold greater prevalence of psychiatric illness in family members than low utilizers. On other measures; including coping strategies, social support, and personality; the two groups were comparable.

Discussion—The study strengthens emerging evidence that disease severity, familial factors related to greater parental education, and psychiatric illness are important factors in high care utilization in patients with sickle cell disease.

Keywords

sickle cell disease; pain; mood disorders; socioeconomic status; health care utilization

Introduction

Sickle cell disease (SCD) is a hematologic illness producing complex multi-system damage and morbidity. There are approximately 100,000 SCD sufferers in the United States, where the disease is heavily concentrated in the African American subpopulation (1, 2). Although

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rare relative to many other chronic medical conditions, it is one of the most common genetic disorders. The illness is caused by a single point substitution in the gene for the hemoglobin beta chain. When this abnormal hemoglobin (S) allele is inherited with another abnormal beta globin allele, most commonly another S allele (SS genotype), clinically significant polymerization of the hemoglobin occurs. The resulting erythrocyte deformation and rigidity cause hemolysis, hyperviscosity, and microvascular hypoperfusion. Sickle cell disease affects every major organ system, including the central nervous system, and shortens the life expectancy of affected people by approximately 30 years (2).

Painful vaso-occlusive crises (VOC) are the best described phenomena associated with SCD. The mechanism by which crises begin, and the chain of events that leads from polymerization of hemoglobin to perception of pain in the central nervous system, are not well understood. Current research suggests highly complex interactions between erythrocytes, the endothelium, immune cells and inflammatory mediators, and the peripheral nervous system are involved (3, 4). The pain of vaso-occlusive crisis is severe and highly unpredictable. There are no objective markers for the presence or severity of VOC. Current standards of care are to accept a patient's report of crisis and treat accordingly, which generally requires parenteral opioids for pain control along with other supportive measures, often in emergency departments or inpatient units (5).

Despite the burden of both chronic and acute pain imposed by SCD, most sufferers manage at home, and only a minority of crises results in acute care visits, usually to hospital emergency departments (6, 7). Despite this, costs for the care of SCD are exceptionally high, and most of these costs are associated with hospital utilization (8–10). As an example, in a recent study of United States emergency department data, Lanzkron, et al. reported that charges for hospital admissions from emergency departments for SCD were on a similar order of magnitude to conditions over 100 times more common (11). This paradox is explained by the skewed distribution of hospital utilization, such that only 10–20% of all SCD patients account for over 50% of the costs of care (10, 12, 13). Rare patients who literally spend more time hospitalized than not can be identified in large samples, and the management of this subpopulation is an often-discussed problem among SCD providers (12, 13).

Although objective markers of disease severity are associated with acute care visits (2), they only partially explain differences in utilization (14–16). For example, Anie and colleagues found that pain severity and complications explained only about 12–24% of the variance in acute care utilization in the United Kingdom (14, 15). Psychiatric explanations are a common resort when clinicians are confronted with high-utilizing, treatment refractory SCD patients, and there is some evidence that psychological factors are related to pain and treatment utilization in SCD (16–20). However, the extant literature provides mostly suggestive associations between measures of psychological distress and treatment utilization, with little guidance as to intervention.

In many other chronic medical conditions, major depression and anxiety disorders are associated with greater health care utilization (21–31). Depressive symptoms are prevalent among SCD patients (18, 20, 32, 33), and have been associated with worsened pain (7, 18, 20, 34), greater opioid use, reduced quality of life, and reduced relief from opioids (6, 18) mostly in cross-sectional studies. In SCD, findings on depressive symptoms and utilization have been mixed (18, 19, 32).

The study of these patients in the United States also is hampered by the rarity of the disease, greatly limiting sample sizes. Use of large government and institutional databases has significant limits on individual-level data (12, 13, 35, 36). In clinical settings, other

investigators have studied samples of a few hundred patients and related dimensional measures of psychological constructs to utilization measures (17, 18). These methods also have limitations imposed by the skewed distribution of utilization, as the high utilizing patients who are most relevant to resource utilization are uncommon enough that even large clinics cannot produce samples of sufficient size for complex analyses.

The present study is a preliminary attempt to addresses some of these problems. A group of high utilizing SCD patients (with more than 4 acute care visits in the prior 12 months) was recruited from the Johns Hopkins Sickle Cell Center for Adults, a large comprehensive SCD treatment center. Based on the literature and experience within the clinic, these participants likely represented the top 10% of patients with respect to utilization. These patients were compared with others with a more typical utilization pattern. A comprehensive set of measures of family history, early life experience, social support, personality, depressive symptoms, and medical severity were used and the similarities and differences between the high-utilizing subpopulation and the comparison group investigated. It was hypothesized that high utilizers would score higher on pain-related catastrophizing, depressive symptoms, violence exposure, and neuroticism; and lower on measures of social support. It was also expected that high utilizers would have greater lifetime prevalence of complications of SCD.

Methods

Participant recruitment

Participants were patients in the Sickle Cell Center for Adults (SCCA) at Johns Hopkins Hospital. The SCCA is a comprehensive sickle cell treatment center that provides outpatient care, acute care in the form of an urgent-care infusion center for evaluation and treatment of VOC, and inpatient services through associations with Johns Hopkins Hospital inpatient units. Patients were approached during treatment at the outpatient infusion center or at regular clinic visits by research staff. Patients in the infusion center were approached only once clinical staff had informed research staff that approach would not disrupt care. No patients were excluded from approach by clinical staff. The clinical staff of the infusion center included the physician assistant and head nurse of the infusion center. Clinical staff examined the hospital electronic medical record and fed back to research staff whether the patients met criteria for the high utilizer group. At outpatient visits, a research staff member accessed the EMR directly to determine the category. Patients were considered high utilizers if they had a history of more than four acute care visits (ED or infusion center) in the past 12 months. Clinical staff informed research staff whether the prospective participant met criteria for the high utilizer category prior to approach. The total sample size was 56, with 27 participants in the comparison group and 29 in the high utilizer group. Six of the participants did not complete all study measures (10.7% of the consented sample). The number of patients approached who did not consent was not tracked, but was lower than the number who consented but did not complete the measures. The study was approved by the Johns Hopkins University Institutional Review Board, and written consent was obtained from all participants.

Study measures

Medical severity and management—A clinical/research database created using hospital and clinician records was reviewed for measures of disease severity, complications, and prior management. Measures included: SCD genotype; lifetime history of avascular necrosis of joints, cerebrovascular accidents, pulmonary hypertension, chronic renal disease, or acute chest syndrome; current use of hydroxyurea or chronic transfusion; and lifetime history of iron overload. Database entries for each participant were checked by chart review by two investigators (Carroll, Hoot) and conflicts were resolved by consensus.

Social, psychological, and psychiatric measures Family background and social support

Parental Relationship: Participants reported whether their parents were ever married.

Maternal and Paternal Education: Participants ranked each parent on highest educational achievement. These reports were categorized as less than high school, high school graduate or equivalent, some college, or bachelor's degree or greater.

Family Psychiatric History: Participants also were asked if there was a known history of psychiatric illness, drug use problems, or alcohol problems in their first degree relatives (parents or siblings) or extended relations. The specific questions were composed of the root: "Did anyone in your [immediate/extended] family (with parenthetic explanation of immediate or extended) ...," followed by 1) "... suffer from a mental illness (such as depression, schizophrenia, bipolar disorder)?," 2) "... drink heavily, have an alcohol problem, or abuse alcohol?", and 3) "... have a problem with illegal or prescription drug use (like cocaine, heroin, sedatives, or others)?"

Violence, Abuse, and Neglect Exposure: Exposure to violence prior to age 18 was measured by four questions derived from the Adverse Childhood Experiences study describing childhood exposure to violence (37–40). The questions followed a progressive pattern, asking whether any adult in the household had been the victim of violence ranging from pushing and slapping to assaults with dangerous weapons. The total number of "yes" responses were summed to provide an index of violence exposure (maximum of 4). Abuse or neglect experienced by the patient during childhood was measured using five items from the ACE study of childhood abuse and neglect (39–42). The questions addressed verbal abuse, violence, whether the patient was ever in foster care, and whether the patient had ever been left alone for more than a day prior to age 16. Again, the total number of "yes" responses was used as an index for the experience of abuse or neglect (maximum of 5).

Social Support: Overall social support was measured using the six item version of the Social Support Questionnaire (SSQ-6) (43). The instrument asks about the number of people participants could rely upon to distract them from their problems, help them relax, accept them, care about them, help them feel better when down in the dumps, and *console them*. There was no stated maximum to the number of people each participant could list in each area. In addition, participants rated their satisfaction with the level of support they received on each subscale on a one to six scale. For the sake of parsimony and to minimize spurious findings from multiple comparisons, total support and satisfaction indices were created by adding together each of the six support and satisfaction scales.

Personal background and function

Educational and Occupational Achievement: Participants reported their highest level of educational achievement and current occupational status. Educational achievement was categorized with the same system as parental education. Participants also were asked whether they had been suspended in school. Participants reported their means of financial support (with options being employment, disability income, family/friends support, informal work and odd jobs, or "other" which provided space for explanation). Note that these were not conceptualized as mutually exclusive, as many participants had multiple sources of income.

Psychological measures

Depressive Symptoms: Current depressive symptoms were quantified by the Beck Depression Inventory version II, a well-validated instrument that is widely used as a screening instrument for major depressive disorder (44, 45). It contains 21 items corresponding to depressive symptoms with a maximum possible score of 63. Participants who screened positive at a cut point of 19 (corresponding to mild-moderate depression(45)) were contacted; those for whom a diagnosis of a depressive illness had been established and were in treatment were given no further intervention. One participant screened positive with no prior diagnosis and was seen by the primary author in consultation and ruled out for a depressive disorder.

Pain Coping Strategies: Pain coping strategies were assessed using the Coping Strategies Questionnaire (46, 47), which provides measures of distraction, catastrophizing, ignoring, distancing, praying, and coping self-statements (48).

Personality: Variation along normal personality dimensions was measured using the NEO-FFI, a 60 item instrument measuring the elements of the Five Factor Model of personality (49, 50). These include Neuroticism (proneness to negative affect), Extraversion (including assertiveness, gregariousness, and positive emotions), Openness to Experience, Agreeableness (including straightforwardness, altruism, and trust), and Conscientiousness (including dutifulness, order, and competence). Responses related to each factor are summed and assigned a T score standardized to a mean of 50 and a standard deviation of 10 relative to the reference population.

Statistical analysis

Categorical measures were compared between high utilizing and comparison groups using Chi-squared tests, and continuous measures were compared using Student's t test. Not all participants completed all study measures; in some cases this was due to lack of knowledge, which was a particular problem with the paternal education items. All completed measures were used in analyses, though this did result in differing sample sizes between analyses of different measures. The sample sizes for each analysis are recorded in Tables 1 and 2. Differences associated with a p value below 0.05 were considered statistically significant. Individual analyses were not corrected for multiple comparisons given the preliminary nature of the study, however the expected number of statistically significant findings by chance would be slightly more than 2. If Bonferroni correction had been used, the revised study-wise alpha level would be approximately 0.001. Because of the sample size and the rarity of the condition being studied, the authors desired a means of pointing out results that were not strictly statistically significant but appeared to be of clinical interest. Thus odds ratios (for proportions) and Cohen's d (for continuous measures) were calculated and reported as measures of effect size. All statistical analyses were performed in the R statistical computing environment (51).

Results

Demographics, family of origin, and early life (see Table 1)

High utilizers were nearly a decade younger on average than the comparison group (28.6 years versus 38.0 years, p=0.002). The parents of high and low utilizers were equally likely to be married. The parents of high utilizers appeared more educated, with more parents completing high school and more mothers having some level of college education (father's education Chi-square = 9.74 on 3 d.f., p=0.021; mother's education Chi-square = 3.67 on 3 d.f., p=0.053). There was little evidence for differences in family history of alcohol or drug problems, though there was dramatically more psychiatric illness in both immediate and

extended families of high utilizers (immediate: 42.9% vs. 7.41%, OR = 9.38, extended: 39.3% vs.11.5%, OR=4.96; for both p<0.05).

Functional and medical status (See Table 1)

The majority of participants were SS genotype (66.7% of high utilizers and 73.1% in the comparison group, p=0.697). Other individual genotypes were of such low frequency as to make statistical comparison fruitless. Although there were no statistically distinguishable differences between high utilizers and the comparison group on lifetime prevalence of complications, the comparison group was numerically more likely to have renal disease and the high utilizers tended to have a greater lifetime prevalence of other complications. In general, high utilizers showed evidence of a more aggressive treatment history, with greater prevalence of iron overload, chronic transfusion, and hydroxyurea exposure, though again these were not statistically distinguishable. There was a suggestion that high utilizers were more likely to receive disability income than low utilizers (62.1% vs. 37.0%, OR = 2.78, p=0.109). As expected, measures of acute care utilization were dramatically higher in the high utilizing patients.

Psychological characteristics (See Table 2)

High utilizers and the comparison group generally were not statistically distinguishable on measures of social support, coping strategies, personality, or depressive symptoms, although effect sizes associated with differences in the coping strategies of distraction (higher in the comparison group), extraversion (higher in the comparison group) and depressive symptoms (higher in the high utilizer group) were of reasonable size. For these analyses in general, a smaller sample size was available due to participants' noncompletion of measures.

Discussion

Implications of demographic differences in high utilizers

The most dramatic difference between high utilizers and the comparison group was the difference in mean age of nearly a decade. This is of particular interest since the life expectancy of SCD sufferers is in the mid 40's. The distribution of ages was much narrower in the high utilizer group, being almost entirely restricted to people in the third decade of life; only 3.45% of high utilizers were above forty years of age whereas 44.4% of low utilizers were. Since frequent hospitalizations are known to be a risk factor for early mortality in SCD (13, 52), any sample from this subpopulation is likely to be younger. In addition, age selection may occur through an "aging out" process. In the primary author's previous work, patients who were frequently admitted to the hospital in a given year tended to be admitted less often in subsequent years, and resumption of high hospital utilization after moderation was atypical (12). Thus while high utilizers have a greater risk of death, those who survive an initial period of high utilization are more likely to drop out of the high utilizing category than to become chronic. Presumably, those patients who do become chronic high utilizers continue to incur the greater risk of death associated with higher utilization as well, further shifting the age of cross-sectional samples younger.

In prior studies, higher-utilizing patients with SCD have had more severe disease and greater disability. In this study, the high utilizers overall had similar or slightly greater lifetime prevalence of complications. Although they reported more reliance on disability income, this was not statistically distinguishable from the comparison group. However, these results should be considered in light of the age differences of the sample. Similar lifetime prevalence of complications and greater disability in a much younger sample suggests a more rapid course of disease.

Early life and psychiatric factors

The greater prevalence of self-reported psychiatric family history in the high utilizers was striking. This was present in both the immediate and extended family and of considerable magnitude. Although high utilizing patients reported a greater prevalence of prior psychiatric contact, this difference was not supported by hypothesis testing and did not appear as robust. Caution should be used as all these data are based on self-report, and might be biased by any number of differences in prior medical contacts and response biases. Prior investigators have noted that children of depressed parents use more medical resources. Although at least some of this excess utilization is in the psychiatric realm, these children also use more medical resources (53), and the mechanism of this relationship remains largely unexplored.

Interestingly, other psychological measures expected to be relevant showed few differences in high utilizers. Although the sample size available for these measures was smaller in general, the absolute differences were unimpressive. There were no detectable differences in personality, coping strategies, or levels of social support. Depressive symptoms in the high utilizers were elevated relative to the comparison group, though not statistically distinguishable. Neither did the indices of abuse or violence exposure differ between groups.

In fact, contrary to the authors' hypotheses, there were a number of indicators associated with greater stability and advantage among the high utilizers. Parental education in general appeared greater, and educational achievement in the high utilizers was comparable to the comparison group.

Role of psychiatric illness

A number of investigators have approached the role of depressive symptoms and anxiety in sickle cell disease. In general, these studies have suggested that there is a link between the level of depressive symptoms, worse pain, reduced quality of life, and greater health care utilization (18, 20, 32). The relationship with health care utilization does appear to be weaker and more inconsistently found than the other associations, however. Although preliminary, the present study suggests one possible explanation.

The best of prior studies have administered screening instruments for psychiatric disorder and used these to prospectively predict pain and hospital utilization (17, 18). Many of these instruments have not been validated in SCD populations, thus their ability to distinguish true psychiatric illness from distress related to SCD is uncertain. If psychiatric illness specifically is related to utilization it would be consistent with the finding that risk factors for psychiatric illness are more strongly related to utilization than more general measures of distress.

Family background

The better education in high utilizers' parents is consonant with prior research in adolescents. Brown and colleagues discovered that adolescent SCD patients' hospital utilization was associated with greater educational achievement in their mothers (16), and other investigators have noted that greater utilization in children with SCD was associated with greater parental knowledge of the disease (54). A suggestive literature also has developed relating children's health care attitudes, particularly their liking of health care, to parents' attitudes toward care (56), and parental health care utilization predicts children's (57). In addition to these more direct effects, parental education probably is a proxy for greater socioeconomic status, which is associated with greater access to and utilization of health care resources (58), although it typically also is associated with better health (59). Parental education probably is an indicator of a number of characteristics that

help break down barriers to access for health care services, such as greater disease knowledge, a more positive attitude toward health care, and greater access to services. These parental characteristics may result in a greater impulse toward care seeking in the child, and with sufficient disease severity and reinforcement, eventual development of a high-utilizing pattern. These hypotheses are well ahead of the current literature, and likely will require longitudinal studies of families with SCD children to settle.

Strengths and limitations

The study faced some limitations. Chiefly, the sample size was small in statistical terms, although assembly of a similar subsample of high utilizers likely would require sampling a clinical population of over three hundred patients. The low number reduced power to detect statistically significant differences and the use of multiple univariate comparisons increases concerns for type I errors. Calculation of effect sizes does give some collateral information regarding clinical significance of the findings and points out those for which a larger sample may have yielded different hypothesis testing results; however, the results of the study should be regarded as preliminary. In some cases the sample size was further reducedwhen participants did not complete all measures. Particularly with the family history measures, the self-report measures used will require replication with more rigorous methods. The participants were a single-clinic convenience sample, and so it is possible that results will not generalize to other settings. Replication of all these results with larger samples across different settings will be necessary.

The study also had significant strengths, particularly in addressing gaps in recent research on this topic. The design allowed specific study of the high utilizing subpopulation, which is central to the issue of healthcare utilization in sickle cell disease. Because of this targeted design, a very broad range of measures could be studied simultaneously, allowing a more detailed assessment of these psychosocial measures than previously reported in larger studies.

Summary

The results of this study, although preliminary, support prior work that suggests that the psychosocial background of high utilizing SCD patients is complex, including both disadvantages and elements ordinarily associated with better outcomes. Evidence is converging to suggest that high-utilizing patients with SCD have greater familial and personal psychiatric comorbidity in addition to a more severe SCD course. High utilization also may be related to greater parental education, though the mechanism of this association is obscure. To move forward and develop a multidisciplinary strategy to improve health care utilization and patient outcomes in SCD, the field will need to apply new methods. Future work on psychiatric factors in health care utilization in SCD will require methods to establish valid psychiatric diagnoses, gauge the independence of these diagnoses from symptoms of SCD, and track changes in symptoms of both over time. To elucidate the complex relationships of parental education and socioeconomic status with utilization, prospective methods studying families of SCD children through adolescence and adulthood likely will be necessary. Possible mediators of these relationships, such as attitudes toward health care, parental health care utilization, and familial resources will have to be measured over time. It is encouraging that in each of these areas possible interventions can be visualized; in particular, early screening and intervention for young patients at risk of psychiatric illness may be an important component of SCD care. If these results are replicated with more robust methods, it is quite likely that such interventions will be costeffective if appropriately targeted, and could improve long-term mortality as well.

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Abbreviations

SCD sickle cell disease	
VOC vaso-occlusive crisis/crises	
SCCA Sickle Cell Center for Adults at Johns He	opkins
ED emergency department	
ACE/ACEs Adverse Childhood Experiences Study	
SSQ-6 Social Support Questionnaire, 6-item ver	sion
NEO-FFI NEO Five Factor Inventory	

References

- Hassell, K. Sickle Cell Disease Population Estimation: Application of Available Contemporary Data to Traditional Methods. Oral Presentation, 35th Anniversary Convention of the National Sickle Cell Disease Program and the Sickle Cell Disease Association of America; 2007.
- Ashley-Koch A, Yang Q, Olney RS. Sickle hemoglobin (HbS) allele and sickle cell disease: a HuGE review. AmJEpidemiol. 2000; 151:839.
- 3. Hebbel RP, Osarogiagbon R, Kaul D. The endothelial biology of sickle cell disease: inflammation and a chronic vasculopathy. Microcirculation. 2004; 11:129–51. [PubMed: 15280088]
- Frenette PS. Sickle cell vaso-occlusion: multistep and multicellular paradigm. Curr Opin Hematol. 2002; 9:101–6. [PubMed: 11844991]
- 5. National Heart L. Blood I., editor. The Management of Sickle Cell Disease. 4 ed. The National Institutes of Health; 2002.
- Smith WR, Penberthy LT, Bovbjerg VE, McClish DK, Roberts JD, Dahman B, Aisiku IP, Levenson JL, Roseff SD. Daily assessment of pain in adults with sickle cell disease. AnnInternMed. 2008; 148:94.
- McClish DK, Smith WR, Dahman BA, Levenson JL, Roberts JD, Penberthy LT, Aisiku IP, Roseff SD, Bovbjerg VE. Pain site frequency and location in sickle cell disease: the PiSCES project. Pain. 2009; 145:246. [PubMed: 19631468]
- Lanzkron S, Haywood C Jr. Segal JB, Dover GJ. Hospitalization rates and costs of care of patients with sickle-cell anemia in the state of Maryland in the era of hydroxyurea. American Journal of Hematology. 2006; 81:927. [PubMed: 16924648]
- Davis H, Moore RM Jr. Gergen PJ. Cost of hospitalizations associated with sickle cell disease in the United States. Public Health Rep. 1997; 112:40. [PubMed: 9018287]
- Woods K, Karrison T, Koshy M, Patel A, Friedmann P, Cassel C. Hospital utilization patterns and costs for adult sickle cell patients in Illinois. Public Health Rep. 1997; 112:44. [PubMed: 9018288]

- Lanzkron S, Carroll CP, Haywood CH Jr. The Burden of Emergency Department Use for Sickle Cell Disease: An Analysis of the National Emergency Department Sample Database. American Journal of Hematology. 2010
- Carroll CP, Haywood C Jr. Fagan P, Lanzkron S. The course and correlates of high hospital utilization in sickle cell disease: Evidence from a large, urban Medicaid managed care organization. American Journal of Hematology. 2009; 84:666. [PubMed: 19743465]
- 13. Carroll CP, Haywood C Jr. Lanzkron S. Prediction of Onset and Course of High Hospital Utilization in Sickle Cell Disease. Journal of Hospital Medicine. 2010 in press.
- Anie KA, Steptoe A, Ball S, Dick M, Smalling BM. Coping and health service utilisation in a UK study of paediatric sickle cell pain. ArchDisChild. 2002; 86:325.
- Anie KA, Steptoe A, Ball S, Dick M, Smalling BM. Coping and health service utilisation in a UK study of paediatric sickle cell pain. Arch Dis Child. 2002; 86:325–9. [PubMed: 11970920]
- 16. Brown RT, Connelly M, Rittle C, Clouse B. A longitudinal examination predicting emergency room use in children with sickle cell disease and their caregivers. JPediatrPsychol. 2006; 31:163.
- Citero Vde A, Levenson JL, McClish DK, Bovbjerg VE, Cole PL, Dahman BA, Penberthy LT, Aisiku IP, Roseff SD, Smith WR. The role of catastrophizing in sickle cell disease--the PiSCES project. Pain. 2007; 133:39. [PubMed: 17408858]
- Levenson JL, McClish DK, Dahman BA, Bovbjerg VE, de A Citero V, Penberthy LT, Aisiku IP, Roberts JD, Roseff SD, Smith WR. Depression and anxiety in adults with sickle cell disease: the PiSCES project. PsychosomMed. 2008; 70:192.
- Hasan SP, Hashmi S, Alhassen M, Lawson W, Castro O. Depression in sickle cell disease. JNatlMedAssoc. 2003; 95:533.
- 20. Wison Schaeffer JJ, Gil KM, Burchinal M, Kramer KD, Nash KB, Orringer E, Strayhorn D. Depression, disease severity, and sickle cell disease. JBehavMed. 1999; 22:115.
- Katon WJ, Lin E, Russo J, Unutzer J. Increased medical costs of a population-based sample of depressed elderly patients. ArchGenPsychiatry. 2003; 60:897.
- 22. Sullivan M, Simon G, Spertus J, Russo J. Depression-related costs in heart failure care. ArchInternMed. 2002; 162:1860.
- Johnson J, Weissman MM, Klerman GL. Service utilization and social morbidity associated with depressive symptoms in the community. Jama. 1992; 267:1478. [PubMed: 1538538]
- Egede LE. Major depression in individuals with chronic medical disorders: prevalence, correlates and association with health resource utilization, lost productivity and functional disability. GenHospPsychiatry. 2007; 29:409.
- 25. Ciechanowski PS, Katon WJ, Russo JE. Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. ArchInternMed. 2000; 160:3278.
- 26. Williams ER, Guthrie E, Mackway-Jones K, James M, Tomenson B, Eastham J, McNally D. Psychiatric status, somatisation, and health care utilization of frequent attenders at the emergency department: a comparison with routine attenders. J Psychosom Res. 2001; 50:161. [PubMed: 11316509]
- Himelhoch S, Weller WE, Wu AW, Anderson GF, Cooper LA. Chronic medical illness, depression, and use of acute medical services among Medicare beneficiaries. MedCare. 2004; 42:512.
- Fleet RP, Dupuis G, Marchand A, Burelle D, Arsenault A, Beitman BD. Panic disorder in emergency department chest pain patients: prevalence, comorbidity, suicidal ideation, and physician recognition. AmJMed. 1996; 101:371.
- 29. Jones GN, Ames SC, Jeffries SK, Scarinci IC, Brantley PJ. Utilization of medical services and quality of life among low-income patients with generalized anxiety disorder attending primary care clinics. IntJPsychiatry Med. 2001; 31:183.
- Ford JD, Trestman RL, Steinberg K, Tennen H, Allen S. Prospective association of anxiety, depressive, and addictive disorders with high utilization of primary, specialty and emergency medical care. Soc Sci Med. 2004; 58:2145. [PubMed: 15047073]
- Deacon B, Lickel J, Abramowitz JS. Medical utilization across the anxiety disorders. JAnxiety Disord. 2008; 22:344. [PubMed: 17420113]

- 32. Belgrave FZ, Molock SD. The role of depression in hospital admissions and emergency treatment of patients with sickle cell disease. JNatlMedAssoc. 1991; 83:777.
- 33. Molock SD, Belgrave FZ. Depression and anxiety in patients with sickle cell disease: conceptual and methodological considerations. JHealth SocPolicy. 1994; 5:39.
- 34. Barakat LP, Patterson CA, Daniel LC, Dampier C. Quality of life among adolescents with sickle cell disease: mediation of pain by internalizing symptoms and parenting stress. HealthQualLifeOutcomes. 2008; 6:60.
- 35. Shankar SM, Arbogast PG, Mitchel E, Ding H, Wang WC, Griffin MR. Impact of proximity to comprehensive sickle cell center on utilization of healthcare services among children with sickle cell disease. PediatrBlood Cancer. 2008; 50:66.
- 36. Shankar SM, Arbogast PG, Mitchel E, Cooper WO, Wang WC, Griffin MR. Medical care utilization and mortality in sickle cell disease: a population-based study. American Journal of Hematology. 2005; 80:262. [PubMed: 16315251]
- Anda RF, Croft JB, Felitti VJ, Nordenberg D, Giles WH, Williamson DF, Giovino GA. Adverse childhood experiences and smoking during adolescence and adulthood. Jama. 1999; 282:1652–8. [PubMed: 10553792]
- Anda RF, Whitfield CL, Felitti VJ, Chapman D, Edwards VJ, Dube SR, Williamson DF. Adverse childhood experiences, alcoholic parents, and later risk of alcoholism and depression. Psychiatr Serv. 2002; 53:1001. [PubMed: 12161676]
- Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, Koss MP, Marks JS. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) Study. Am J Prev Med. 1998; 14:245–58. [PubMed: 9635069]
- Foege WH. Adverse childhood experiences. A public health perspective. Am J Prev Med. 1998; 14:354–5. [PubMed: 9635083]
- 41. Anda RF, Felitti VJ, Bremner JD, Walker JD, Whitfield C, Perry BD, Dube SR, Giles WH. The enduring effects of abuse and related adverse experiences in childhood. A convergence of evidence from neurobiology and epidemiology. Eur Arch Psychiatry Clin Neurosci. 2006; 256:174–86. [PubMed: 16311898]
- 42. Weiss MJ, Wagner SH. What explains the negative consequences of adverse childhood experiences on adult health? Insights from cognitive and neuroscience research. Am J Prev Med. 1998; 14:356–60. [PubMed: 9635084]
- 43. Sarason IG, Sarason BR, Shearin EN, Pierce GR. A Brief Measure of Social Support: Practical and Theoretical Implications. Journal of Social and Personal Relationships. 1987; 4:497.
- Storch EA, Roberti JW, Roth DA. Factor structure, concurrent validity, and internal consistency of the Beck Depression Inventory-Second Edition in a sample of college students. DepressAnxiety. 2004; 19:187.
- Beck, AT.; Steer, RA.; Brown, GK. Beck Depression Inventory Second Edition Manual. The Psychological Corporation; San Antonio, Texas: 1996.
- 46. Anderson LP, Rehm LP. The relationship between strategies of coping and perception of pain in three chronic pain groups. JClinPsychol. 1984; 40:1170.
- Geisser ME, Robinson ME, Henson CD. The Coping Strategies Questionnaire and chronic pain adjustment: a conceptual and empirical reanalysis. Clin J Pain. 1994; 10:98–106. [PubMed: 8075472]
- 48. Robinson ME, Riley JL 3rd, Myers CD, Sadler IJ, Kvaal SA, Geisser ME, Keefe FJ. The Coping Strategies Questionnaire: a large sample, item level factor analysis. ClinJPain. 1997; 13:43.
- 49. Costa, PT.; McCrae, RR. NEO PI/FFI manual supplement. 1989.
- Costa, PT.; McCrae, RR. Revised NEO Personality Inventory and NEO Five-Factor Inventory Professional Manual. Psychological Assessment Resources; Odessa, FL: 1992.
- 51. Team RDC. R: A language and environment for statistical computing. Vienna, Austria: 2010.
- Houston-Yu P, Rana SR, Beyer B, Castro O. Frequent and prolonged hospitalizations: a risk factor for early mortality in sickle cell disease patients. American Journal of Hematology. 2003; 72:201. [PubMed: 12605392]

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- 53. Olfson M, Marcus SC, Druss B, Alan Pincus H, Weissman MM. Parental depression, child mental health problems, and health care utilization. Med Care. 2003; 41:716–21. [PubMed: 12773837]
- Logan DE, Radcliffe J, Smith-Whitley K. Parent factors and adolescent sickle cell disease: associations with patterns of health service use. J Pediatr Psychol. 2002; 27:475–84. [PubMed: 12058011]
- 55. Allison SM, Koenig LJ, Marhefka SL, Carter RJ, Abrams EJ, Bulterys M, Tepper V, Palumbo PE, Bachanas PJ, Farley JJ. Assessing Medication Adherence of Perinatally HIV-Infected Children Using Caregiver Interviews. J Assoc Nurses AIDS Care. 2010
- Fiscella K, Franks P, Clancy CM. Skepticism toward medical care and health care utilization. Med Care. 1998; 36:180–9. [PubMed: 9475472]
- 57. Janicke DM, Finney JW, Riley AW. Children's health care use: a prospective investigation of factors related to care-seeking. Med Care. 2001; 39:990–1001. [PubMed: 11502956]
- Alter DA, Naylor CD, Austin P, Tu JV. Effects of socioeconomic status on access to invasive cardiac procedures and on mortality after acute myocardial infarction. N Engl J Med. 1999; 341:1359–67. [PubMed: 10536129]
- Mackenbach JP, Stirbu I, Roskam AJ, Schaap MM, Menvielle G, Leinsalu M, Kunst AE. Socioeconomic inequalities in health in 22 European countries. N Engl J Med. 2008; 358:2468–81. [PubMed: 18525043]

Table 1

Demographics, family characteristics, early life, social history, and medical history in samples of high utilizers and comparison patients

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Demographics	Comparison	Hign Utilizers	3	d	5	н
Age	38.0 (13.3)	28.6 (5.10)	0.959	0.002	27	59
Male	37.0%	31.0%	0.765	0.848	27	29
Parents Married	63.0%	65.5%	1.12	0.936	27	29
Maternal Education						
Less than high school	18.5%	0.00%		0.053	27	27
High School	33.3%	22.2%				
Some College	22.2%	29.6%				
Bachelor or above	25.9%	48.1%				
Paternal Education						
Less than high school	26.3%	0.00%		0.021	19	24
High School	21.1%	54.2%				
Some College	31.6%	33.3%				
Bachelor or above	21.1%	12.5%				
Psychiatric History						
Primary Family Mental Illness	7.41%	42.9%	9.38	0.007	27	28
Primary Family Alcoholism	37.0%	41.4%	1.20	0.953	27	29
Primary Family Drug Problem	37.0%	44.8%	1.38	0.749	27	29
Personal Psychiatric Treatment	11.1%	31.0%	3.60	0.136	27	29
Early Life						
Violence Exposure Index	0.615 (1.17)	1.07 (1.39)	0.359	0.194	26	29
Abuse Index	0.654 (1.09)	1.14(1.43)	0.385	0.163	26	29
Suspension from School	81.5%	53.6%	0.262	0.055	27	28
Sources of Support						
Disability	37.0%s	62.1%	2.78	0.109	27	29

						a
	Comparison	High Utilizers	ES	d	Co	ΗU
Employed	40.7%	31.0%	0.655	0.632	27	29
Informal Work	11.1%	17.2%	1.67	0.785	27	29
Family Support	29.6%	20.7%	0.620	0.643	27	29
Complications and Treatment						
Avascular Necrosis	37.0%	31.0%	0.765	0.848	27	29
CVA	3.70%	10.3%	3.00	0.656	27	29
Renal Disease	29.6%	10.3%	0.274	0.139	27	29
Acute Chest Syndrome	44.4%	62.1%	2.05	0.292	27	29
Pulmonary Hypertension	18.5%	34.5%	2.32	0.296	27	29
Iron Overload	7.41%	17.2%	2.60	0.479	27	29
Hydroxyurea	0.00%	3.45%	Inf	0.500	27	29
Chronic Transfusion	11.1%	24.1%	2.55	0.356	27	29
Utilization (past 12 months)						
ED visits	0.778 (0.847)	8.69 (9.77)	1.14	<0.001	27	29
Infusion Center Visits	1.15 (1.03)	10.8 (10.5)	1.30	<0.001	27	29
Hospitalizations	0.593 (0.797)	4.28 (3.86)	1.32	<0.001	27	29

Categorical data are represented by percents. Values for continuous measure are summarized as mean (standard deviation). The measures of effect size (ES) for categorical values is the odds ratio (OR), for continuous measures it is Cohen's *d*. The far right columns represent the number in each group for each comparison; "Co" represents the comparison group and "HU" the high utilizers. "Inf" denotes an uninterpretable odds ratio due to zero prevalence in the comparison group.

Table 2

Social support, coping, depressive symptoms, and personality measures in samples of high utilizers and comparison patients

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	Comparison	High Utilizers	ES	d	Co	ΗU
Social Support						
Extent	19.6 (13.4)	17.1 (10.5)	0.208	0.488	24	23
Satisfaction	11.3 (7.21)	12.7 (7.80)	0.190	0.525	24	23
Coping Strategies						
Distraction	15.3 (7.85)	13.1 (6.36)	0.316	0.295	24	23
Catastrophizing	13.6 (7.97)	13.8 (7.58)	0.026	0.930	24	23
Ignoring	12.5 (7.06)	11.8 (5.94)	0.106	0.724	24	23
Distancing	6.83 (6.71)	4.70 (4.85)	0.374	0.216	24	23
Coping Self-Statements	15.6 (6.34)	15.3 (3.74)	0.055	0.855	24	23
Praying	14.5 (4.22)	14.3 (3.77)	0.050	0.867	24	23
Depressive Symptoms						
Beck Depression Inventory	10.8 (9.39)	14.8 (12.6)	0.368	0.222	24	23
Personality						
Neuroticism	50.2 (10.4)	51.9 (12.0)	0.158	0.602	23	23
Extraversion	47.1 (13.2)	42.0 (7.81)	0.483	0.120	23	23
Openness	50.5 (9.11)	47.6 (8.98)	0.333	0.274	23	23
Agreeableness	45.7 (12.9)	46.7 (11.1)	0.078	0.798	23	23
Conscientiousness	50.5 (10.2)	47.4 (9.87)	0.314	0.302	23	23
Values are summarized as mean (standard deviation). The measures of effect size is Cohen's d . The fi	n (standard devi	ation). The measu	res of eff	ect size is	s Cohei	n's <i>d</i> . Tl

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The far right columns represent the number in each group for each comparison; "Co" represents the Ġ. comparison group and "HU" the high utilizers. s are