ILLNESS IDENTITY AND PSYCHOLOGICAL ADAPTATION IN INDIVIDUALS WITH HYPERMOBILE EHLERS DANLOS SYNDROME OR HYPERMOBILITY SPECTRUM DISORDER

by

Alexis R. Heidlebaugh

A thesis submitted to Johns Hopkins University in conformity with the requirements for the degree of Master of Science

Baltimore, Maryland

March 2020

ABSTRACT

Background: Much of the research literature in the hEDS and HSD populations focuses on diagnostic classification and quantifying patients' physical and psychological functioning. Little is known about the psychological processes and outcomes of individuals living with these illnesses.

Objective: Our study aims to explore factors related to illness identity and psychological adaptation in individuals with hEDS or HSD.

Methods: We distributed an online survey through the EDS Society to adults with hEDS or HSD.

Results: Overall, 399 individuals participated in our study. Participants viewed their illness as threatening, perceived moderate uncertainty, had moderate confidence in their coping ability, moderate anxiety, mild depression, and moderate adaptation. Higher rejection identity was significantly correlated with lower number of illness characteristics, greater perceived impact of illness characteristics, more threatening illness perceptions, and more uncertainty. In regression analysis, individuals who felt threatened by and uncertain about their illness were significantly more likely to reject their illness as part of their identity. Higher acceptance identity was significantly correlated with less uncertainty and less coping self-efficacy. In regression analysis, individuals who had higher coping self-efficacy were less likely to accept their illness as part of their identity. Higher engulfment identity was significantly correlated with higher number of illness characteristics, less perceived impact of illness characteristics, less threatening illness perceptions, more uncertainty, and more coping self-efficacy. In regression analysis, individuals who viewed their illness as uncertain and had higher coping self-efficacy were more likely to

become engulfed by their illness. Additionally, individuals who perceived their illness as threatening were less likely to become engulfed by their illness. Higher enrichment identity was correlated with more threatening illness perceptions and less coping self-efficacy. In regression analysis, individuals with higher coping self-efficacy were less likely to be enriched by their illness.

Discussion: Further research is needed to understand the unexpected relationships among the illness identity states, coping self-efficacy, and emotional distress. Our study contributes to better understanding of illness identity and psychological adaptation in individuals with hEDS or HSD. This may allow genetic counselors to better care for their patients and potentially provide opportunities for psychotherapeutic intervention.

THESIS COMMITTEE

William Klein, PhD [lead advisor, associate investigator]

Lori Erby, PhD, ScM, CGC [co-advisor, associate investigator]

Debra Roter, DrPH [principal investigator, committee member]

Joann Bodurtha, MD, MPH [committee member]

Christy H. Smith, ScM, CGC [committee member]

Weiyi Mu, ScM, CGC [committee member]

THESIS READERS

William Klein, PhD

Jill Owczarzak, PhD

ACKNOWLEDGEMENTS

To our participants and the EDS Society: Thank you so much for your participation in our research study. Your journeys with hEDS and HSD have inspired our research study and we hope our study will contribute to better understanding your needs as a community. Thank you to the EDS Society for partnering with us to provide guidance on our study and for distributing our survey.

To my thesis advisors: Thank you Bill for your wisdom, guidance, and enthusiasm for my research study. Your support throughout this process has been integral to its success. Thank you Lori for your insight and encouragement throughout my research study.

To my thesis committee and readers: Thank you Debra, Dr. Bodurtha, Christy, and Weiyi, for your time, dedication, and insight throughout my thesis development and completion. Thank you Jill for providing thoughtful and critical commentary on my thesis manuscript.

To the faculty and staff of the JHU/NIH Genetic Counseling Training Program: Thank you for your support throughout my thesis development and completion and for your dedication to training genetic counselors to think critically and support patients empathically.

To my classmates: Thank you Hannah, Diana, and Laynie for your support and encouragement throughout our training program. I am so grateful for each and every one of you and I am so glad that we are friends and now colleagues.

To my family and friends: Thank you Dad, Mom, Sam, Isaac, and my other family members and friends for always believing in me and for being a source of encouragement and support through my genetic counseling training and life.

TABLE OF CONTENTS

TABLES

FIGURES

BACKGROUND

Current Research on hEDS and HSD

Description & Diagnosis

Despite being the one of the most common heritable connective tissue disorders, accurate recognition and diagnosis of Hypermobile Ehlers Danlos syndrome (EDS Hypermobility type or hEDS) remains an ongoing challenge[1-8]. Often, hEDS is used as a "default" diagnosis to explain individuals with chronic pain and generalized joint hypermobility when other conditions have been ruled out[3, 6, 9, 10]. Generalized joint hypermobility is a non-specific feature of many connective and non-connective tissue disorders, therefore a diagnosis of hEDS must also include multiple systemic connective tissue findings[2, 5, 11]. Sleep disturbance, fatigue, postural orthostatic tachycardia syndrome (POTS), functional gastrointestinal disorders, dysautonomia, anxiety, and depression have all been associated with but are non-specific to hEDS[2, 7, 10, 11]. Additionally, variability in clinical features is substantial which makes it difficult to distinguish between conditions and predict prognosis.

Molecular confirmation is available for most types of Ehlers Danlos Syndrome (EDS) and other connective tissue disorders, however definitive causative genes are unknown for the vast majority of individuals with hEDS. Diagnosis of hEDS is based solely on clinical diagnostic criteria[2, 4]. In 2017, Malfait and other experts revised and purposefully made more stringent, the diagnostic criteria for hEDS in an effort to reduce heterogeneity with hopes to better facilitate gene discovery[2]. Individuals not meeting criteria for hEDS are given the diagnostic label of Hypermobility Spectrum Disorder (HSD)[1, 4]. Both hEDS and HSD lie on a continuum of conditions featuring joint hypermobility and clinical management is the same regardless of the

diagnosis[1]. However, identification of an underlying genetic cause(s) is valuable for molecular confirmation and distinction from other conditions featuring joint hypermobility. Patients' perceptions of uncertainty in their diagnosis and their ability to cope with these uncertainties have yet to be explored in the research literature in the hEDS and HSD populations.

Illness Chronicity & Impact

While there is a phenotypic spectrum, hEDS and HSD have been associated with musculoskeletal and non-musculoskeletal problems, which vary in extent, severity, and pain[2, 7, 11, 12]. Chronic pain and fatigue are prevalent problems and have a significant impact on physical, emotional/psychological, and social functioning in individuals with hEDS or HSD[7-9, 13-22]. A qualitative interview study of individuals with EDS explored their experiences living with pain; many of them explaining the constant nature of their pain, "learning" to live with pain and being limited in their educational pursuits, job opportunities, and social activities[19]. In addition to the significant impact on physical and psychological functioning, chronic pain and fatigue have the potential to become disabling. Baeza-Velasco and colleagues reviewed 33 studies examining the psychological factors related to chronic pain and disability in individuals with hEDS[9]. Chronic pain and fatigue were associated with reduction in cognitive abilities, increased somatosensory amplification and pain catastrophizing, high levels of negative emotions, symptoms of anxiety and depression, and fluctuations in activity levels leading to hypervigilant or avoidant behaviors[9]. These cognitive, emotional, and behavioral aspects contribute to overall psychological functioning in individuals with hEDS or HSD.

The biopsychosocial model of health explains the bidirectional relationship between physical and psychological functioning. In a retrospective chart review study, Hershenfeld and

colleagues identified mental health concerns in just less than half (42.5%) of individuals with hEDS or HSD, the most common being anxiety and depression[23]. In response to the significant psychological impact of living with hEDS or HSD, a few studies have investigated the use of psychotherapeutic interventions such as Cognitive-Behavioral Therapy (CBT). Positive outcomes were observed with reduction in anxiety, depression, catastrophizing, and an improvement in self-efficacy[9, 24], however, these studies have small sample sizes and are limited in generalizability. While there is strong evidence for the relationship between chronic pain and fatigue with physical and psychological functioning, there is little research exploring patients' perspectives on their illness and its effect on their identity and life.

Conceptual Framework

The conceptual framework for our study drew from several different theories with the aim to explore illness identity and psychological adaptation in individuals with hEDS or HSD [see **FIGURE 1**]. The foundation for this framework builds from Lazarus and Folkman's Transactional Model of Stress and Coping (TMSC)[25, 26] and the Common Sense Model of SelfRegulation (CSM) by Leventhal and colleagues[27, 28]. A chronic illness such as hEDS or HSD, threatens the body and disrupts an individual's sense of self[29]. Stress is the result of the interaction between an individual (their physiological, cognitive, affective, and psychological selves) and their environment[25, 26]. A chronic illness is a source of stress[25, 26, 29]. The relationship between stress and the environment can be explained by the processes of cognitive appraisals and coping[25-28]. An individual's evaluation of the relevance or risk of a stressor to themselves is known as primary appraisal. A stressor can either be appraised as a threat to self or as an opportunity for growth. An individual's evaluation of their resources to deal with stress is known as secondary appraisal. Individuals utilize various internal and external resources such as coping

strategies and social support to deal with stress [25, 26]. Selection of coping strategies is directed by individuals' appraisals of stress. Being able to effectively cope with stress benefits various health and psychological outcomes[25, 26]. The TMSC and CSM are valuable models to use in the study of patient populations as appraisals, coping, and behaviors are mutable and therefore appropriate targets of interventions to improve health and psychological outcomes of patients. Our research study aims to assess relationships among various types of appraisals and outcomes to understand how individuals integrate their illness into their identity and adapt to living with hEDS or HSD..

Appraisals

The constructs used in our research study to capture the appraisal process consist of Illness Perceptions, Uncertainty in Illness, and Coping Self-Efficacy [see **FIGURE 1**]. The construct of Illness Perceptions, from Leventhal's CSM, assesses individuals' cognitive and emotion representations of an illness[27, 30, 31]. The five attributes of illness perceptions include 1) identity of the disease (ie. symptoms, labels), 2) timeline (ie. onset, duration, recovery time), 3) perceived cause(s) (ie. germs, genetic variants), 4) consequences (ie. death, disability, pain, social and economic loss), and 5) controllability (ie. intractable vs. susceptible to self-treatment, medication, surgery)[30, 31]. Primary appraisals focus on the nature of the stressor therefore the construct of Illness Perceptions can be used to assess how individuals with hEDS or HSD perceive their illness. One study by Hope and colleagues found that individuals with hEDS or HSD perceived their illness to be complex and chronic[32]. Affected individuals felt they had moderate personal and treatment control over their illness[32]. This study provides insight into individuals' perceptions of living with hEDS or HSD yet the researchers do not relate these perceptions to either health or psychological outcomes. To potentially target illness perceptions through interventions, it is first necessary to understand its relationship with measurable

outcomes. Our study evaluates the relationships among illness perceptions and two primary outcomes: illness identity and psychological adaptation [see **FIGURE 1**]. In addition to illness perceptions, individuals with hEDS or HSD may perceive uncertainty in their illness due to the erratic nature of symptomatology and ambiguity in symptoms and diagnosis[33]. Individuals with hEDS or HSD may experience multiple levels of uncertainty in the cause, prognosis, consequences, outcomes, and meaning of their illness[33-37]. Uncertainty has the ability to invade one's ability to cope and adapt to living with an illness[34-36]. The construct of Uncertainty in Illness, from Mishel's Uncertainty in Illness theory, assesses individuals' perceptions of uncertainty in illness[34-36]. Secondary appraisals focus on the abilities and resources of individuals to deal with a stressor therefore the construct of Uncertainty in Illness can be used to assess perceptions of uncertainty in individuals with hEDS or HSD. Although uncertainty likely contributes to many challenges faced by individuals with hEDS or HSD, it has not previously been quantifiably studied. Our study evaluates the relationships among uncertainty in illness and two primary outcomes: illness identity and psychological adaptation [see **FIGURE 1**].

Due to symptoms, comorbidities, and other challenges of living with hEDS or HSD, affected individuals may utilize a variety of cognitive and behavioral efforts to deal with their illness. Hypervigilance or avoidance are common behaviors of affected individuals when seeking medical care and management however both are associated with poor outcomes that can potentially lead to disability[9]. Little is known about the coping strategies and behaviors utilized by individuals with hEDS or HSD and the effect of these efforts on health and psychological outcomes. Being able to cope effectively to stress or a health threat leads to positive outcomes as demonstrated by Lazarus' TMSC[25, 26]. The construct of Coping Self-Efficacy assesses an individual's confidence in their ability to cope effectively[38]. Secondary appraisals focus on the

abilities and resources of individuals to deal with a stressor therefore the construct of Coping Self-Efficacy can be used to assess confidence in coping of individuals with hEDS or HSD. Our study evaluates the relationships among coping self-efficacy and two primary outcomes: illness identity and psychological adaptation [see **FIGURE 1**].

Illness Identity

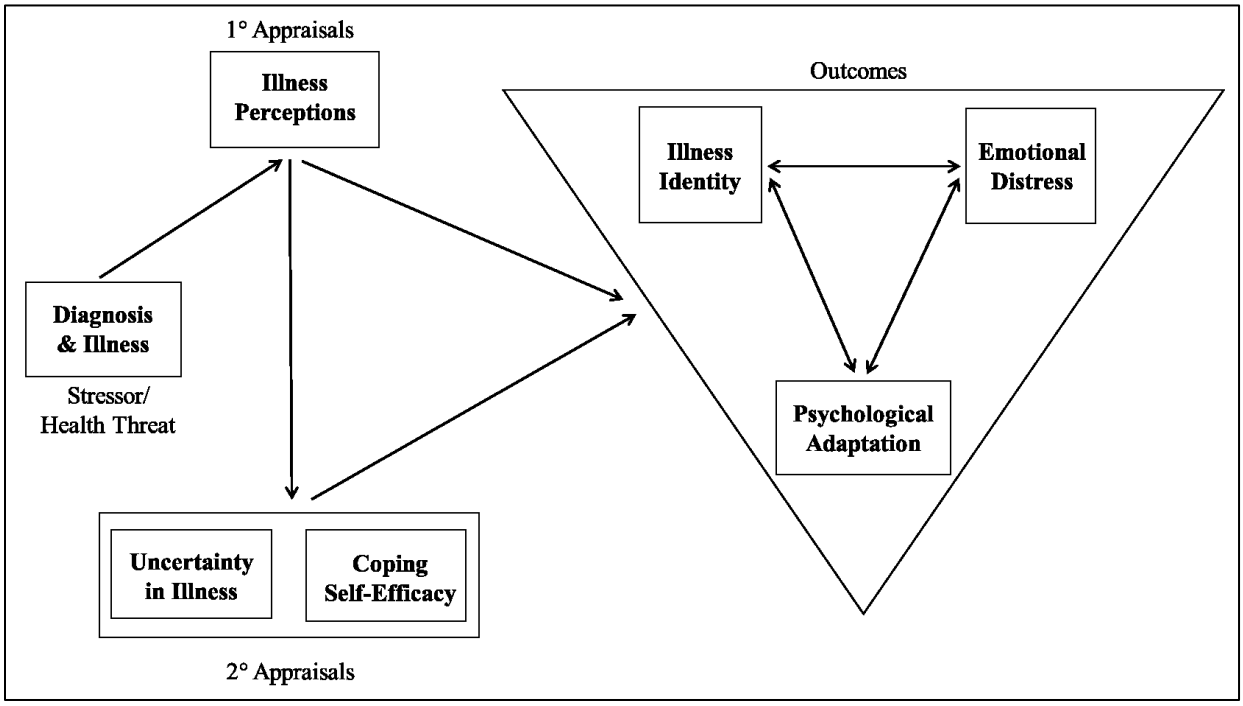
"Chronic illness assaults the body and threatens the integrity of self"[29]. From bodily losses to loss of relationships, individuals with chronic illness repeatedly experience loss[29]. In response to loss, individuals question and redefine their identities[29]. According to Erikson, identity refers to the degree to which individuals integrate personality, social interactions, and life experiences into a coherent sense of self which guides values and behaviors[39]. A chronic illness interferes with identity formation and creates tension between body and self. According to Charmaz's theory on Body, Identity, and Self, there are a variety of ways individuals manage the tension between body and self: some ignore, minimize, or struggle against their illness whereas others reconcile, surrender or embrace their illness[29]. Successful adaptation occurs when individuals are able to live with their illness and are not be defined by it, resulting in optimal physical and psychological functioning[29]. Individuals with hEDS or HSD feel they are "living a restricted life" due to living in fear, living with pain, feeling stigmatized, experiencing lack of affirmation from the healthcare community, and feeling limited in education, career opportunities, and social activities[19]. All of these challenges may contribute to tension between body and self when living with a chronic condition therefore interfering with physical and psychological functioning.

Little is known about how individuals with hEDS or HSD incorporate their illness into their identity, what factors influence illness identity, and how illness identity affects health and psychological outcomes. Our research study uses the construct of Illness Identity to capture how illness influences sense of self and the degree to which it is included in identity formation[29, 40, 41]. The construct of Illness Identity includes 4 different states: rejection, engulfment, acceptance, and enrichment. Rejection, or the degree to which an illness is rejected as part of one's identity, and engulfment, or the degree to which an illness dominates one's identity capture negative illness identities or less adaptive forms of illness integration[40, 41]. Acceptance, or the degree to which an illness is accepted as part of one's identity, and enrichment, or the degree to which an illness positively affects one's identity, capture positive illness identities or more adaptive illness integration[40, 41]. The construct of Illness Identity has been evaluated in a few populations including adolescents and emerging adults with type 1 diabetes[40], adults with chronic illness[42], young adults with refractory epilepsy[43], and adults with congenital heart disease[44]. These studies demonstrated differentiation among the 4 illness identity states. Additionally, these studies showed that the degree to which an illness is integrated into a one's identity is associated with physical and psychological functioning as well as behavioral outcomes such as treatment adherence and healthcare utilization [40-42, 44, 45]. Our study evaluates the relationships among illness perceptions, uncertainty in illness, coping self-efficacy and the outcome of illness identity in individuals with hEDS or HSD [see **FIGURE 1**]. Also, our study evaluates the relationships between the outcomes of illness identity, emotional distress, and psychological adaptation [see **FIGURE 1**].

Psychological Adaptation

Individuals' ability to effectively manage their illness and its potential stress is known as psychological adaptation. Adaptation is more than just optimal physical functioning and psychological well-being. According to Lazarus' TMSC[25, 26], adaptation is the outcome of appraising stressors or health threats and using coping strategies effectively. However, adaptation can also be viewed as a process. According to Taylor's Theory of Cognitive Adaptation (TCA)[46], searching for meaning, regaining control, and rebuilding self-esteem is the process of adaptation. This ongoing process fluctuates throughout life and with different stressors[46]. However, many individuals are able to find restoration and hopefulness through the process of adaptation[46, 47]. The construct of Psychological Adaptation assesses how individuals adapt to a chronic condition[48]. Biesecker and Erby suggest that successful coping, restored self-esteem, spiritual and psychological well-being, and social integration are all indicators of a well-adapted individual[48, 49]. Individuals with hEDS or HSD experience many physical[7, 11, 12, 17], psychological[9, 22], and social challenges[19, 50] and little is known about their adaptation to living with a chronic illness. . Our study evaluates the relationships among illness perceptions, uncertainty in illness, coping self-efficacy and the outcome of psychological adaptation in individuals with hEDS or HSD [see **FIGURE 1**]. Also, our study evaluates the relationships between the outcomes of psychological adaptation, emotional distress, and illness identity [see **FIGURE 1**].

FIGURE 1: Conceptual Framework



Significance

Much of the research literature in the hEDS and HSD populations focuses on the description and diagnosis of these conditions, patients' experiences of illness chronicity, and its effect on physical and psychological functioning. Affected individuals have chronic pain and fatigue among other co-morbidities that contribute to the chronic and complex nature of hEDS and HSD. Additionally, they experience challenges including uncertainty in diagnosis, lack of access to knowledgeable healthcare providers, limited treatment and management options, and potential for substantial disability. As a result of these comorbidities and challenges, physical and psychological functioning is negatively affected in these individuals. Further research is needed to explore how affected individuals perceive their illness, appraise uncertainty and their ability to cope, integrate their illness into their identity, and adapt to living with a chronic illness. The objectives of our study are to contribute to a greater understanding of how these concepts interact with each other and provide insight into the perspectives and needs of patients with hEDS or HSD which may allow genetic counselors to provide better clinical care for individuals with these illnesses.

OBJECTIVE AND SPECIFIC AIMS

Much of the research literature in the hEDS and HSD populations has concentrated on two main topics: diagnosis and illness chronicity. Individuals experience challenges regarding uncertainty in diagnosis[51], lack of access to knowledgeable healthcare providers[51-53], limited treatment and management options[51-53], and potential for substantial disability[15]. Further exploration of these challenges is warranted to understand if and how individuals incorporate their illness into their identity and adapt to living with hEDS or HSD.

Aim 1: To examine the relationships between predictors [diagnosis and illness characteristics and primary and secondary appraisals] and outcome of illness identity.

*In our study, primary appraisals is captured by a measure of illness perceptions and secondary appraisals is captured by measures of uncertainty in illness and coping self-efficacy.

Hypothesis: Individuals with greater number and impact of symptoms, greater perceptions of their illness as threatening, greater uncertainty in their illness, and lower coping self-efficacy will have higher scores in the rejection or engulfment identities.

Aim 2: To examine relationships between illness identity and outcomes of emotional distress and psychological adaptation.

*In our study, emotional distress is captured by measures of anxiety and depression.

Hypothesis: Individuals who have higher scores in the rejection or engulfment identities will experience more symptoms of anxiety and depression and will be less adapted to living with their illness.

METHODS

Study Design

Our cross-sectional study used an online survey to examine illness identity and psychological adaptation in individuals with hEDS or HSD. Potential participants for the main study were recruited from the Ehlers Danlos Society (EDS Society) [see **APPENDIX 1**]. The EDS Society posted the link to the survey in the research section on their website and on Instagram. Participants completed an online survey consisting of several validated measures of concepts from within the conceptual framework. The survey was developed using the survey software, Qualtrics. Estimated time to complete the survey was 30-40 minutes. Participants who completed the survey were eligible to receive a $5.00 electronic gift card.

Pilot Study

A pilot study was conducted before the main study was distributed. The purpose of the pilot study was to ensure that the questions and instructions on the survey were clear to participants. Pilot participants were asked to complete the survey and provide feedback by responding with any questions or comments about the survey. Participants for the pilot study were recruited from the Johns Hopkins Department of Genetic Medicine. Two genetic counselors, Christy H. Smith, ScM, CGC and Weiyi Mu, ScM, CGC, and one geneticist, Joann Bodurtha, MD, MPH, invited potential pilot participants either in person during their appointment or via email [see **APPENDIX 1**].

Study Sample

The study participants were individuals with a self-reported clinical diagnosis of hEDS or HSD. Inclusion criteria specified individuals age 18 years or older with a clinical diagnosis of hEDS or HSD. Exclusion criteria specified individuals who did not have a clinical diagnosis of hEDS or HSD, individuals under the age of 18 years, and individuals who did not speak or understand written English. There were no eligibility restrictions based on demographics such as race, ethnicity, and sex.

The proposed sample size for our study was 250 individuals. A power calculation for regression analysis was conducted to specifically assess the relationship between illness identity and psychological adaptation [see **TABLE 1**]. Holding alpha at 0.05 and power at 0.80, a small ($r = 0.1$) to medium ($r = 0.3$) effect size was reasonable for this study based on previous studies evaluating factors associated with psychological adaptation[54-60] and acceptable benchmarks for social and behavioral science research[61]. This power calculation was also appropriate to use in the assessment of relationships between our other study variables.

TABLE 1: Power Calculations for Regression Analysis

	Sample Size (N)	Alpha	Power	SD (regression errors)	SD (independent variables)	Estimated Effect Size
1	787	0.05	0.8	1	1	0.1
2	198	0.05	0.8	1	1	0.2
3	89	0.05	0.8	1	1	0.3
4	51	0.05	0.8	1	1	0.4
5	33	0.05	0.8	1	1	0.5

SD: standard deviation

Measures

Demographics

Participants were asked a series of 6 single-answer questions regarding their current age, sex, race, ethnicity, marital status, and highest level of education.

Diagnosis Characteristics

Participants were asked a series of 6 single-answer questions regarding their diagnosis of hEDS or HSD [see **APPENDIX 3**]. These questions included "Have you been given a formal clinical diagnosis of hEDS or HSD by a healthcare provider?", "For the healthcare provider who diagnosed your condition, which condition did he or she diagnose you with?", "What other diagnoses have you been given in the past?", "At what age did you first notice signs or symptoms of hEDS or HSD?", "At what age were you diagnosed with hEDS or HSD?", and "How much time has passed since your diagnosis of hEDS or HSD?".

Illness Characteristics

Participants were provided a list of 21 symptoms/comorbidities that have been associated with hEDS or HSD [see **APPENDIX 3**]. This list was developed for our specific study. Symptoms/co-morbidities were selected based on the clinical diagnostic criteria[2], the research literature[8, 11, 12, 21, 62], and in consultation with geneticist, Dr. Joann Bodurtha, and genetic counselor, Christy H. Smith. Participants were asked if they experienced the symptom/co-morbidity (0 = "No" and 1 = "Yes") and its degree of impact on their health by responding to a 5-point Likert scale (1 = "strongly disagree" to 5 = "strongly agree"). The score for each symptom/comorbidity was simply the response to the question. An overall score was calculated

for total count of illness characteristics and total impact of illness characteristics by adding each response respectively. A higher score for total count of illness characteristics reflects a high amount of symptoms/comorbidities experiences whereas a lower score reflects a lower amount of symptoms/comorbidities experiences. A higher score for total impact of illness characteristics reflects a greater perceived impact of symptoms/comorbidities whereas a lower score reflects a lesser perceived impact of symptoms/comorbidities.

Illness Perceptions

Participants were asked a series of 9 questions through a previously validated scale, Illness Perceptions Questionnaire-Brief Form (IPQ-B)[31], to assess participants' perceptions of living with hEDS or HSD. Each question corresponds to a specific dimension of the IPQ-B scale assessing participants cognitive and emotional representations of living with their illness [see **APPENDIX 3**]. These dimensions consist of (1) Consequences, (2) Timeline, (3) Personal Control, (4) Treatment Control, (5) Identity, (6) Concern, (7) Coherence, (8) Emotional Representations, and (9) Causes. Participants were asked to respond to each question (except Causes) on an 11-point Likert scale. An example of a survey question is "How much control do you feel you have over your illness?" (Dimension: Personal Control). For the Causes question, participants were asked to list in rank order the 3 most important factors that they believe caused their illness. The score for each dimension (except Causes) is simply the response to the question. An overall score was calculated by reverse scoring questions 3, 4, and 7 and adding them to questions 1, 2, 5, 6, and 8. A higher score reflects a more threatening view of the illness whereas a lower score reflects a more benign view. For the causes question, responses were grouped into categories based on thematic content analysis. Internal reliability (Cronbach's alpha) of the IPQ scale has been reported to range from 0.702 to 0.720 in published research

literature[59, 63, 64]. A systematic review and meta-analysis of 188 studies, found good concurrent and predictive validity[65].

Uncertainty in Illness

Participants were asked a series of 22 questions through a previously validated scale, Mishel Uncertainty in Illness Scale-Community Form (MUIS-C)[36], to assess participants perceived uncertainty in their hEDS or HSD. The first 14 questions correspond to the dimension of Ambiguity/Future Uncertainty whereas the last 8 questions correspond to the dimension of Unpredictability [see **APPENDIX 3**]. Participants were asked to respond to each question on a 5-point Likert scale (1 = "strongly disagree" to 5 = "strongly agree"). An example of a survey question is "I have a lot of questions without answers" (Dimension: Ambiguity/Future Uncertainty). The score for the Ambiguity/Future Uncertainty dimension was calculated by adding the responses to each question. The score for the Unpredictability dimension was calculated by reverse scoring all questions and then adding them together. An overall scale score was calculated by adding the 2 dimension scores. A higher score reflects greater perceived uncertainty in illness whereas a lower score reflects less perceived uncertainty. Internal reliability (Cronbach's alpha) of the MUIS scale has been reported to range from 0.71 to 0.91 in the published research literature[66].

Coping Self-Efficacy

Participants were asked a series of 13 questions through a previously validated scale, Coping Self-Efficacy (CSE)[38], to assess participants confidence in their ability to cope effectively. The first 6 questions correspond to the dimension of Use of Problem-Focused Coping, the next 4 questions correspond to the dimension of Stopping Unpleasant Emotions and

Thoughts, and the last 3 questions correspond to the dimension of Getting Support from Friends and Family [see **APPENDIX 3**]. Participants were asked to respond to each question on an 11-point Likert scale (1 = "cannot do at all" to 11 = "certainly can do"). An example of a survey question is "Break an upsetting problem down into smaller parts" (Dimension: Use of Problem-Focused Coping). The score for each dimension was calculated by averaging the responses to each question. An overall scale score was calculated by averaging the 3 dimension scores. A higher score reflects greater confidence in their ability to effectively cope whereas a lower score reflects less confidence in their coping ability. Internal reliability (Cronbach's alpha) of the CSE scale has been reported to range from 0.88 to 0.97 in the published research literature[38, 58, 67].

Illness Identity

Participants were asked a series of 25 questions through a validated scale, Illness Identity Questionnaire (IIQ)[40], to assess the degree to which they integrate hEDS or HSD into their identity. The construct of Illness Identity includes 4 different states: rejection, engulfment, acceptance, and enrichment. The first 5 questions capture the illness identity state of Rejection or the degree to which an illness is rejected as part of one's identity. The next 5 questions capture the illness identity state of Acceptance or the degree to which an illness is accepted as part of one's identity The next 8 questions capture the illness identity state of Engulfment or the degree to which an illness dominates one's identity The last 7 questions capture the illness identity state of Enrichment, or the degree to which an illness positively affects one's identity [see **APPENDIX 3**]. Participants were asked to respond to each question on a 5-point Likert scale (1 = "strongly disagree" to 5 = "strongly agree"). Examples of survey questions are "I refuse to see my illness as part of myself" (State: Rejection), "My illness is a part of who I am" (State: Acceptance), "My illness dominates my life" (State: Engulfment), and "Because of my illness, I

have grown as a person" (State: Enrichment).The score for each illness identity state was calculated by averaging the responses to each question. A higher score on any of the illness identity states reflects support for that illness identity state whereas a lower score reflects lack of support for that illness identity state. The dimensions of the IIQ demonstrate good internal reliability (Cronbach's alpha) in the published research literature [Rejection (range from 0.75 to 0.84), Acceptance (range from 0.81 to 0.85), Engulfment (range from 0.90 to 0.92), Enrichment (range from 0.90 to 0.95)][40-42, 44, 45].

Emotional Distress

Participants were asked a series of 16 questions through validated scales, PROMIS Anxiety-Short Form 8a (PROMIS Anx.)[68] and Depression-Short Form 8a (PROMIS Dep.)[68], to assess participants emotional distress. The first 8 questions are from the Anxiety short form and the last 8 questions are from the Depression short form [see **APPENDIX 3**]. Participants were asked to respond to each question on a 5-point Likert scale (1 = "never" to 5 = "always"). An example of a survey question is "My worries overwhelmed me" (Anxiety short form). The score for anxiety and depression for each participant is calculated through the HealthMeasures Scoring Service (available at http://www.healthmeasures.net/index.php) which utilizes Item Response Theory. PROMIS scores have a mean of 50 and standard deviation (SD) of 10 in the general population. A higher score reflects more symptoms of anxiety or depression whereas a lower score reflects less symptoms[69]. A development and calibration study of the PROMIS Emotional Distress measures demonstrated good internal consistency and validity of the Anxiety and Depression short forms[70].

Psychological Adaptation

Participants were asked a series of 20 questions through a validated scale, Psychological Adaptation Scale (PAS)[48], to assess participants adaptation to living with hEDS or HSD. The first 5 questions correspond to the dimension of Coping Self-Efficacy, the next 5 questions correspond to the dimension of Self-Esteem, the next 5 questions correspond to the dimension of Social Integration, and the last 5 questions correspond to the dimension of Spiritual Well-Being [see **APPENDIX 3**]. Participants were asked to respond to each question on a 5-point Likert scale (1 = "strongly disagree" to 5 = "strongly agree"). An example of a survey question is "Helped me learn how to handle difficult times" (Dimension: Self-Esteem). The score for each dimension was calculated by averaging the responses to each question. An overall scale score was calculated by averaging the 4 dimensions scores. A higher score reflects better adaptation to illness whereas a lower score reflects poorer adaptation to illness. Internal reliability (Cronbach's alpha) of the PAS scale has been reported to range from 0.73 to 0.97 in the published research literature[48, 55, 56, 58-60, 71].

Statistical Analyses

Responses from the survey were analyzed to examine relationships between 2 main groups of predictors and outcomes. The first aim of our study was to examine how diagnosis and illness characteristics and primary and secondary appraisals are related to illness identity. In our study, the primary appraisal was illness perceptions and the secondary appraisals were uncertainty in illness and coping self-efficacy. The second aim of our study was to examine how illness identity related to emotional distress and psychological adaptation. In our study, emotional distress were symptoms of anxiety and depression. Statistical analyses were completed using STATA Version 15[72].

Descriptive Statistics

Frequencies and percentages were calculated to characterize the population based on demographics and diagnosis and illness characteristics. Also, means of each subscale and scale were calculated to characterize the population based on illness perceptions, uncertainty in illness, coping self-efficacy, illness identity, anxiety and depression, and psychological adaptation.

Internal Reliability of Scales

Internal reliability for each of the scales used in this study was calculated by Cronbach's alpha coefficients of reliability[73]. A Cronbach's alpha of 0.70 or higher is considered acceptable (high internal reliability) in most social science research[73].

Correlation Analysis

A Pearson pairwise correlation analysis was conducted to understand associations among all of our study variables except demographics and diagnosis characteristics. These variables included the count and impact of illness characteristics, total score for illness perceptions, total score for uncertainty in illness, total score for coping self-efficacy, scores for each illness identity state, total score for anxiety, total score for depression, and total score for psychological adaptation. Significant associations were determined by $p < 0.05$.

Regression Analysis

Several multiple linear regression models were constructed to examine the associations between predictors and outcomes in each aim of our study. Significant associations were determined by $p < 0.05$.

Ethics Statement

Our research study was reviewed and approved by the Institutional Review Board of the Bloomberg School of Public Health, Johns Hopkins University [JHSPH IRB#: 00009644] and the Scientific Committee of the EDS Society. Participants were informed that reading a description of the study [see **APPENDIX 2**] and completion of the survey indicated their consent to the study. Documentation of written consent was waived by the JHSPH IRB.

Funding

Our research study was supported by the Intramural Research Program of the National Human Genome Research Institute, National Institutes of Health.

RESULTS

Participant Characteristics

Pilot Study

Of the 9 potential participants approached for the pilot survey, 2 completed the survey. Both individuals indicated they had a diagnosis of hEDS. The outcome of the pilot study consisted of only minor changes related to clarification of wording in a few questions.

Recruitment

Of the 591 total participants who accessed the survey, 160 participants completed less than 50% of the survey. Of the 431 participants who remained, 399 participants were included in the study. For inclusion in statistical analyses, each participant needed to complete each measure used in the statistical analysis.

Demographics

Of the 399 participants, the majority were female (93.73%), white (93.23%), and not Hispanic or Latino (92.7%) [see **TABLE 2**]. Ages of participants included 18-25 years (26.57%), 26-30 years (18.05%), 31-40 years (28.07%), 41-50 years (16.29%), and greater than 50 years (11.03%). Marital status of participants included single or never married (37.34%), partnered (16.29%), married (39.85%), separated or divorced (6.27%), and widowed (0.25%). Highest level of education of participants included less than college (16.08%), some college (29.9%), college graduate (32.16%), and post-graduate (21.86%).

TABLE 2: Participant Demographics [N = 399]

Category	Frequency	Percent
Age		
18 - 25 years	106	26.57
26 - 30 years	72	18.05
31 - 40 years	112	28.07
41 - 50 years	65	16.29
> 50 years	44	11.03
Sex		
Female	374	93.73
Race		
White	372	93.23
Ethnicity		
Not Hispanic or Latino	368	92.7
Marital Status		
Single / Never Married	149	37.34
Partnered	65	16.29
Married	159	39.85
Separated / Divorced	25	6.27
Widowed	1	0.25
Highest Level of Education		
< College	64	16.08
Some College	119	29.9
College Graduate	128	32.16
Post - Graduate	87	21.86

Descriptive Statistics

Diagnosis Characteristics

Most participants indicated receiving a formal clinical diagnosis of hEDS or HSD by a healthcare provider (95.49%) and the majority were diagnosed with hEDS (79.7%) [see **TABLE 3**]. Participants indicated a range of previous diagnosis including hEDS (19.73%), HSD (9.46%), different type of EDS (5.14%), immune deficiency or autoimmune disorder (15.14%), and other (50.27%). Age at onset of symptoms varied with 57.14% indicating at less than 10 years old, 29.07% indicating at 10-18 years old, 10.53% indicating at 19-30 years old, and 3.26% indicating at greater than 30 years old. Age at diagnosis varied with 16.58% indicating 10-18 years old, 40.45% indicating 19-30 years old, 24.85% indicating 31-40 years old, and 18.84% indicating greater than 40 years old. Amount of time since diagnosis varied with 25.31% indicating less than 1 year, 24.06% indicating 1-2 years, 22.81% indicating 3-5 years, 16.04% indicating 5-10 years, and 11.78% indicating greater than 10 years.

TABLE 3: Diagnosis Characteristics [N = 399]

Characteristic	Frequency	Percent
Formal Clinical Diagnosis		
Yes	381	95.49
Diagnosis		
hEDS	318	79.7
Previous Diagnosis		
hEDS	73	19.73
HSD	35	9.46
Different Type of EDS	19	5.14
Immune Deficiency or Autoimmune Disorder	56	15.14
Other	186	50.27
Age of Symptom Onset		
< 10 years old	228	57.14
10 - 18 years old	116	29.07
19 - 30 years old	42	10.53
> 30 years old	13	3.26
Age at Diagnosis		
< 10 years old	5	1.26
10 - 18 years old	66	16.58
19 - 30 years old	161	40.45
31 - 40 years old	99	24.87
> 40 years old	67	16.84
Time Since Diagnosis		
< 1 year	101	25.31
1 - 2 years	96	24.06
3 - 5 years	91	22.81
5 - 10 years	64	16.04
> 10 years	47	11.78

Illness Characteristics

Of the participants who completed the survey, greater than 90% indicated they experience pain, joint hypermobility, joint dislocations or subluxations, fatigue, gastrointestinal issues, skin manifestations, and emotional difficulties [see **TABLE 4**]. More than 75% of participants indicated that they experience cardiovascular issues, neurological issues, and sleeping difficulties. Additionally, greater than 50% indicated they experience arthritis, Temporomandibular Joint disorder (TMJ), and immunological issues..

Symptoms and co-morbidities that had the greatest impact ($M > 5$) on participant's life were pain ($M = 6.291$, $SD = 1.474$), joint hypermobility ($M = 5.865$, $SD = 1.5540$), joint dislocations or subluxations ($M = 5.591$, $SD = 2.115$), fatigue ($M = 6.211$, $SD = 1.573$), gastrointestinal issues ($M = 5.546$, $SD = 2.115$), neurological issues ($M = 5.441$, $SD = 2.251$), emotional difficulties ($M = 5.474$, $SD = 2.123$), and sleeping difficulties ($M = 5.075$, $SD = 2.600$) [see **TABLE 4**].

TABLE 4: Illness Characteristics [N = 399]

	IC. Count		IC. Impact	
Symptom / Co-morbidity	**Frequency**	**Percent**	**Mean**	**SD**
Pain (Limb or Joint)	392	98.25	6.291	1.474
CRPS / RSD	80	23.32	1.083	2.305
Fibromyalgia	169	45.31	2.516	3.090
Joint Hypermobility	389	97.49	5.865	1.554
Joint Dislocations or Subluxations	365	91.94	5.591	2.115
Fatigue	386	97.23	6.211	1.573
Arthritis	217	57.26	3.060	3.005
Scoliosis	172	46.74	2.000	2.565
TMJ	271	71.88	3.521	2.738
Locked Jaw	143	39.18	1.787	2.547
Endometriosis	88	24.51	1.261	2.482
Vulvodynia	53	15.1	0.712	1.918
Infertility	51	14.7	0.687	1.901
Gastrointestinal Issues	361	91.62	5.546	2.115
Cardiovascular Issues	330	85.05	4.932	2.507
Neurological Issues	353	89.14	5.441	2.251
Organ Prolapse	76	20.88	1.050	2.253
Skin Manifestations	362	91.88	4.145	2.075
Immunological Issues	222	59.2	3.431	3.175
Emotional Difficulties	362	92.82	5.474	2.123
Sleeping Difficulties	330	84.18	5.075	2.600

IC. Count: total count of illness characteristics
IC. Impact: total impact of illness characteristics

CRPS / RSD: Complex Regional Pain syndrome / Reflex Sympathetic Dystrophy
TMJ: Temporomandibular Joint disorder

Gastrointestinal Issues: Irritable Bowel syndrome (IBS), Gastroesophageal Reflux disorder (GERD), gastroparesis, diarrhea, constipation, nausea, other functional bowel problems
Cardiovascular Issues: shortness of breath, tachycardia, palpitations, Postural Orthostatic Tachycardia syndrome (POTS)
Neurological Issues: headaches/migraines, dizziness, nerve compression, Neurally-mediated Hypotension (NMH), syncope
Organ Prolapse: uterine, bladder, rectal
Skin Manifestations: easy bruising, easy scarring, soft / velvety skin
Immunological Issues: immune deficiency, autoimmune disorder, Mast Cell Activation syndrome (MCAS)
Emotional Difficulties: anxiety, depression, trouble focusing, brain fog, other mood disorder
Sleeping Difficulties: insomnia, Restless Leg syndrome (RLS)

Means of Scales

Overall, participants viewed hEDS and HSD as threatening (IPQ: $M = 62.688$, $SD = 8.603$). More specifically, participants indicated that their illness has a severe impact on their lives (Consequences: $M = 9.135$, $SD = 1.859$). Participants perceived hEDS and HSD as lasting forever (Timeline: $M = 10.570$, $SD = 1.399$). Participants felt they had a moderate amount of personal control over their illness (Personal Control: $M = 7.463$, $SD = 2.357$) and felt their treatment could moderately help their illness (Treatment Control: $M = 6.618$, $SD = 2.522$). Participants indicated they experienced many severe symptoms (Identity: $M = 9.000$, $SD = 1.719$). This finding is consistent with the count and impact of illness characteristics described in the previous section. Participants indicated they are moderately concerned about their hEDS or HSD (Concern: $M = 8.191$, $SD = 2.324$). Participants felt they had little understanding of their illness (Coherence: $M = 3.586$, $SD = 2.347$). Participants felt their hEDS or HSD moderately affected them emotionally (Emotional Representations: $M = 8.105$, $SD = 2.373$).

When asked to "list in rank-order the three most important factors that you believe caused your illness", the majority of participants indicated "genetics" as the most important causal factor that caused hEDS or HSD [see **TABLE 5**]. Other causal factors ranked first included physical stress/injury (4.92%) and psychological stress/trauma (2.73%). Other causal factors ranked second included physical stress/injury (21.40%), lack of diagnosis/knowledgeable healthcare providers (18.95%), psychological stress/trauma (8.77%), immune dysfunction (6.67%), and diet/nutrition/lifestyle (5.26%). Other causal factors ranked third included lack of diagnosis/knowledgeable healthcare providers (16.67%), physical stress/injury (15.85%), diet/nutrition/lifestyle (6.91%), psychological stress/trauma (6.10%), and immune dysfunction (4.47%).

TABLE 5: Causal Attributions

Causal Attribution	Frequency	Percent
Causal Factor 1 [n = 366]		
Genetics	319	87.16
Physical Stress / Injury	18	4.92
Psychological Stress / Trauma	10	2.73
Causal Factor 2 [n = 285]		
Genetics	67	23.51
Physical Stress / Injury	61	21.40
Lack of Diagnosis / Knowledgeable Healthcare Providers	54	18.95
Psychological Stress / Trauma	25	8.77
Immune Dysfunction	19	6.67
Diet / Nutrition / Lifestyle	15	5.26
Causal Factor 3 [n = 246]		
Genetics	57	23.17
Lack of Diagnosis / Knowledgeable Healthcare Providers	41	16.67
Physical Stress / Injury	39	15.85
Diet / Nutrition / Lifestyle	17	6.91
Psychological Stress / Trauma	15	6.10
Immune Dysfunction	11	4.47

Overall, participants perceived moderate uncertainty in their hEDS or HSD (MUIS: *M* = 59.080, *SD* = 10.834). More specifically, participants perceived moderate ambiguity/future uncertainty (Ambiguity/Future Uncertainty: *M* = 36.792, *SD* = 8.628) and moderate unpredictability in their illness (Unpredictability: *M* = 22.263, *SD* = 4.730).

Overall, participants had moderate levels of confidence in their ability to cope (CSE: *M* = 6.168, *SD* = 2.234). More specifically, participants indicated moderate levels of confidence in using problem-focused coping (*M* = 36.792, *SD* = 8.628), stopping unpleasant thoughts (*M* = 5.725, *SD* = 2.721), and getting support from friends and family (M = 5.971, SD = 2.754).

Overall, participants had moderate scores on 3 out of the 4 illness identity dimensions (Acceptance: *M* = 2.440, *SD* = 0.646; Engulfment: *M* = 2.727, *SD* = 0.854; Enrichment: *M* = 2.279, *SD* = 0.855). Participants had moderately high scores on the Rejection Identity (*M* = 3.579, *SD* = 0.839).

Overall, participants had moderate levels of anxiety (*M* = 61.469, *SD* = 8.518) and mild levels of depression (*M* = 58.614, *SD* = 9.148).

Overall, participants were moderately adapted to living with their hEDS or HSD (PAS: *M* = 2.617, *SD* = 0.770). More specifically, participants had moderate levels of coping self-efficacy (*M* = 2.592, *SD* = 0.857). This finding is consistent with the scores on the Coping Self-Efficacy scale described previously in this section. They also had moderate levels of self-esteem (*M* = 2.511, *SD* = 0.945), and social integration (*M* = 2.253, *SD* = 0.801). Participants indicated they had moderately high levels of spiritual well-being (*M* = 3.111, *SD* = 0.966).

Internal Reliability of Scales

Most scales showed good internal reliability with $\alpha > 0.70$. The CSE scale had an $\alpha = 0.9408$, the IIQ Rejection state had an $\alpha = 0.809$, the IIQ Engulfment state had an $\alpha = 0.8892$, the IIQ Enrichment state had an $\alpha = 0.9042$, the PROMIS Anxiety scale had an $\alpha = 0.9273$, the PROMIS Depression scale had an $\alpha = 0.9441$, and the PAS had an $\alpha = 0.9447$. The IPQ scale had an $\alpha = 0.5712$ which indicated poor internal reliability. To increase internal reliability, questions 2, 4, and 7 [see **APPENDIX 3**] were dropped from the total score based on low item-total correlations which improved internal reliability to an $\alpha = 0.717$, indicating better internal reliability. All further analyses used the modified IPQ scale. The MUIS "Unpredictability" subscale had an $\alpha = 0.5947$ which indicated poor internal reliability. The subscale could not be effectively modified and was dropped from all further analyses. The MUIS "Ambiguity/Future Uncertainty" subscale had an $\alpha = 0.8285$, indicating good internal reliability. This subscale was used in all further analyses.

Correlation Analysis

Relationships with Illness Identities

Correlations were examined to assess relationships between predictor variables and each of the illness identity states (rejection, acceptance, engulfment, and enrichment) [see **TABLE 6**]. Predictors were diagnosis characteristics, total count of illness characteristics, total impact of illness characteristics, total score for illness perceptions, total score for uncertainty, and total score for coping self-efficacy. Higher scores in the rejection identity was related to lower number of illness characteristics ($r = -0.2451$, $p < 0.001$), more perceived impact of illness characteristics ($r = 0.2773$, $p < 0.001$), more threatening illness perceptions ($r = 0.2511$, $p < 0.001$), and more

uncertainty ($r = 0.1571$, $p = 0.002$). The rejection identity was not related to coping self-efficacy ($r = 0.0357$, $p = 0.4768$). Higher scores in the acceptance identity was related to less uncertainty ($r = -0.1540$, $p = 0.0031$), and less coping self-efficacy ($r = -0.1722$, $p = 0.005$). The acceptance identity was not related to number of illness characteristics ($r = -0.004$, $p = 0.9433$), perceived impact of illness characteristics ($r = -0.0382$, $p = 0.4467$), or illness perceptions ($r = 0.031$, $p = 0.5389$). Higher scores in the engulfment identity was related to higher number of illness characteristics ($r = 0.1501$, $p = 0.008$), less perceived impact of illness characteristics ($r = -0.2329$, $p < 0.001$), less threatening illness perceptions ($r = -0.5070$, $p < 0.001$), more uncertainty ($r = 0.4223$, $p < 0.001$), and more coping self-efficacy ($r = 0.4617$, $p < 0.001$). Higher scores in the enrichment identity was related to more threatening illness perceptions ($r = 0.1091$, $p = 0.0299$) and less coping self-efficacy ($r = -0.3952$, $p < 0.001$). The enrichment identity was not related to number of illness characteristics ($r = -0.0204$, $p = 0.7197$), impact of illness characteristics ($r = -0.0322$, $p = 0.521$), and uncertainty ($r = -0.0446$, $p = 0.3817$).

TABLE 6: Correlation of Predictor Variables and Illness Identity [n=300]

	IC. Count	IC. Impact	IPQ	MUIS	CSE	IIQ Reject.	IIQ. Accept.	IIQ Engulf.	IIQ Enrich.
IC. Count	1								
IC. Impact	-0.8276*	1							
	0								
IPQ	-0.3356*	0.4349*	1						
	0	0							
MUIS	0.0405	-0.0509	-0.2861*	1					
	0.4832	0.3183	0						
CSE	0.1068	-0.088	-0.2940*	0.2712*	1				
	0.0599	0.0792	0	0					
IIQ Reject.	-0.2451*	0.2773*	0.2511*	0.1571*	0.036	1			
	0	0	0	0.002	0.477				
IIQ Accept.	-0.004	-0.0382	0.031	-0.1504*	-0.1722*	-0.4001*	1		
	0.9433	0.4467	0.5389	0.0031	0.0000	0			
IIQ Engulf.	0.1501*	-0.2329*	-0.5070*	0.4223*	0.4617*	0.0259	-0.1161*	1	
	0.008	0	0	0	0	0.6063	0.0203		
IIQ Enrich.	-0.0204	-0.0322	0.1091*	-0.0446	-0.3952*	-0.0796	0.2908*	-0.1673*	1
	0.7197	0.521	0.0299	0.3817	0	0.1123	0	0.0008	

IC. Count: total count of illness characteristics
IC. Impact: total impact of illness characteristics
IPQ: modified Illness Perceptions Questionnaire – brief form
MUIS: ambiguity/future uncertainty subscale of the Mishel Uncertainty in Illness scale – community form
CSE: Coping Self-Efficacy Scale
IIQ Reject: Illness Identity – Rejection dimension
IIQ Accept: modified Illness Identity – Acceptance dimension
IIQ Engulf: Illness Identity – Engulfment dimension
IIQ Enrich: Illness Identity – Enrichment dimension

Relationships with Emotional Distress and Psychological Adaptation

Correlations were examined to assess relationships between each of the illness identities and outcomes [see **TABLE 7**]. Outcomes were emotional distress (anxiety and depression) and psychological adaptation. More anxiety was related to higher acceptance identity ($r = 0.1993$, $p = 0.002$), lower engulfment identity ($r = -0.4590$, $p < 0.001$), and higher enrichment identity ($r = 0.1980$, $p = 0.0001$). Anxiety was not related to the rejection identity ($r = -0.0637$, $p = 0.2113$). More depression was related to higher acceptance identity ($r = 1896$, $p = 0.0001$), lower engulfment identity ($r = -0.6047$, $p < 0.001$), and higher enrichment identity ($r = 0.3237$, $p < 0.001$). Depression was not related to the rejection identity ($r = -0.0436$, $p = 0.3854$). More psychological adaptation was related to higher acceptance identity ($r = 0.2891$, $p < 0.001$), lower engulfment identity ($r = -0.2051$, $p < 0.001$), higher enrichment identity ($r = 0.8078$, $p < 0.001$), more anxiety ($r = 0.2242$, $p < 0.001$), and more depression ($r = 0.3434$, $p < 0.001$). Psychological adaptation was not related to the rejection identity ($r = -0.0611$, $p = 0.223$), .

TABLE 7: Correlation of Illness Identity and Outcomes [N=399]

	IIQ Reject.	IIQ Accept.	IIQ Engulf.	IIQ Enrich.	Anxiety	Depression	PAS
IIQ Reject.	1						
IIQ Accept.	-0.4001*	1					
	0						
IIQ Engulf.	0.0259	-0.1161*	1				
	0.6063	0.0203					
IIQ Enrich.	-0.0796	0.2908*	-0.1673*	1			
	0.1123	0	0.0008				
Anxiety	-0.0627	0.1883*	-0.4590*	0.1980*	1		
	0.2113	0.0002	0	0.0001			
Depression	-0.0436	0.1896*	-0.6047*	0.3237*	0.7203*	1	
	0.3854	0.0001	0	0	0		
PAS	-0.0611	0.2891*	-0.2051*	0.8078*	0.2242*	0.3434*	1
	0.223	0	0	0	0	0	

IIQ Reject: Illness Identity – Rejection dimension
IIQ Accept: modified Illness Identity – Acceptance dimension
IIQ Engulf: Illness Identity – Engulfment dimension
IIQ Enrich: Illness Identity – Enrichment dimension
Anxiety: PROMIS Anxiety t-score
Depression: PROMIS Depression t-score
PAS: Psychological Adaptation Scale

Regression Analysis

Outcome: Illness Identities

Regression models were built to assess predictors of each of the illness identities (rejection, acceptance, engulfment, and enrichment). Predictors were diagnosis characteristics, total count of illness characteristics, total impact of illness characteristics, total score for illness perceptions, total score for uncertainty, and total score for coping self-efficacy. Individuals who perceived their illness as threatening ($\beta = 0.0244$, $t = 2.96$, $p = 0.003$) and uncertain ($\beta = 0.0304$, $t = 4.27$, $p < 0.001$) had higher rejection identity. Individuals with higher coping self-efficacy had lower acceptance identity ($\beta = -0.0602$, $t = -2.75$, $p = 0.006$). Individuals who perceived their illness as uncertain had higher engulfment identity ($\beta = 0.0291$, $t = 5.4$, $p < 0.001$).Individuals who perceived their illness as threatening had lower engulfment identity ($\beta = -0.0341$, $t = -5.45$, $p < 0.001$).Individuals with higher coping self-efficacy had higher engulfment identity ($\beta = 0.1104$, $t = 5.84$, $p < 0.001$). Individuals with higher coping self-efficacy had lower enrichment identity ($\beta = -0.1627$, $t = -7.22$, $p < 0.001$)..

Outcome: Emotional Distress

Regression models were built to examine the relationships between each illness identity state (rejection, acceptance, engulfment, and enrichment) and emotional distress (anxiety and depression). Individuals with a higher acceptance identity ($\beta = 1.3346$, $t = 2.21$, $p = 0.027$) and higher enrichment identity ($\beta = 0.9330$, $t = 2.02$, $p = 0.045$) had higher anxiety. Individuals with a higher engulfment identity had less anxiety ($\beta = -4.2888$, $t = -9.62$, $p < 0.001$). Individuals with a higher enrichment identity ($\beta = 2.2540$, $t = 5.2$, $p < 0.001$) had more depression and those with a higher engulfment identity had less depression ($\beta = -6.0122$, $t = -14.4$, $p < 0.001$).

Outcome: Psychological Adaptation

Regression models were built to examine the relationships between each illness identity (rejection, acceptance, engulfment, and enrichment) and psychological adaptation. Individuals with higher acceptance identity ($\beta = 0.0719$, $t = 1.98$, $p = 0.048$) and higher enrichment identity ($\beta = 0.7026$, $t = 25.15$, $p < 0.001$) had higher psychological adaptation. Individuals with higher engulfment identity had lower psychological adaptation ($\beta = -0.0610$, $t = -2.27$, $p = 0.024$).

DISCUSSION

Goals of the Study

This is the first research study to explore many of the concepts used in our study, including uncertainty in illness, coping self-efficacy, illness identity, and psychological adaptation in the hEDS and HSD populations. One of the goals of our study was to understand if and how individuals incorporate their illness into their identity and adapt to living with hEDS or HSD. To better understand these processes and outcomes, several concepts were examined in the context of the Transactional Model of Stress and Coping (TMSC). These concepts consisted of diagnosis and illness characteristics, illness perceptions (as a primary appraisal), uncertainty in illness and coping self-efficacy (as secondary appraisals), and emotional distress (anxiety and depression) and psychological adaptation (as outcomes). An additional goal of our study was to examine how the concept of illness identity may relate or contribute to concepts in the TMSC. Illness identity has not previously been examined with many of the concepts used in our study including illness perceptions, uncertainty in illness, coping self-efficacy, and psychological adaptation. Illness identity has also not previously been examined in the hEDS and HSD populations.

Summary of Results

Characterization of Study Sample

Our study included 399 participants. Most participants were female, white, not Hispanic or Latino, and had a diagnosis of hEDS. Participants varied on all other demographic variables and diagnosis characteristics. Symptoms of pain, joint hypermobility, joint dislocations or subluxations, fatigue, gastrointestinal issues, neurological issues, emotional difficulties, and

sleeping difficulties were reported by most participants and were perceived as having the greatest impact. These demographic, diagnosis, and illness characteristics are consistent with other research studies within the hEDS and HSD populations[12, 21, 32, 62, 74].

Overall, participants viewed hEDS and HSD as threatening (M = 62.688, SD = 8.603). More specifically, participants viewed their illness as severe, lasting forever, and experienced many severe symptoms. There was a general perception of having moderate personal control and treatment control over their illness. Participants felt moderately concerned about their illness, indicated that they had little understanding of their illness, and felt their illness moderately affected them emotionally. These results are consistent with the illness characteristics reported previously in our study. Additionally, these results are consistent with a study by Hope and colleagues investigating subjective health complaints and illness perceptions among adults with hEDS or HSD[32].

Participants perceived moderate uncertainty in their illness and were moderately confident in their ability to cope effectively with their illness. Participants had moderate scores on 3 out of the 4 illness identity states (Acceptance: M = 2.440, SD = 0.646; Engulfment: M = 2.727, SD = 0.854; Enrichment: M = 2.279, SD = 0.855). Participants had moderately high scores on the Rejection Identity (M = 3.579, SD = 0.839). A study by Oris and colleagues investigating illness identity in adults with multisystem connective tissue disorders (specifically systemic lupus erythematosus and systemic sclerosis) found similar scores on the illness identity states[42]. Participants had moderate levels of anxiety and mild levels of depression. Many studies have reported that a significant minority of individuals with hEDS or HSD have clinically significant levels of anxiety and depression[9, 22, 23, 75-77]. Lastly, participants were moderately adapted to living with their hEDS or HSD.

Illness Identity as an Outcome

We hypothesized that individuals with greater number and impact of illness characteristics, greater perceptions of their illness as threatening, greater uncertainty in their illness, and lower coping self-efficacy would have higher scores in the rejection or engulfment identities. As hypothesized, higher scores in rejection were significantly correlated with greater perceived impact of illness characteristics, more threatening illness perceptions, and more uncertainty. Contrary to hypothesis, higher scores in rejection were significantly correlated with lower number of illness characteristics. Also contrary to hypothesis, the rejection identity was not correlated with coping self-efficacy. In regression analysis, individuals who felt threatened by and uncertain about their illness were significantly more likely to reject hEDS and HSD as part of their identity. As hypothesized, higher scores in acceptance were significantly correlated with less uncertainty. Contrary to hypothesis, higher scores in acceptance were significantly correlated with less coping self-efficacy. Also contrary to hypothesis, the acceptance identity was not correlated with number or perceived impact of illness characteristics or illness perceptions. In regression analysis, individuals who had higher coping self-efficacy were less likely to accept hEDS and HSD as part of their identity. As hypothesized, higher scores in engulfment were significantly correlated with higher number of illness characteristics and more uncertainty. Contrary to hypothesis, higher scores in engulfment were significantly correlated with less perceived impact of illness characteristics, less threatening illness perceptions, and more coping self-efficacy. In regression analysis, individuals who viewed their illness as uncertain and had higher coping self-efficacy were more likely to become engulfed by hEDS or HSD. Additionally, individuals who perceived their illness as threatening were less likely to become engulfed by hEDS or HSD. Contrary to hypothesis, higher scores in enrichment were correlated with more

threatening illness perceptions and less coping self-efficacy. Also contrary to hypothesis, the engulfment identity was not correlated with number or perceived impact of illness characteristics or uncertainty. In regression analysis, individuals with higher coping self-efficacy were less likely to be enriched by hEDS or HSD.

A unique finding in our study was the unexpected relationships among coping self-efficacy and the illness identity states. We expected that individuals who had more confidence in their ability to cope would be more likely to accept their illness as a part of their identity or become enriched by it. Our results indicated that individuals who had higher coping self-efficacy were more likely to become engulfed by their illness. One possible explanation for this finding may be the unique characteristics of the study population. We recruited our participants from the EDS Society which is a very active patient advocacy organization. Individuals involved in the EDS Society may be more likely to indicate greater confidence in their coping abilities due to the available resources and social support. However, the availability of these resources and individuals' confidence in their coping ability may not translate into the processes of coping and integrating their illness into their identity. More research is needed to understand the relationships among coping self-efficacy and the illness identity states. Additionally, more research is needed to understand how individuals with hEDS or HSD coping with their illness and integrate it into their identity.

Relationships Among Illness Identity, Emotional Distress, and Psychological Adaptation

We hypothesized that individuals who have higher scores in the rejection or engulfment identities would experience more symptoms of anxiety and depression and be less adapted to living with their illness. Contrary to hypothesis, the relationships among the illness identity states

and symptoms of anxiety and depression were not as expected. The acceptance and enrichment identities were significantly correlated with more symptoms of anxiety and depression. The engulfment identity was significantly correlated with less symptoms of anxiety and depression. The rejection identity was not related to symptoms of anxiety and depression. In regression analysis, these findings were recapitulated and individuals with more anxiety were more likely to accept hEDS or HSD into their identity or be enriched by it and less likely to be engulfed by it. Additionally, individuals with more depression were more likely to be enriched by their hEDS or HSD and less likely to become engulfed by it. As hypothesized, the acceptance and enrichment identities were significantly correlated with more psychological adaptation. The engulfment identity was significantly correlated with less psychological adaptation. Contrary to hypothesis, the rejection identity was not related to psychological adaptation. In regression analysis, these findings were recapitulated and individuals who were more likely to accept hEDS or HSD into their identity or be enriched by it had more psychological adaptation than those who are engulfed by their illness.

A unique finding in our study was the unexpected relationships among the illness identity states and symptoms of anxiety and depression. We expected that individuals who were more likely to accept their illness as part of their identity or be enriched by it would have less symptoms of anxiety and depression. Our results indicated that individuals who were more likely to be engulfed by their illness had less symptoms of anxiety and depression. One possible explanation for this finding may be that the measures used to capture symptoms of anxiety and depression are representative of the state of emotional distress rather than the trait of emotional distress. A state of emotional distress is a temporary reaction to a situation in a specific moment whereas a trait of emotional distress is a consistent personality attribute. State and trait emotional

distress are not always directly correlated. It is possible that the PROMIS measures used in our study to capture symptoms of anxiety and depression represents state emotional distress. More research is needed to understand the relationships among the illness identity states and emotional distress.

Clinical Implications

The results from our research study have implications for clinical care of individuals with hEDS or HSD. It is well recognized that hEDS and HSD are chronic conditions and greatly affect physical and psychological functioning. Previous research has identified that affected individuals experience challenges in managing their condition due to diagnostic uncertainty, lack of awareness of hEDS and HSD, lack of access to knowledgeable healthcare providers, limited treatment and management options, and potential for disability[3, 6, 9, 14, 15, 17, 19, 21-24, 32, 50, 51, 75-79]. These challenges negatively affect physical functioning and psychological well-being[3, 6, 9, 14, 15, 17, 19, 21-24, 32, 50, 51, 75-79]. Understanding how individuals with hEDS or HSD perceive their illness, appraise uncertainty and their ability to cope, integrate their illness into their identity, and adapt to living with a chronic illness, may allow healthcare providers to intervene in hopes of improving health outcomes. For example, Cognitive-Behavior Therapy (CBT) has been shown to reduce anxiety, depression, catastrophizing, and improve self-efficacy in individuals with hEDS or HSD[9, 24]. While CBT is widely used in the psychotherapy field, some of its principles may also be used by other healthcare providers such as genetic counselors. Genetic counselors can utilize CBT principles to affect downstream effects of adaptation such as medical management and behavior change[49, 80]. Genetic counselors may facilitate adaptation by helping affected individuals identify coping strategies and resources that fit with their perceptions of their illness. Furthermore, this intervention may also lead to changes in behavior such as treatment adherence.

As discussed, findings from our research study provide insight into illness identity integration and adaptation. Psychotherapeutic interventions have the potential to influence downstream clinical outcomes in individuals with hEDS or HSD.

Limitations

Although there is extensive research evidence and theories supporting the concepts of illness identity and psychological adaptation[27, 34, 38, 41, 81, 82], nuances still remain. Studying these concepts in different populations and under different circumstances may provide greater theoretical understanding and potentially identify more opportunities to affect clinical outcomes. The findings from our research study, specifically the unexpected relationships among coping self-efficacy, emotional distress, and the illness identity states, need further evaluation. More research is needed to determine if the findings from our study are reflective of the hEDS and HSD populations or if there are other psychological factors contributing. Despite the important clinical and theoretical implications of our research study, there are several limitations. In terms of sex, race, ethnicity, and clinical diagnosis our study population was fairly homogenous. Although our study population varied on other demographic and diagnostic characteristics, the findings may not be generalizable across different groups of individuals with hEDS or HSD. Furthermore, recruitment from the EDS Society may contribute to limitations in generalizability as well as result in response bias. Individuals not actively involved in the EDS Society may differ in key aspects from those who are and those who have participated in our research study. As mentioned previously, individuals who are involved in the EDS Society may be more motivated to seek resources and social support as a means of coping with their hEDS or HSD. Further research is needed to understand the effect of involvement in a patient advocacy organization on psychological and health outcomes. Additionally, the self-reported nature of the

diagnosis and illness characteristics may contribute to limitations in accurate interpretation or translation of our study findings. Lastly, the course of an illness, like hEDS or HSD, changes over time. The cross-sectional nature of our study only captures one point in time and may not comprehensively evaluate the processes of illness identity integration or adaptation overtime. Further research is needed to understand our study's unique findings and address some of its limitations.

Areas for Future Research

Our research study is the first to examine relationships among concepts within the Transactional Model of Stress and Coping (TMSC) in the hEDS and HSD populations. Additionally, this research study is the first to examine the relationships among illness identity and concepts within the TMSC. While this research study provides some insight into the relationships among concepts in the hEDS and HSD populations, it raises potential nuances in and important questions. Further research is needed to better understand how the concepts relate to each other and in this specific population.

Further research is needed to explore how other appraisals, such as uncertainty in diagnosis, contribute to adaptive illness identity integration and adaptation in individuals with hEDS or HSD. Given the 2017 revision of the hEDS clinical diagnostic criteria[2], the creation of the diagnostic label of HSD[1, 4], and lack of identifiable genetic cause(s) of hEDS and HSD[2, 10, 11, 62], it is reasonable to suspect that some affected individuals may experience uncertainty in their diagnosis. Bhise and colleagues define diagnostic uncertainty as a "subjective perception of an inability to provide an accurate explanation of the patient's health problem"[83]. Accurate recognition and diagnosis of hEDS and HSD is an ongoing challenge[1-8]. Little is known about

how healthcare providers communicate diagnostic uncertainty, how patients perceive diagnostic uncertainty, and how diagnostic uncertainty affects health outcomes. Furthermore, diagnostic uncertainty is not unique to individuals with hEDS or HSD. Many other patients with health conditions, suspected genetic or otherwise, may experience diagnostic uncertainty. Despite significant advances in medical knowledge and technology, many patients still lack an etiologic explanation for their health condition. More research is needed to evaluate the effect of diagnostic uncertainty on different health outcomes. In the interim, healthcare providers can help patients by facilitating adaptation to living with uncertainty.

Other psychological and social factors, such as perceived social stigma, may affect how individuals integrate their illness into their identity and adapt to living with hEDS or HSD. The chronic pain, fatigue, and comorbidities associated with hEDS and HSD have the potential to become disabling for some individuals[15, 19, 24, 78]. Some individuals feel as though they live a "restricted life" due to being limited in their educational pursuits, job opportunities, and social activities[19]. In addition to disability, lack of awareness, understanding, and respect from healthcare providers, other professionals, and peers may lead to feelings of stigmatization in individuals with hEDS or HSD[8, 50, 51]. Rybarczyk and colleagues define perceived social stigma as a "perception that others hold negative stereotypic attitudes about him or her as a result of a disability"[84]. Individuals with hEDS or HSD may experience stigmatization for a variety of reasons[8, 15, 19, 24, 50, 51, 78]. Based on previous work on illness, identity, and self in other populations[29], it is reasonable to suspect that perceived social stigma may influence illness identity integration and adaptation in individuals with hEDS or HSD. More research is needed to understand if and how individuals with hEDS or HSD experience stigma and its relation to

different health outcomes. In the meantime, healthcare providers can listen to patients' narratives and provide resources as necessary to help patients deal with stigma.

CONCLUSIONS

Our study is one of the only studies to assess psychological processes and outcomes in the hEDS and HSD populations. Exploration of relationships between diagnosis and illness characteristics, illness perceptions, illness uncertainty, and coping self-efficacy with illness identity revealed unique findings. Unexpectedly, higher coping self-efficacy was related the rejection and engulfment illness identities whereas lower coping self-efficacy was related to acceptance and enrichment illness identities. Additionally, exploration of relationships between illness identity, emotional distress, and psychological adaptation revealed unique findings. Unexpectedly, more symptoms of anxiety and depression were related to acceptance and enrichment identities whereas less symptoms of anxiety and depression were related to rejection and engulfment identities. More research is needed to understand these unique findings. Our study contributes to better understanding of the illness experiences of individuals with hEDS or HSD and provides a possible opportunity for genetic counselors to facilitate illness integration into identity and adaptation.

APPENDIX 1

RECRUITMENT LETTER

Dear Potential Research Participant,

You are invited to participate in a study conducted by researchers at the Johns Hopkins Bloomberg School of Public Health and the National Human Genome Research Institute. The purpose of this study is to learn more about the experiences of individuals living with Hypermobile Ehlers Danlos Syndrome (hEDS) or Hypermobility Spectrum Disorder (HSD). The information you provide may help to improve our understanding of the patient's perspective with regards to having a diagnosis and the impact of these conditions.

The study involves filling out a survey, which we anticipate will take about 30-40 minutes to complete. The survey asks questions about your diagnosis, symptoms, and thoughts and feelings about living with your condition. Individuals who join in this study will receive a $5.00 gift card as a token of our appreciation for their time.

You may participate in the study if:

1. You are 18 years or older
2. You can read and write English
3. You have a diagnosis of hEDS or HSD

The survey can be found online at _____.

If you are willing to take part in the study, please read the study information form on the first page of the survey and check the box to show that you have read and voluntarily agreed to participate.

Sincerely,

Alexis Heidlebaugh

Student Investigator

Johns Hopkins Bloomberg School of Public Health

National Human Genome Research Institute

alexis.heidlebaugh@nih.gov

William Klein, PhD

Associate Investigator

National Cancer Institute

National Human Genome Research Institute

kleinwm@mail.nih.gov

Lori Erby, PhD, ScM

Associate Investigator

National Human Genome Research Institute

lori.erby@nih.gov

APPENDIX 2

STUDY INFORMATION FORM

You are invited to participate in a study conducted by researchers at the Johns Hopkins Bloomberg School of Public Health and the National Human Genome Research Institute.

Why is this study being done? To learn more about the lived experiences of individuals with Hypermobile Ehlers Danlos Syndrome (hEDS) or Hypermobility Spectrum Disorder (HSD).

Who can participate in the study? We are interested in hearing from individuals who have been told by a healthcare provider that they have hEDS or HSD. You must be 18 years of age or older and able to read and write in English.

What is involved in the study? There is one survey that takes approximately 30-40 minutes to complete. The survey asks questions about your diagnosis, symptoms, and thoughts and feelings about living with your condition.

What are the risks to the study? There are no known risks of taking part in the study. If taking the survey causes any discomfort, you can stop taking the survey at any time. If you have questions or concerns regarding your diagnosis or have other medical health concerns, please contact your specialist who manages your condition or your primary care provider. If you are looking for more information regarding hEDS or HSD, please contact the EDS HelpLine at (866-616-1735). If you feel upset or anxious after taking the survey, please contact the EDS HelpLine at (866-616-1735) or free crisis support services at (800-273-8255). If you feel upset or anxious after taking the survey you can contact the researcher using the information provided below.

Are there benefits to taking part in the study? You will not personally receive any benefits from taking part in this study. However, we hope to learn more about the lived experiences of individuals with these conditions and that this knowledge will advance science and improve genetic services.

Do I have to participate? You do not have to participate in this study. You can skip any question or stop taking the survey at any time. Choosing not to participate will not affect your participation in any other research study or your healthcare.

Will I be paid for being part of this research study? You will be offered the opportunity to receive a $5.00 gift card after completing the survey. You will be asked at the end of the survey to provide your email address to receive the gift card electronically. Any contact information you give to the researchers will be destroyed after the gift card is sent and will not be linked in any way to your survey responses. You are not required to receive a gift card to take part in the study.

Who else will know that I am in the study? You will not be required to give your name or contact information to participate in the study if you prefer not to. If you provide us with your name and/or contact information by contacting the researchers directly or accepting the gift card, we will not link your name, email, and/or other contact information with your responses. We will not share your contact information with anyone outside the research team or use it for any other purpose than giving you the survey and/or the gift card. Your responses to the survey will not be part of any medical record. When we report our research results, it will be done without reporting any identifiable information from individual participants.

How do I participate? The survey can be completed by advancing to the next screen.

Will I be told about the study findings? After the study is complete, we plan on posting the summary of findings to the EDS Society website.

Please check the box below if you have read and understand the information presented in this study information form

- □ I understand the purpose and procedures of the study.

If you are interested in participating in other research studies or being involved in the EDS Society's Global Registry please follow the links below.

https://www.ehlers-danlos.com/research/

https://www.ehlers-danlos.com/eds-global-registry/

Thank you for your interest and time! Please contact the researchers (contact information below) with any questions or concerns.

Researchers Contact Information:

Alexis Heidlebaugh

Student Investigator

Johns Hopkins Bloomberg School of Public Health

National Human Genome Research Institute

alexis.heidlebaugh@nih.gov

William Klein, PhD

Associate Investigator

National Cancer Institute

National Human Genome Research Institute

kleinwm@mail.nih.gov

Lori Erby, PhD, ScM

Associate Investigator

National Human Genome Research Institute

lori.erby@nih.gov

APPENDIX 3

SURVEY INSTRUMENT

Section 1: Eligibility Screen

Instructions: Please answer the following questions to determine your eligibility to participate in this study.

1. Have you been told by a healthcare provider that you have hEDS or HSD?
   - □ Yes
   - □ No
2. Are you 18 years of age or older?
   - □ Yes
   - □ No

Section 2: Demographic Information

Instructions: Please indicate which categories you identify with.

1. Current Age
    - □ 18-25
    - □ 26-30
    - □ 31-40
    - □ 41-50
    - □ 51-60
    - □ >60
2. Sex
    - □ Male
    - □ Female
    - □ Other
3. Race (Check all that apply)
    - □ American Indian/Native Alaskan
    - □ Asian
    - □ Black/African American
    - □ Native Hawaiian/Pacific Islander
    - □ White
    - □ Other
4. Ethnicity
    - □ Hispanic or Latino
    - □ Not Hispanic or Latino
5. Marital Status
    - □ Single/Never Married
    - □ Partnered
    - □ Married
    - □ Separated/Divorced
    - □ Widowed
6. Highest Level of Education
    - □ Elementary/Junior High
    - □ High School/GED
    - □ Technical School
    - □ Some College
    - □ College Graduate
    - □ Post-Graduate

Section 3: Diagnosis Characteristics

Instructions: These questions ask about your experience with receiving a diagnosis of hEDS or HSD. Please select one answer for each of the following questions below.

1. Have you been given a formal clinical diagnosis of hEDS or HSD by a healthcare provider?
    - □ Yes
    - □ No
    - □ Unsure
2. For the healthcare provider who diagnosed your condition, which condition did he or she diagnose you with?
    - □ hEDS
    - □ HSD
    - □ Other (please explain)
3. What other diagnoses have you been given in the past?
    - □ hEDS
    - □ HSD
    - □ Marfan Syndrome/Loeys-Dietz Syndrome
    - □ Different Type of EDS
    - □ Immune Deficiency or Autoimmune Disorder
    - □ Other (please explain)
4. At what age did you first notice signs or symptoms of hEDS or HSD?
    - □ <10
    - □ 10-18
    - □ 19-30
    - □ 31-40
    - □ 41-50
    - □ 51-60
    - □ >60
5. At what age were you diagnosed with hEDS or HSD?
    - □ <10
    - □ 10-18
    - □ 19-30
    - □ 31-40
    - □ 41-50
    - □ 51-60
    - □ >60
6. How much time has passed since your diagnosis of hEDS or HSD?
    - □ <1 Year
    - □ 1-2 Years
    - □ 3-5 Years
    - □ 5-10 Years
    - □ >10 Years

Section 4: Illness Characteristics

Instructions: These questions ask about the symptoms of your hEDS or HSD. Please select one answer for each of the following questions below.

		I have experienced this symptom		(Only if yes is selected for previous response) This symptom has a significant impact on my life.				
		Yes	No	Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree
1	Pain (limb or joint)							
2	CRPS/RSD							
3	Fibromyalgia							
4	Joint Hypermobility							
5	Joint Dislocations or Subluxations							
6	Fatigue							
7	Arthritis							
8	Scoliosis							
9	TMJ							
10	Locked Jaw							
11	Endometriosis							
12	Vulvodynia							
13	Infertility							
14	Gastrointestinal Issues (one or more of the following: IBS, GERD, gastroparesis, diarrhea, constipation, nausea, other functional bowel problems)							
15	Cardiovascular Issues (one of more of the following: shortness of breath, tachycardia, palpitations, POTS)							
16	Neurological Issues (one or more of the following: headaches/migraines, dizziness, nerve compression, NMH, syncope)							
17	Organ Prolapse (one of more if the following: uterine, bladder, rectal)							
18	Skin Manifestations (one or more of the following: easy bruising, easy scarring, soft/velvety skin)							
19	Immunological Issues (one or more of the following: immune deficiency, autoimmune disorder, MCAS)							
20	Emotional Difficulties (one of more of the following: anxiety, depression, trouble focusing, brain fog, other mood disorder)							

21	Sleeping Difficulties (one of more of the following: insomnia, RLS)							

Section 5: Brief Illness Perceptions Questionnaire (IPQ-B)

Instructions: Please indicate which response best corresponds to your views of hEDS or HSD.

Consequences	No Effect At All (0)	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	Severely Affects My Life (10)
1	How much does your illness affect your life?											
Timeline	A Very Short Time (0)	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	Forever (10)
2	How long do you think your illness will continue?											
Personal Control	Absolutely No Control (0)	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	Extreme Amount of Control (10)
3	How much control do you feel you have over your illness?											
Treatment Control	Not At All (0)	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	Extremely Helpful (10)
4	How much do you think your treatment can help your illness?											
Identity	No Symptoms At All (0)	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	Many Severe Symptoms (10)
5	How much do you experience symptoms from your illness?											
Concern	Not At All Concerned (0)	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	Extremely Concerned (10)
6	How concerned are you about your illness?											
Coherence	Don't Understand At All (0)	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	Understand Very Clearly (10)
7	How well do you feel you understand your illness?											
Emotional Representations	Not At All Affected Emotionally (0)	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	Extremely Affected Emotionally (10)
8	How much does your illness affect you emotionally (does it make you feel angry, scared, upset, depressed)?											
Causes												

9	Please list in rank-order the three most important factors that you believe caused your illness.											

Section 6: Mishel Uncertainty in Illness-Community Form (MUIS-C)

Instruction. Please indicate how uncertain you are about the following aspects of hEDS or HSD.

		Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree
Ambiguity/Future Uncertainty						
1	I don't know what is wrong with me					
2	I have a lot of questions without answers					
3	I am unsure if my illness is getting worse of better					
4	The explanations they give seem hazy to me					
5	My symptoms continue to change unpredictably					
6	The doctors say things to me that could have many meanings					
7	My treatment is too complex to figure out					
8	It is difficult to know if the treatments of medication I am getting are helping me					
9	Because of the unpredictability of my illness, I cannot plan for the future					
10	The course of my illness keeps changing, I have my good and bad days					
11	It is not clear what is going to happen to me					
12	The effectiveness of the treatment is undetermined					
13	Because of the treatment, what I can do and cannot do keeps changing					
14	They have not given me a specific diagnosis					
Unpredictability						
1	I can predict how long my illness will last					
2	I usually know if I am going to have a good or bad day					
3	I can generally predict the course of my illness					
4	My physical distress is predictable, I know when it is going to get better or worse					
5	My diagnosis is definite and will not change					
6	The seriousness of my illness has been determined					
7	I'm certain that they will not find anything else wrong with me					
8	The doctors and nurses use everyday language so I can understand what they are saying					

Section 7: Coping Self-Efficacy Scale (CSE)

Instructions: When things are not going well for you, or when you're having problems, how confident or certain are you that you can do the following:

		Cannot Do At All (0)	(1)	(2)	(3)	(4)	Moderately Can Do (5)	(6)	(7)	(8)	(9)	Certain Can Do (10)
Use Problem-Focused Coping												
1	Break an upsetting problem down into smaller parts											
2	Sort out what can be changed, and what cannot be changed											
3	Make a plan of action and follow it when confronted with a problem											
4	Leave options open when things get stressful											
5	Think about one part of the problem at a time											
6	Find solutions to your most difficult problems											
Stop unpleasant emotions and thoughts												
1	Make unpleasant thoughts go away											
2	Take your mind off unpleasant thoughts											
3	Stop yourself from being upset by unpleasant thoughts											
4	Keep from feeling sad											
Get support from friends and family												
1	Get friends to help you with the things you need											
2	Get emotional support from friends and family											
3	Make new friends											

Section 8: Illness Identity Questionnaire (IIQ)

Instructions: We want to know how hEDS or HSD is a part of you. Please indicate how much you agree or disagree with the following statements.

		Strongly Disagree	Disagree	Neither Agree or Disagree	Agree	Strongly Agree
Rejection						
1	I refuse to see my illness as part of myself					
2	I'd rather not think of my illness					
3	I hate being talked to about my illness					
4	I never talk to others about my illness					
5	I just avoid thinking about my illness					
Acceptance						
1	My illness simply belongs to me as a person					
2	My illness is part of who I am					
3	I accept being a person with illness					
4	I am able to place my illness in my life					
5	I have learned to accept the limitations imposed by my illness					
Engulfment						
1	My illness dominates my life					
2	My illness has a strong impact on how I see myself					
3	I am preoccupied with my illness					
4	My illness influences all my thoughts and feelings					
5	My illness completely consumes me					
6	It seems as if everything I do, is influenced by my illness					
7	My illness prevents me from doing what I would really like to do					
8	My illness limits me in many things that are important to me					
Enrichment						
1	Because of my illness, I have grown as a person					
2	Because of my illness, I know what I want out of life					
3	Because of my illness, I have become a stronger person					
4	Because of my illness, I realize what is really important in life					
5	Because of my illness, I have learned a lot about myself					
6	Because of my illness, I have learned to work through problems and not just give up					
7	Because of my illness, I have learned to enjoy the moment more					

Section 9: PROMIS Emotional Distress

Instructions: Please indicate how often you have felt the following statements in the past 7 days.

		Never	Rarely	Sometimes	Often	Always
Anxiety-Short Form 8a						
1	I felt fearful					
2	I found it hard to focus on anything other than my anxiety					
3	My worries overwhelmed me					
4	I felt uneasy					
5	I felt nervous					
6	I felt like I needed help for my anxiety					
7	I felt anxious					
8	I felt tense					
Depression-Short Form 8a						
1	I felt worthless					
2	I felt helpless					
3	I felt depressed					
4	I felt hopeless					
5	I felt like a failure					
6	I felt unhappy					
7	I felt that I had nothing to look forward to					
8	I felt that nothing could cheer me up					

Section 10: Psychological Adaptation Scale (PAS)

Instructions: Please indicate how much you agree or disagree with the following statements.

Living with hEDS or HSD has…

		Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree
Coping Efficacy						
1	Helped me accept the way things work out					
2	Helped me learn to deal better with uncertainty					
3	Taught me how to adjust to things I cannot change					
4	Helped me take things as they come					
5	Helped me to look at things in a more positive way					
Self-Esteem						
1	Helped me learn to handle difficult times					
2	Helped me become more comfortable with who I am					
3	Helped me become a stronger person					
4	Helped me feel better about my ability to handle problems					
5	Helped me to become a better person					
Social Integration						
1	Helped me know who I can count on in times of trouble					
2	Makes me more willing to help others					
3	Helped relationships become more meaningful					
4	Helped me become closer to people I care about					
5	Helped me become more aware of the love and support available from other people					
Spiritual Well-Being						
1	Helped me learn my life is more meaningful					
2	Given me a greater appreciation for life					
3	Helped me develop a deeper sense of purpose in life					
4	Helped me feel peaceful					
5	Helped me find strengths in my faith or spiritual beliefs					

BIBLIOGRAPHY

1 Castori M, Tinkle B, Levy H, Grahame R, Malfait F, Hakim A. A framework for the classification of joint hypermobility and related conditions. American Journal of Medical Genetics Part C: Seminars in Medical Genetics. 2017;175(1):148-57.
2 Malfait F, Francomano C, Byers P, et al. The 2017 international classification of the Ehlers–Danlos syndromes. American Journal of Medical Genetics Part C: Seminars in Medical Genetics. 2017;175(1):8-26.
3 Gazit Y, Jacob G, Grahame R. Ehlers–Danlos Syndrome—Hypermobility Type: A Much Neglected Multisystemic Disorder. Rambam Maimonides Medical Journal. 2016 10/31;7(4):e0034.
4 Forghani I. Hypermobile Ehlers Danlos Syndrome. Balkan medical journal. 2018 Jul 31.
5 Colombi M, Dordoni C, Chiarelli N, Ritelli M. Differential diagnosis and diagnostic flow chart of joint hypermobility syndrome/ehlers-danlos syndrome hypermobility type compared to other heritable connective tissue disorders. American Journal of Medical Genetics Part C: Seminars in Medical Genetics. 2015;169(1):6-22.
6 Challal S, Minichiello E, Funalot B, Boissier M-C. Ehlers–Danlos syndrome in rheumatology: Diagnostic and therapeutic challenges. Joint Bone Spine. 2015 2015/10/01/;82(5):305-7.
7 Tinkle B, Castori M, Berglund B, et al. Hypermobile Ehlers–Danlos syndrome (a.k.a. Ehlers–Danlos syndrome Type III and Ehlers–Danlos syndrome hypermobility type): Clinical description and natural history. American Journal of Medical Genetics Part C: Seminars in Medical Genetics. 2017;175(1):48-69.
8 Castori M, Morlino S, Celletti C, et al. Re-writing the natural history of pain and related symptoms in the joint hypermobility syndrome/Ehlers–Danlos syndrome, hypermobility type. American Journal of Medical Genetics Part A. 2013;161(12):2989-3004.
9 Baeza-Velasco C, Bulbena A, Polanco-Carrasco R, Jaussaud R. Cognitive, emotional, and behavioral considerations for chronic pain management in the Ehlers–Danlos syndrome hypermobility-type: a narrative review. Disability and Rehabilitation. 2018:1-9.
10 Tinkle BT, Bird HA, Grahame R, Lavallee M, Levy HP, Sillence D. The lack of clinical distinction between the hypermobility type of Ehlers–Danlos syndrome and the joint hypermobility syndrome (a.k.a. hypermobility syndrome). American Journal of Medical Genetics Part A. 2009 2009/11/01;149A(11):2368-70.
11 Levy HP. Hypermobile Ehlers-Danlos Syndrome. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews((R)). Seattle (WA): University of Washington, Seattle; 1993.
12 Castori M, Camerota F, Celletti C, et al. Natural history and manifestations of the hypermobility type Ehlers-Danlos syndrome: a pilot study on 21 patients. American journal of medical genetics Part A. 2010 Mar;152a(3):556-64.
13 Hakim A, De Wandele I, O'Callaghan C, Pocinki A, Rowe P. Chronic fatigue in Ehlers–Danlos syndrome—Hypermobile type. American Journal of Medical Genetics Part C: Seminars in Medical Genetics. 2017;175(1):175-80.
14 Johannessen EC, Reiten HS, Løvaas H, Maeland S, Juul-Kristensen B. Shoulder function, pain and health related quality of life in adults with joint hypermobility syndrome/Ehlers–Danlos syndrome-hypermobility type. Disability and Rehabilitation. 2016 2016/07/02;38(14):1382-90.
15 Scheper MC, de Vries JE, Verbunt J, Engelbert RHH. Chronic pain in hypermobility syndrome and Ehlers–Danlos syndrome (hypermobility type): it is a challenge. Journal of Pain Research. 2015 08/20;8:591-601.

16 Syx D, De Wandele I, Rombaut L, Malfait F. Hypermobility, the Ehlers-Danlos syndromes and chronic pain. Clinical and experimental rheumatology. 2017 Sep-Oct;35 Suppl 107(5):116-22.
17 Voermans NC, Knoop H, Bleijenberg G, van Engelen BG. Pain in ehlers-danlos syndrome is common, severe, and associated with functional impairment. Journal of pain and symptom management. 2010 Sep;40(3):370-8.
18 Rombaut L, Malfait F, Cools A, De Paepe A, Calders P. Musculoskeletal complaints, physical activity and health-related quality of life among patients with the Ehlers-Danlos syndrome hypermobility type. Disabil Rehabil. 2010;32(16):1339-45.
19 Berglund B, Nordstrom G, Lutzen K. Living a restricted life with Ehlers-Danlos syndrome (EDS). Int J Nurs Stud. 2000 Apr;37(2):111-8.
20 Muriello M, Clemens JL, Mu W, et al. Pain and sleep quality in children with non-vascular Ehlers-Danlos syndromes. American journal of medical genetics Part A. 2018 Sep;176(9):1858-64.
21 Murray B, Yashar BM, Uhlmann WR, Clauw DJ, Petty EM. Ehlers-Danlos syndrome, hypermobility type: A characterization of the patients' lived experience. American journal of medical genetics Part A. 2013 Dec;161a(12):2981-8.
22 Baeza-Velasco C, Bourdon C, Montalescot L, et al. Low- and high-anxious hypermobile Ehlers–Danlos syndrome patients: comparison of psychosocial and health variables. Rheumatology International. 2018 May 01;38(5):871-8.
23 Hershenfeld SA, Wasim S, McNiven V, et al. Psychiatric disorders in Ehlers–Danlos syndrome are frequent, diverse and strongly associated with pain. Rheumatology International. 2016 March 01;36(3):341-8.
24 Scheper MC, Juul-Kristensen B, Rombaut L, Rameckers EA, Verbunt J, Engelbert RH. Disability in Adolescents and Adults Diagnosed With Hypermobility-Related Disorders: A Meta-Analysis. Archives of Physical Medicine and Rehabilitation. 2016 2016/12/01/;97(12):2174-87.
25 Lazarus RS, Folkman S. Stress, appraisal, and coping. 1984 [cited; Available from: http://www.dawsonera.com/depp/reader/protected/external/AbstractView/S9780826141927
26 Folkman S, Lazarus RS, Gruen RJ, DeLongis A. Appraisal, coping, health status, and psychological symptoms. Journal of personality and social psychology. 1986;50(3):571.
27 Leventhal H, Nerenz, D.R., Steele, D.J. Illness representations and coping with health threats. In: Baum A TS, Singer JE. , editor. Handbook of Psychology and Health: Social Psychological Aspects of Health. Hillsdale, NJ: Earlbaum; 1984. p. 219-52.
28 Leventhal H, Leventhal EA, Contrada RJ. Self-regulation, health, and behavior: A perceptual-cognitive approach. Psychology & health. 1998 1998/07/01;13(4):717-33.
29 Charmaz K. The Body, Identity, and Self: Adapting to Impairment. The Sociological Quarterly. 1995;36(4):657-80.
30 Weinman J, Petrie KJ, Moss-morris R, Horne R. The illness perception questionnaire: A new method for assessing the cognitive representation of illness. Psychology & health. 1996 1996/03/01;11(3):431-45.
31 Broadbent E, Petrie KJ, Main J, Weinman J. The Brief Illness Perception Questionnaire. Journal of psychosomatic research. 2006;60(6):631-7.
32 Hope L, Juul-Kristensen B, Løvaas H, Løvvik C, Maeland S. Subjective health complaints and illness perception amongst adults with Joint Hypermobility Syndrome/Ehlers–Danlos Syndrome-HypermobilityType – a cross-sectional study. Disability and Rehabilitation. 2017:1-8.

33 Han PKJ, Klein WMP, Arora NK. Varieties of Uncertainty in Health Care:A Conceptual Taxonomy. Medical Decision Making. 2011;31(6):828-38.
34 Mishel MH. Uncertainty in Illness. Image: the Journal of Nursing Scholarship. 1988;20(4):225-32.
35 Mishel MH. Uncertainty in chronic illness. Annual review of nursing research. 1999;17:269-94.
36 Mishel MH. The measurement of uncertainty in illness. Nursing research. 1981 Sep-Oct;30(5):258-63.
37 Han PK, Umstead KL, Bernhardt BA, et al. A taxonomy of medical uncertainties in clinical genome sequencing. Genet Med. 2017 Jan 19.
38 Chesney MA, Neilands TB, Chambers DB, Taylor JM, Folkman S. A validity and reliability study of the coping self-efficacy scale. British journal of health psychology. 2006;11(Pt 3):421-37.
39 Erikson EH. Identity : youth and crisis; 1968.
40 Oris L, Rassart J, Prikken S, et al. Illness Identity in Adolescents and Emerging Adults With Type 1 Diabetes: Introducing the Illness Identity Questionnaire. Diabetes Care. 2016;39(5):757-63.
41 Van Bulck L, Luyckx K, Goossens E, Oris L, Moons P. Illness identity: Capturing the influence of illness on the person's sense of self. European Journal of Cardiovascular Nursing. 2019;18(1):4-6.
42 Oris L, Luyckx K, Rassart J, et al. Illness Identity in Adults with a Chronic Illness. Journal of clinical psychology in medical settings. 2018 Feb 21.
43 Luyckx K, Oris L, Raymaekers K, et al. Illness identity in young adults with refractory epilepsy. Epilepsy & Behavior. 2018 2018/03/01/;80:48-55.
44 Van Bulck L, Goossens E, Luyckx K, Oris L, Apers S, Moons P. Illness Identity: A Novel Predictor for Healthcare Use in Adults With Congenital Heart Disease. Journal of the American Heart Association. 2018 May 22;7(11).
45 Luyckx K, Oris L, Raymaekers K, et al. Illness identity in young adults with refractory epilepsy. Epilepsy & behavior : E&B. 2018 Mar;80:48-55.
46 Taylor SE. Adjustment to threatening events: A theory of cognitive adaptation. American Psychologist. 1983;38(11):1161-73.
47 Taylor SE, Brown JD. Illusion and well-being: A social psychological perspective on mental health. Psychological bulletin. 1988;103(2):193-210.
48 Biesecker BB, Erby LH, Woolford S, et al. Development and validation of the Psychological Adaptation Scale (PAS): use in six studies of adaptation to a health condition or risk. Patient Education and Counseling,. 2013 Nov;93(2):248-54.
49 Biesecker BB, Erby L. Adaptation to living with a genetic condition or risk: a mini-review. Clinical Genetics,. 2008 Nov;74(5):401-7.
50 Berglund B, Anne-Cathrine M, Randers I. Dignity not fully upheld when seeking health care: experiences expressed by individuals suffering from Ehlers-Danlos syndrome. Disabil Rehabil. 2010;32(1):1-7.
51 Terry RH, Palmer ST, Rimes KA, Clark CJ, Simmonds JV, Horwood JP. Living with joint hypermobility syndrome: patient experiences of diagnosis, referral and self-care. Family Practice. 2015 04/24;32(3):354-8.

52 Chopra P, Tinkle B, Hamonet C, et al. Pain management in the Ehlers–Danlos syndromes. American Journal of Medical Genetics Part C: Seminars in Medical Genetics. 2017;175(1):212-9.
53 Bovet C, Carlson M, Taylor M. Quality of life, unmet needs, and iatrogenic injuries in rehabilitation of patients with Ehlers–Danlos Syndrome hypermobility type/Joint Hypermobility Syndrome. American Journal of Medical Genetics Part A. 2016;170(8):2044-51.
54 Turriff A, Levy HP, Biesecker B. Factors associated with adaptation to Klinefelter syndrome: the experience of adolescents and adults. Patient Education and Counseling,. 2015 Jan;98(1):90-5.
55 Yanes T, Humphreys L, McInerney-Leo A, Biesecker BJJoGC. Factors Associated with Parental Adaptation to Children with an Undiagnosed Medical Condition. 2017 August 01;26(4):829-40.
56 Truitt M, Biesecker B, Capone G, Bailey T, Erby L. The role of hope in adaptation to uncertainty: the experience of caregivers of children with Down syndrome. Patient Education and Counseling,. 2012 May;87(2):233-8.
57 Lamb AE, Biesecker BB, Umstead KL, Muratori M, Biesecker LG, Erby LH. Family functioning mediates adaptation in caregivers of individuals with Rett syndrome. Patient Educ Couns. 2016 Nov;99(11):1873-9.
58 Peay HL, Meiser B, Kinnett K, Furlong P, Porter K, Tibben A. Mothers' psychological adaptation to Duchenne/Becker muscular dystrophy. European journal of human genetics : EJHG. 2016 May;24(5):633-7.
59 Peay HL, Rosenstein DL, Biesecker BB. Adaptation to bipolar disorder and perceived risk to children: a survey of parents with bipolar disorder. BMC Psychiatry. 2013 2013/12/02;13(1):327.
60 Shapira R, Turbitt E, Erby LH, Biesecker BB, Klein WMP, Hooker GWJFC. Adaptation of couples living with a high risk of breast/ovarian cancer and the association with risk-reducing surgery. 2018 October 01;17(4):485-93.
61 Cohen J. Statistical power analysis for the behavioral sciences. Hillsdale, N.J.: L. Erlbaum Associates; 1988.
62 De Wandele I, Rombaut L, Malfait F, De Backer T, De Paepe A, Calders P. Clinical heterogeneity in patients with the hypermobility type of Ehlers-Danlos Syndrome. Research in Developmental Disabilities. 2013 2013/03/01/;34(3):873-81.
63 Løchting I, Garratt A, Storheim K, Werner E, Grotle MJJPR. Evaluation of the brief illness perception questionnaire in sub-acute and chronic low back pain patients: data quality, reliability and validity. 2013;2(122):2167-0846.1000122.
64 Tiemensma J, Gaab E, Voorhaar M, Asijee G, Kaptein AAJIjocopd. Illness perceptions and coping determine quality of life in COPD patients. 2016;11:2001.
65 Broadbent E, Wilkes C, Koschwanez H, Weinman J, Norton S, Petrie KJ. A systematic review and meta-analysis of the Brief Illness Perception Questionnaire. Psychology & health. 2015;30(11):1361-85.
66 Wright LJ, Afari N, Zautra A. The illness uncertainty concept: A review. Current Pain and Headache Reports. 2009 2009/03/14;13(2):133.
67 Nicholls AR, Polman R, Levy AR. Coping self-efficacy, pre-competitive anxiety, and subjective performance among athletes. European Journal of Sport Science. 2010 2010/03/01;10(2):97-102.

68 Cella D, Choi SW, Condon DM, et al. PROMIS((R)) Adult Health Profiles: Efficient Short-Form Measures of Seven Health Domains. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2019 May;22(5):537-44.
69 Ader DN. Developing the Patient-Reported Outcomes Measurement Information System (PROMIS). 2007;45(5):S1-S2.
70 Pilkonis PA, Choi SW, Reise SP, Stover AM, Riley WT, Cella D. Item Banks for Measuring Emotional Distress From the Patient-Reported Outcomes Measurement Information System (PROMIS®): Depression, Anxiety, and Anger. 2011;18(3):263-83.
71 Turriff A, Levy HP, Biesecker B. Factors associated with adaptation to Klinefelter syndrome: the experience of adolescents and adults. Patient education and counseling. 2015;98(1):90-5.
72 StataCorp. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC; 2017.
73 Cronbach LJJp. Coefficient alpha and the internal structure of tests. 1951;16(3):297-334.
74 Fontana A, Copetti M, Grammatico P, Morlino S, Colombi M, Castori M. Severity classes in adults with hypermobile Ehlers–Danlos syndrome/hypermobility spectrum disorders: a pilot study of 105 Italian patients. 2019.
75 Bulbena A, Baeza-Velasco C, Bulbena-Cabré A, et al. Psychiatric and psychological aspects in the Ehlers–Danlos syndromes. American Journal of Medical Genetics Part C: Seminars in Medical Genetics. 2017;175(1):237-45.
76 Berglund B, Pettersson C, Pigg M, Kristiansson P. Self-reported quality of life, anxiety and depression in individuals with Ehlers-Danlos syndrome (EDS): a questionnaire study. BMC Musculoskeletal Disorders. 2015;16:89.
77 Sinibaldi L, Ursini G, Castori M. Psychopathological manifestations of joint hypermobility and joint hypermobility syndrome/ Ehlers-Danlos syndrome, hypermobility type: The link between connective tissue and psychological distress revised. American journal of medical genetics Part C, Seminars in medical genetics. 2015 Mar;169c(1):97-106.
78 Berglund B, Mattiasson AC, Nordstrom G. Acceptance of disability and sense of coherence in individuals with Ehlers-Danlos syndrome. Journal of clinical nursing. 2003 Sep;12(5):770-7.
79 Voermans NC, Knoop H. Both pain and fatigue are important possible determinants of disability in patients with the Ehlers-Danlos syndrome hypermobility type. Disabil Rehabil. 2011;33(8):706-7.
80 Haakonsen Smith C, Turbitt E, Muschelli J, et al. Feasibility of Coping Effectiveness Training for Caregivers of Children with Autism Spectrum Disorder: a Genetic Counseling Intervention. J Genet Counsel. 2018;27(1):252-62.
81 Lazarus RS, Folkman S. Stress, appraisal, and coping. New York: Springer Pub. Co.; 1984.
82 Hall SS, Burns DD, Reiss AL. Modeling family dynamics in children with fragile x syndrome. Journal of abnormal child psychology. 2007 Feb;35(1):29-42.
83 Bhise V, Rajan SS, Sittig DF, Morgan RO, Chaudhary P, Singh H. Defining and Measuring Diagnostic Uncertainty in Medicine: A Systematic Review. Journal of General Internal Medicine. 2018;33(1):103-15.
84 Rybarczyk B, Nyenhuis DL, Nicholas JJ, Cash SM, Kaiser J. Body image, perceived social stigma, and the prediction of psychosocial adjustment to leg amputation. Rehabilitation Psychology. 1995;40(2):95-110.

CURRICULUM VITAE

ALEXIS R. HEIDLEBAUGH
80 Mount Zion Road York, PA 17402
717.855.8260
aheidle1@jhmi.edu
alexis.heidlebaugh@nih.gov

EDUCATION:

Johns Hopkins University / National Institutes of Health
Baltimore, MD / Bethesda, MD — Aug 2017-Jan 2020
Master of Science in Genetic Counseling
Program Director: Lori Erby, PhD, ScM, CGC
Thesis: Illness Identity and Psychological Adaptation in Individuals with Hypermobile Ehlers Danlos Syndrome or Hypermobility Spectrum Disorder
Thesis Advisors: William Klein, PhD and Lori Erby, PhD, ScM, CGC

Thomas Jefferson University
Philadelphia, PA — Aug 2009-May 2013
Bachelor of Science in Pre-Medical Studies
Program Director: Diana Cundell, PhD
Minor Concentration in Genetics, Honors Program

GENETIC COUNSELING ROTATION EXPERIENCE:

Kennedy Krieger Institute
Baltimore, MD — Oct 2019-Dec 2019
Clinical Setting: Pediatric Neurodevelopment Disorders

Children's National Medical Center Rare Disease Institute
Washington, DC — Sep 2019–Oct 2019
Clinical Setting: Pediatric Oncology, Pediatric/General Genetics
Case Presentation: Congenital Anomaly or Cystic Nephroma: Ruling Out DICER1

National Institute of Allergy and Infectious Diseases, National Institutes of Health
Bethesda, MD — Jun 2019–Aug 2019
Clinical Research Setting: Multiple Sclerosis, Immunodeficiencies, Autoimmune Disorders

Inova Cardiovascular Genomics Center / Pediatric Specialists of Virginia
Fairfax-Falls Church, VA — Mar 2019–May 2019
Clinical Setting: Cardiovascular Genetics, Pediatric/General Genetics

National Cancer Institute, National Institutes of Health
Bethesda, MD — Jan 2019–Mar 2019
Clinical Research Setting: Hereditary Diffuse Gastric Cancer, Lung Cancer, Mesothelioma

Johns Hopkins Institute of Genetic Medicine
Baltimore, MD — Oct 2018–Dec 2018

Clinical Setting: Pediatric/General Genetics, Metabolism

Medstar Washington Hospital Center, Cancer Institute
Washington, DC Sep 2018–Oct 2018
Clinical Setting: Oncology

Johns Hopkins Internal Medicine / Institute of Genetic Medicine
Lutherville-Timonium, MD / Baltimore, MD Jun 2018–Jul 2018
Clinical Setting: Internal Medicine, Connective Tissue Disorders

GeneDx
Gaithersburg, MD Mar 2018-May 2018
Laboratory Setting
Project & Presentation: Primary Ciliary Dyskinesia

Greater Baltimore Medical Center Prenatal Diagnostic Center
Towson, MD Oct 2017-Mar 2018
Clinical Setting: Prenatal Genetics

RESEARCH EXPERIENCE:

National Human Genome Research Institute, National Institutes of Health
Social and Behavioral Research Branch
Bethesda, MD Oct 2015–Jul 2017

Post-Bac Research Fellow (Intramural Research Training Award)
Genetic Services Research Unit
Principal Investigator: Barbara Biesecker, PhD, MS

- Analyze social and behavioral qualitative data for ClinSeq Exome Sequencing Study, POI RCT Consent Study, and CCGO Secondary Findings Analysis and Return Study
- Maintain database, collect survey data, and return negative secondary findings in CCGO Secondary Findings Analysis and Return Study
- Prepare and revise manuscripts for publication
- Mentor and supervise summer college students conducting social and behavioral research

Genetic Counseling Training Program Coordinator
Johns Hopkins University / National Institutes of Health
Genetic Counseling Training Program
Program Director: Barbara Biesecker, PhD, MS

- Provide administrative support for genetic counseling students and NIH faculty
- Assist with genetic counseling student thesis research
- Organize and participate in weekly Genetic Counseling Seminar course

Thomas Jefferson University
Philadelphia, PA Aug 2012-May 2013

Student Researcher
Research Advisor: Frank Wilkinson, PhD

- Conduct research on polycomb-group proteins in drosophila and yeast
- Learn and implement molecular biology techniques such as electrophoresis, real-time PCR, and yeast two-hybrid assay

PUBLICATIONS:

Lewis KL, **Heidlebaugh AR**, Epps S, et al. Knowledge, motivations, expectations, and traits of an African, African-American, and Afro-Caribbean sequencing cohort and comparisons to the original ClinSeq® cohort. *Genetics in Medicine,* 2019;21(6):1355-62.

Sapp JC, Johnston JJ, Driscoll K, **Heidlebaugh AR**, et al. Evaluation of Recipients of Positive and Negative Secondary Findings Evaluations in a Hybrid CLIA-Research Sequencing Pilot. *American Journal of Human Genetics,* 2018;103(3):358-66.

Biesecker BB, Lewis KL, Umstead KL, Johnston JJ, Turbitt E, Fishler KP, Patton JH, Miller IM, **Heidlebaugh AR**, Biesecker LG. Web Platform vs In-Person Genetic Counselor for Return of Carrier Results From Exome Sequencing: A Randomized Clinical Trial. *JAMA Internal Medicine,* 2018;178(3):338-46.

Turbitt E, Chrysostomou PP, Peay HL, **Heidlebaugh AR**, Nelson LM, Biesecker BB. A randomized controlled study of a consent intervention for participating in an NIH genome sequencing study. *European Journal of Human Genetics* 2018;26(5):622-30.

Lawal TA, Lewis KL, Johnston JJ, **Heidlebaugh AR**, et al. Disclosure of cardiac variants of uncertain significance results in an exome cohort. *Clinical Genetics,* 2018;93(5):1022-29.

POSTERS & PRESENTATIONS:

Alexis Heidlebaugh, Joann Bodurtha, Christy Smith, Weiyi Mu, Debra Roter, Lori Erby & William Klein. Illness Identity and Psychological Adaptation in Individuals with Hypermobile Ehlers Danlos Syndrome or Hypermobility Spectrum Disorder. Poster. *NHGRI Research Symposium*, Bethesda, MD, November 2019.

Alexis Heidlebaugh. Health Care Transition of Adolescents and Young Adults with Special Health Care Needs. Oral Presentation. *NHGRI Post-Clinic Case Conference*, Bethesda, MD, October 2019.

Alexis Heidlebaugh. Facilitating Decision Making for Pregnant Women with Depression. Oral Presentation. *NHGRI Post-Clinic Case Conference,* Bethesda, MD, February 2018.

Alexis Heidlebaugh. Recruiting African Americans, Africans, and Afro-Caribbeans to Participate in a Genome Sequencing Study: Lessons Learned. Oral Presentation. *Social and Behavioral Research Branch Works-In Progress*, Bethesda, MD, December 2016.

Alexis R Heidlebaugh, Charlotte L Hepler, Katie L Lewis, Leslie G Biesecker, Barbara B Biesecker. Motivations for Participating in a Genome Sequencing Study: Views of African American, African, and Afro-Caribbean Participants. Poster. *NHGRI Research Symposium*, Bethesda, MD, November 2016.

Heidlebaugh A, Wilkinson F. Positive Interactions among Pho, Psq, and dRybp. Poster. *St. Joseph University Sigma Xi Student Research Symposium,* Philadelphia PA, April 2013.

Coia T, **Heidlebaugh A**, Moncada L, Pantalone L, Werdann A, Zapulla A, Shain R, Wilkinson F. An Undergraduate Exercise Incoporating IRB Approval for Genotypic Analysis of Phenylthiocarbamide Tasting. *St. Joseph University Sigma Xi Student Research Symposium*, Philadelphia, PA, April 2012.

COUNSELING EXPERIENCE:

EveryMind
Rockville, MD May 2016 – Jun 2017
Hotline Call Specialist

Olivia's House Children's Grief and Loss Center
York, PA Jul 2014 – Oct 2015
Companion Volunteer

Visiting Angels Living Assistance Services
York, PA Mar 2014 – Mar 2015
Caregiving Professional for the Elderly and those with Disabilities

TEACHING EXPERIENCE:

York Suburban School District
York, PA Sep 2014-Jan 2015
Middle School Science & Math Teaching Aide

Thomas Jefferson University
Philadelphia, PA Aug 2010-May 2013
Teaching Assistant, Academic Peer Tutor, Laboratory Course Preparation Student

HONORS & AWARDS :

Summa Cum Laude	May 2013
Distinguished Honors Scholar	May 2013
Academic Excellence in Pre-Medical Studies Preceptorship Award	May 2013
Gerda L and Frederick T Cundell Scholarship	Aug 2012-May 2013
Academic and Faculty Scholarships for Academic Excellence	Aug 2009-May 2013

PROFESSIONAL MEMBERSHIPS:

Omicron Delta Kappa, National Leadership Society	Jan 2013-Present
Alpha Lambda Delta, National Freshman Honor Society	Jan 2010-Present

SERVICE:

Leukemia and Lymphoma Society Oct 2010-Oct 2015
York, PA
Light the Night Walk Team Co-Captain

Servants, Inc July 2014
Red Lion, PA
Missions Trip to Guatemala

Thomas Jefferson University Asclepius Pre-Medical Studies Society
Philadelphia, PA Aug 2009-May 2013
President, Member

Thomas Jefferson University American Cancer Society Colleges Against Cancer and Relay for Life
Philadelphia, PA Jan 2010-May 2013
Team Captain, Survivorship & Advocacy Committee Member