Health State Utilities and Disease Duration in Systemic Sclerosis: Is There an Association?

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ABSTRACT. ***Objective.*** Health state utility values (HSUV) are used as weightings to calculate quality-adjusted life years in economic evaluations. Evidence suggests that patients' perceptions of a new diagnosis for a chronic disease, while initially poor, may improve over time. The objective of this study was to examine the association between disease duration and direct HSUV scores in patients with systemic sclerosis (SSc).

Methods. Our study included patients with SSc from a US SSc center. An interviewer administered direct HSUV techniques including the visual analog scale (VAS), time tradeoff (TTO), and standard gamble (SG). We calculated the Short Form 6D HSUV from the Medical Outcomes Study Short Form-36. Additional clinical and demographic variables were collected.

Results. The mean age of the SSc sample (n = 223) was 51 years (SD 16) with the majority being women (84%). Median disease duration was 5 years (interquartile range 1.5–9). Mean (SD) HSUV were 0.67 (0.19) for the VAS, 0.76 (0.28) for the TTO, 0.84 (0.22) for the SG, and 0.65 (0.13) for the SF-6D. In patients with early disease (defined as < 2 yrs, n = 77), the mean HSUV values were 0.64 (VAS), 0.70 (TTO), 0.80 (SG), and 0.63 (SF-6D) versus for those with a longer disease duration: 0.69, 0.79, 0.87, and 0.67, respectively. In multivariate analysis, the SG measure showed a significant and positive association with disease duration measured as a continuous variable and using a threshold of 2 years (p = 0.047 and p = 0.023, respectively).

Conclusion. Greater disease duration showed a positive association with a direct measure (SG) of utility elicitation after a period of 2 years. (J Rheumatol First Release xxxx; doi:10.3899/jrheum.160162)

Key Indexing Terms:
QUALITY OF LIFE DISEASE DURATION SYSTEMIC SCLEROSIS

Systemic sclerosis (SSc) is a rare connective tissue disease that has a prevalence of between 286–659 cases per million people in the United States[1]. Patients are typically classified as having limited cutaneous (lcSSc) or diffuse cutaneous SSc (dcSSc). In general, the subclassification is based on skin involvement and is a surrogate for internal organ involvement. Typically, patients with dcSSc have higher morbidity and mortality. There is no effective treatment for this disease, meaning that most treatment offered is symptom-dependent[2]. It is well established that patients with SSc have a decreased health-related quality of life (HRQOL) compared with the general population[3].

Preference-based measures of health assess the desirability of a particular health state and summarize HRQOL as a single number: the health state utility value (HSUV)[4]. HSUV can be measured directly using methods such as the visual analog scale (VAS), the time-tradeoff method (TTO), or the standard gamble method (SG). Multidimensional measures, such as the Short Form 6D (SF-6D), can also be used to estimate utilities indirectly[5]. The advantage of these measures is that they are easy to administer, easy to understand, and have low respondent burden. HSUV can also be derived using algorithms for general health questionnaires such as the SF-12v2 Health Survey or the Medical Outcomes Study Short Form-36 (SF-36)[5]. Values estimated from these different measures do not align perfectly[6]. HSUV estimated using such measures form an important component to the economic evaluation of health interventions, specifically cost-utility analyses. These values are used as a weight to incorporate quality and length of life into a single metric (the quality-adjusted life year) to facilitate comparison among competing healthcare options[7]. Results of cost-utility

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analyses are often used to inform reimbursement decisions of new health interventions, so it is essential that methods for identifying patients' utility are well understood.

Patients often perceive higher HRQOL for their health states than the general population perceives for the same health states[3,8]. Part of this difference has been attributed to the influence of adaptation over time, a phenomenon whereby either the values or preferences associated with one's own health state or choices made between alternative health states may change as a result of experiencing that state[9]. "Response shift" may also occur when patients internally alter their ideas about their own HRQOL[10]. Our study sought to analyze whether the patients' duration of disease was associated specifically with their direct HSUV (SG and TTO). In particular, we sought to analyze the idea that patients with SSc would initially have strong preferences for other health states over their own. More recently, diagnosed patients might be more willing to "trade off" or "gamble" for another health state. Therefore, our *a priori* hypothesis was that patients with a shorter disease duration would have lower utility estimates with these direct measures than patients with a longer disease duration.

MATERIALS AND METHODS

Patients with rheumatologist-confirmed SSc were recruited at the University of California at Los Angeles (UCLA) for the UCLA Scleroderma Quality of Life study[11,12]. The study was a single-center, longitudinal, observational study in which consecutive patients with SSc were invited to participate during their clinic visits. Participants completed written consent and Health Insurance Portability and Accountability Act (HIPAA) forms (HIPAA is designed to increase availability and continuity of health insurance coverage for US residents). The study was approved by the UCLA Institutional Review Board (IRB).

Inclusion criteria included adult patients (≥ 18 yrs) with a diagnosis of SSc by SSc clinicians (Drs. Clements and Khanna). The exclusion criteria included the inability to read and write English. Patients with SSc were further stratified into lcSSc, dcSSc, and overlap syndrome. The study defined lcSSc as skin thickening distal, but not proximal, to the knees and elbows, with or without facial involvement; dcSSc was defined as skin thickening distal and proximal to the knees and elbows with or without facial involvement. Overlap syndrome was defined as patients with SSc and another rheumatic disease [such as inflammatory myositis or rheumatoid arthritis (RA)]. All patients signed UCLA IRB-approved written consent and HIPAA forms.

Physician's assessment of skin severity. The modified Rodnan skin score (mRSS) is the most widely used measure to assess skin thickening. The examiner palpates the skin in 17 areas (face, chest, abdomen, and fingers, hands, forearms, arms, feet, legs, and thighs for both sides of the body) and scores the level of thickening from 0–3 (from "uninvolved" to "severe thickening"). The total skin score is the sum of the skin scores of the individual areas with the maximum possible score being 51[13]. The mRSS is a measure of severity of skin thickness and in dcSSc, higher mRSS is associated with internal organ involvement and is considered a surrogate for overall disease severity[14].

Patient-reported outcome measures. The Health Assessment Questionnaire-Disability Index (HAQ-DI) assesses a patient's ability to function[15]. There is a total of 20 questions in 8 categories that ask the patients about their ability to carry out daily tasks, to determine the detrimental effect on their health[15]. The HAQ-DI has been validated for use in a number of diseases including SSc[16]. The HAQ-DI has a range of 0 to 3.0, with higher scores being worse than lower. The Center for Epidemiologic Studies Depression Scale (CES-D) is a patient-reported measure that is designed to identify symptoms of depression in the general population[17]. The Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT Fatigue Scale) is a brief measure (13 items) to identify patients' level of fatigue; it has been validated in patients with rheumatic diseases[18].

Direct HSUV instruments. Direct utility elicitation tasks were performed using the software package UMaker[19]. For all HSUV measures, a higher score indicates better health with a score of "1" indicating perfect health. Patients were first asked to complete a VAS that asked them to mark a point on a scale (0–100 mm) that best described their health in daily life over the past week.

Patients were then directed to complete a TTO exercise. This exercise asks patients their willingness to accept a shorter life in a state of perfect health. The TTO was presented as 2 bars, 1 longer (the current health state) and a bar representing shorter length of life in better health. The patients were asked a series of these questions until an indifference point was reached between the length of life in their current health state and the time the patient would spend in perfect health.

An SG exercise was then completed by the patients. This HSUV elicitation method forces the participant to choose between their life expectancy in their current health state versus a period of perfect health with a probability of immediate death. This probability was represented as a pie chart (or wheel) and users could alter the probability until a point of indifference was achieved between this possibility and their current health state. The associated utility was simply 1 minus this probability. Further details of this process are available in Khanna, *et al*'s study[20].

Indirect HSUV instruments. Patients were asked to answer the SF-36 Health survey, which is commonly used to assess patients' health. Using an established algorithm, the SF-36 was converted into the SF-6D to obtain an HSUV score[5]. The SF-6D has 6 domains (physical functioning, role limitations, bodily pain, vitality, social functioning, and mental health) and 18,000 possible health states.

Analysis. Descriptive statistics were calculated for the study population. Parametric and nonparametric (Wilcoxon Mann Whitney) tests were used where appropriate, based on the variable distributions, to compare differences in HSUV values between measures. Chi-square tests were used for evaluating associations between categorical variables. A series of univariate and multivariate linear regression models were constructed to examine the effect of disease duration on each of the HSUV measures adjusting for potential demographic confounders, including age (continuous), sex (categorical, 2 levels), income (categorical, 6 levels), and education level (categorical, 6 levels). Covariates were considered for the multivariate model if they met a threshold in univariate analysis ($p < 0.2$) and were added stepwise by comparing the Akaike information criterion of each specification. Spearman correlation coefficients were compared for explanatory variables to be included in the model to identify the presence of multicollinearity. Heteroscedasticity was tested for using the White test and normality among the regression residuals was assessed by kernel density plots. We analyzed disease duration as a continuous variable and then using a categorical variable at 1 and 2 years based on our *a priori* hypothesis. These thresholds were based on clinical observation (DK) that patients generally accept living with a chronic disease over a period of 2 years. The primary analyses focused on using the SG and TTO as dependent variables. Secondary analyses used the SF-6D and VAS as dependent variables. Statistical significance was achieved for p values (2-tailed) < 0.05 (α). All analyses were done in SAS version 9.3 (SAS Institute).

RESULTS

A total of 223 patients were recruited into our study (Table 1). The mean age in this patient population was 50.9 years (SD 15.5) and 84.3% of the patients were women. More than 80% of patients had at least some college education and about

Table 1. Study participant characteristics (n = 223).

Variable	Value
Age, yrs, mean (SD)	50.9 (15.5)
Female, %	84.30
Disease duration, yrs, mean (SD)	7.37 (7.85)
Alcohol use, %	48
Marital status, married, %	58.80
Education, %	
Less than high school graduate	4.10
High school graduate	12.70
Postsecondary education	83.20
Income, %, US$/year	
< 25,000	19.90
25,000 to < 50,000	16.80
50,000 to < 75,000	14.90
> 75,000	48.40
Insurance type, %	
Private	56.70
Medicare/Medi-Cal	24.30
Medicare + private	12.40
None	1.40
Ethnicity, %	
White	71.70
Black/African American	6.30
Asian	12.10
More than one	2.20
Unknown	6.30
SSc type, n (%)	
Localized SSc	1 (0.46)
Diffuse SSc	90 (41.29)
Limited SSc	112 (51.38)
Sine SSc	4 (2.29)
Overlap	10 (4.59)

SSc: systemic sclerosis.

two-thirds of patients had an annual income > $50,000 (US). The median time since patients were diagnosed with SSc was 5 years (interquartile range 1.5–9) and 44% of patients had dcSSc. Twenty-six percent (n = 58) of patients reported not having worked in the past 5 years because of their disease; < 1% of patients reported being hospitalized in the previous 12 months.

Mean HSUV estimates in the patient population ranged from 0.654 (SF-6D) to 0.844 (SG; Figure 1). Seventy-three patients (33%) reported being in perfect health (HSUV = 1) with at least 1 of the HSUV measures. Thirty-five patients (16%) reported perfect health with 2 or more measures. No patients reported perfect health in all 4 HSUV measures. More patients reported perfect health (HSUV = 1) with the TTO and SG [48 (22%) and 59 (27%), respectively] than the VAS and the SF-6D. The number of patients reporting perfect health using the VAS and SF-6D were 8 (4%) and 3 (1%), respectively. To discern whether HSUV measures were different by disease type (lcSSc vs dcSSc), we conducted pairwise tests to examine significant differences in HSUV scores between these 2 patient groups. HSUV scores from the VAS, TTO, SG, and SF-6D were all significantly higher in the lcSSc group than the dcSSc group, indicating that they do distinguish well between the 2 disease types (all $p < 0.05$).

A priori, our study hypothesis was that disease duration would have a positive association with HSUV scores, particularly with the SG method of utility elicitation. To test this hypothesis, 3 different measures of disease duration were used: continuous disease duration, duration > 1 year, and duration greater than 2 years (Table 2). The univariate results for disease duration as a continuous variable and the threshold at 2 years of disease duration (n = 145, 70%) were in accordance with this hypothesis ($p < 0.05$; Table 2). Results using the 1-year threshold (n = 161, 78%) showed trends for both the SG and TTO measures, but were not statistically significant ($p = 0.70$ and 0.29, respectively). The TTO and SG were found to be significantly and positively associated with disease duration > 2 years compared with disease duration < 2 years, with coefficients of 0.084 and 0.076, respectively ($p < 0.05$). Regression coefficients for disease duration (for both specifications) with the VAS and SF-6D as outcomes were not significant ($p > 0.05$). A clinical measure of SSc skin severity (mRSS) and patient-reported measures (FACIT Fatigue Scale, CES-D, HAQ-DI) were also significantly associated with all HSUV measures in the expected direction (Table 2). Patient characteristics such as age, sex, and income were not significantly associated with TTO and SG values, and results were mixed for the VAS and the SF-6D (Table 2).

In the main multivariate analysis (Table 3), there was a significant association between SG and disease duration as a continuous variable ($p = 0.047$) and disease duration as a categorical variable using a threshold of 2 years ($p = 0.023$). Disease duration > 2 years was associated with a 7-point increase in the SG score, which reflects the *a priori* hypothesis of our study. For the TTO, multivariate analyses did not produce significant associations for disease duration when included as a continuous variable or as a categorical value (using a 2-yr threshold; $p = 0.762$ and 0.081, respectively), but the regression coefficients were in the expected direction (0.001 and 0.072, respectively).

To see if there were differences between SSc types, a subgroup analysis was done for each of these diagnoses. In patients with dcSSc (n = 90), no significant associations were found for disease duration > 2 years (all $p > 0.1$). However, in patients with lcSSc (n = 118), disease duration > 2 years was positively associated with the SG, TTO, and the SF-6D measures after controlling for covariates (coefficients 0.109, 0.118, and 0.061, respectively; $p < 0.05$ for all).

DISCUSSION

To our knowledge, ours is the first study to elicit direct and indirect HSUV and examine associations with disease duration in patients with SSc. We found that disease duration had a significantly positive association with the SG scores, suggesting that after a period of time after SSc diagnosis,

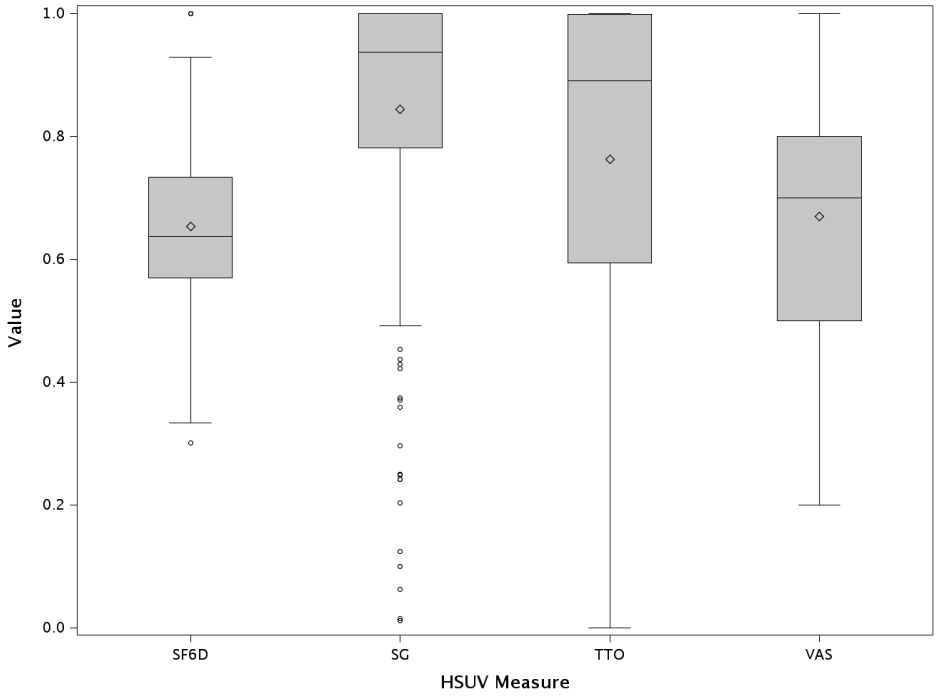

Figure 1. Boxplot of HSUV scores by measure. SF-6D, n = 211. SG, n = 222. TTO, n = 222. VAS, n = 222. HSUV: health state utility value; SF-6D: Short Form 6D; SG: standard gamble; TTO: time tradeoff; VAS: visual analog scale.

Table 2. Regression coefficients and 95% CI of univariate analyses with each HSUV measure as the outcome. Values are coefficient (95% CI).

Variable	SG	TTO	SF-6D	VAS
Duration, cont.	**0.004 (0.0001–0.008)**	0.004 (–0.001 to 0.009)	0.002 (–0.001 to 0.004)	–0.001 (–0.005 to 0.002)
Duration, > 1*	0.015 (–0.06 to 0.089)	0.051 (–0.043 to 0.144)	**0.056 (0.012–0.101)**	0.008 (–0.058 to 0.075)
Duration, > 2*	**0.076 (0.009–0.142)**	**0.084 (0–0.167)**	0.036 (–0.005 to 0.076)	0.033 (–0.027 to 0.092)
Age, yrs	–0.001 (–0.003 to 0.001)	–0.001 (–0.003 to 0.002)	0.0002 (–0.001 to 0.001)	–0.002 (–0.004 to –0.0001)
Sex	–0.037 (–0.121 to 0.046)	0.028 (–0.077 to 0.133)	–0.009 (–0.058 to 0.040)	0.014 (–0.059 to 0.087)
Income	0.014 (–0.013 to 0.042)	0.012 (–0.022 to 0.047)	**0.031 (0.016–0.046)**	**0.028 (0.005–0.052)**
Education	0.022 (–0.003 to –0.046)	0.028 (–0.003 to 0.059)	**0.018 (0.003–0.032)**	0.008 (–0.015 to 0.030)
SSc type†	**–0.089 (–0.152 to –0.026)**	**–0.120 (–0.199 to –0.041)**	**–0.04 (–0.076 to –0.004)**	–0.035 (–0.091 to 0.021)
mRSS, cont.	**–0.005 (–0.009 to –0.002)**	**–0.007 (–0.011 to –0.003)**	**–0.003 (–0.005 to –0.001)**	**–0.004 (–0.007 to 0)**
HAQ-DI	**–0.092 (–0.133 to –0.049)**	**–0.161 (–0.212 to –0.111)**	**–0.106 (–0.127 to –0.086)**	**–0.106 (–0.141 to –0.070)**
CES-D	**–0.001 (–0.015 to –0.005)**	**–0.014 (–0.020 to –0.008)**	**–0.015 (–0.017 to 0.013)**	**–0.015 (–0.019 to –0.011)**
FACIT Fatigue Scale	**–0.005 (–0.007 to –0.003)**	**–0.009 (–0.011 to –0.006)**	**–0.008 (–0.009 to –0.007)**	**–0.007 (–0.009 to –0.005)**
Ethnicity	–0.033 (–0.103 to 0.037)	–0.038 (–0.126 to 0.050)	**–0.068 (–0.108 to –0.028)**	–0.037 (–0.099 to 0.024)
Marital status**	0.019 (–0.043 to 0.081)	–0.014 (–0.092 to 0.064)	0.018 (–0.018 to 0.054)	0.004 (–0.050 to 0.059)

* For these variables, the variable is equal to 1 if the condition is met. † SSc type is equal to 0 for lcSSc and equal to 1 for dcSSc. ** Marital status is equal to 1 if married and 0 if otherwise. Significant data are in bold face ($p < 0.05$). HSUV: health state utility value; SG: standard gamble; TTO: time tradeoff; SF-6D: Short Form 6D; VAS: visual analog scale; cont.: continuous variable; SSc: systemic sclerosis; mRSS: modified Rodnan skin score; HAQ-DI: Health Assessment Questionnaire–Disability Index; CES-D: Center for Epidemiologic Studies Depression Scale; FACIT: Functional Assessment of Chronic Illness Therapy.

patients may adapt to their health state and are less willing to "trade" for a better health state. However, the results of our study also suggest that disease severity, as assessed by the mRSS, appears to be more important in determining the association with HSUV in the multivariate models, particularly in patients with dcSSc. In subgroup analyses, patients with lcSSc showed a positive association between disease duration greater than 2 years and HSUV scores (SG, TTO, SF-6D).

Adaptation is a phenomenon in which values or preferences associated with the evaluation of one's own health state or "tradeoffs" made between alternative health states may change as a result of experiencing that state[9]. This change has been observed in studies evaluating the HRQOL of

Table 3. Regression coefficients for primary and subgroup analyses with 95% CI for disease duration in multivariate analyses with each HSUV measure as the outcome. Adjusted for age, sex, mRSS, education, CES-D, and HAQ-DI.

Variables	SG		TTO		SF-6D		VAS	
	Coeff	95% CI	Coeff	95% CI	Coeff	95% CI	Coeff	95% CI
Primary analysis								
Duration*	**0.004**	**0.00004–0.007**	0.0007	–0.004 to 0.005	0.001	–0.0002 to 0.003	0.002	–0.005 to 0.0009
Duration > 2 yrs**	**0.072**	**0.010–0.138**	0.072	–0.009 to 0.153	**0.037**	**0.014–0.068**	0.061	–0.017 to 0.089
Subgroup analysis								
Patients with dcSSc only								
Duration*	0.005	–0.004 to 0.014	–0.006	–0.017 to 0.004	0.002	–0.002 to 0.006	0.001	–0.005 to 0.006
Duration > 2 yrs**	0.062	–0.056 to 0.180	0.039	–0.105 to 0.183	0.033	–0.007 to 0.073	0.056	–0.021 to 0.133
Patients with lcSSc only								
Duration*	0.030	–0.001 to 0.007	0.003	–0.002 to 0.008	0.002	–0.00002 to 0.004	–0.003	–0.007 to 0.0003
Duration > 2 yrs**	**0.109**	**0.029–0.188**	**0.118**	**0.015–0.220**	**0.061**	**0.018–0.104**	0.038	–0.046 to 0.123

* Disease duration modeled as continuous variable. ** Disease duration modeled as categorical variable (equal to 1 if greater than 2 yrs). Significant data are in bold face ($p < 0.05$). HSUV: health state utility value; mRSS: modified Rodnan skin score; CES-D: Center for Epidemiologic Studies Depression Scale; HAQ-DI: Health Assessment Questionnaire–Disability Index; SG: standard gamble; TTO: time tradeoff; SF-6D: Short Form 6D; VAS: visual analog scale; Coeff: regression coefficient; SSc: systemic sclerosis; dcSSc: diffuse cutaneous SSc; lcSSc: limited cutaneous SSc.

individuals sustaining serious accidents leading to paraplegia or quadriplegia[21], as well as individuals sustaining limb loss[22] or burn injuries[23]. Response shift, a similar phenomenon, includes changes in the meaning of one's self-evaluation of quality of life resulting from changes in internal standards, values, or conceptualization of their health[10].

Several elements of adaptation can render patients' ratings of HRQOL higher; typically, patients perceive higher HRQOL in their health states than is perceived by the general population[8]. This has been observed in SSc and corroborated here with our study. The general public reported mean (SD) HSUV scores of 25.3–69.7 (15.2–16.3) for the VAS, 0.36–0.80 (0.25–0.31) for the TTO, and 0.50–0.81 (0.26–0.32) for the SG, depending on disease severity[3], compared with the mean scores from patients with SSc in our current study of 0.67 (0.19), 0.76 (0.28), and 0.84 (0.22), respectively. These scores that fell in the least severe SSc categories in the previous study by Khanna, *et al*[3]. For context, Marra, *et al*[6] reported on minimally important differences (MID) for several utility measures in patients with RA. While the analysis did not report on the SG measure, the MID for the SF-6D measure (Table 3) was found to be 0.03 to 0.05, depending on the methodology used, similar to results from earlier studies[24]. These MID values are comparable to the result from our study of 0.037 (95% CI 0.014–0.068) for effect of disease duration greater than 2 years on the SF-6D score (Table 3).

Of particular interest, based on our *a priori* hypothesis, was the association between the SG utility score and disease duration. We anticipated that patients with shorter disease duration would be willing to "gamble" more substantially than those with longer disease duration because of the real or perceived desirability of other health states. This desirability reflects that treatment for SSc involves a marked amount of risk with no certainty of improvement. Univariate analysis (Table 2) using a categorical variable for disease duration over 2 years yielded results that were consistent with our hypothesis. In multivariate analysis, the SG measure showed positive and statistically significant associations with disease duration greater than 2 years. The mRSS appeared to be the most consistently significant correlate of HSUV scores, suggesting that the progressive nature of SSc may outweigh the effect of adaptation over time. This idea was confirmed when we performed a subgroup analysis of lcSSc versus dcSSc. While patients may adapt somewhat to their disease state, for those patients with concurrent disease progression (and associated pain), the net effect may be a decrease in HSUV scores. However, in patients with lcSSc, a disease subtype with milder SSc, disease duration greater than 2 years was positively associated with HSUV.

The results of our study have practical implications for cost-utility analyses involving patients with SSc. Utility estimates obtained immediately after SSc diagnosis may not be stable over time. Cost-utility analyses should, therefore, appreciate this phenomenon and ensure that analyses that span a patient's lifetime incorporate changing HSUV. Failure to do so may mean that the results of cost-utility analyses may be prone to error. Previous studies have shown that the choice of utility elicitation method may generate different results[25] and our study adds that, for patients with SSc, there are nuances within specific measures that must be well understood.

There are several limitations to our study. First, the study was not designed specifically to answer the question of adaptation. The nonsignificant results in the subgroup analyses, for example, especially with dcSSc, may be due to lack of power to show such effects. Second, patients were required to respond to a survey that was of considerable length. While most questions were quite easily answered, it is possible that this proved to be burdensome. However, response rates, particularly to HSUV measures, were high,

with the lowest observed with the SF-6D (95%). Third, the cross-sectional design of our investigation does not allow us to view changes in the HSUV and clinical measures of disease severity in individual patients over time. It also does not allow for us to investigate whether the changes in direct and indirect utility measures are similar and if these changes are reflected in the clinical measures of disease severity (and vice versa). We recognize that this type of study design has the potential for bias (i.e., the healthy worker effect), but because recruitment was done exclusively from an SSc clinic, this should be minimized. Fourth, we did not systematically identify which patients declined to participate in our study and also acknowledge that the method and location of recruitment might mean that these results are not generalizable to all patients with SSc. Finally, information on treatments that patients may have been receiving for comorbid diseases may have been beneficial to know what effect, if any, these treatments were having on patients' quality of life.

Our study showed that certain methods of obtaining HSUV appreciate patients' perceptions of their disease, particularly in the period immediately after diagnosis. For the primary analyses, both univariate and multivariate analyses showed that disease duration > 2 years was positively associated with the TTO and SG HSUV measures in accordance with our hypothesis. Our analysis also showed, however, that disease severity, as measured by skin severity, was consistently and significantly negatively associated with all HSUV measures, suggesting that while disease duration may influence patients' HSUV scores, patients' disease severity may mitigate this effect.

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