

Utility and Its Relationship With Disease Activity and Physical Disability of Patients With Psoriatic Arthritis in Thailand

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Abstract

Physical disability and severity of skin disease are important factors for evaluating healthy utility in psoriatic arthritis (PsA) patient. This study aims to estimate health utility and its related factors incorporating both rheumatologic and dermatologic factors in PsA. This cross-sectional study performed in PsA patients in Thailand. EQ-5D-5L, Health Assessment Questionnaire Disability Index (HAQ-DI), and Psoriasis Area and Severity Index (PASI) tools were used to collect health utility, physical disability, and severity of psoriatic skin lesions by face-to-face interviewed. Linear regression analysis was performed to relate health utility and its related factors.

Of 84 patients enrolled, 49 (58.3%) were female, 67 (79.8%) had remission or low disease activity. Eighty-three patients (98.8%) received conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) or biologic DMARDs (bDMARDs). The mean \pm SD overall utility was 0.87 ± 0.15 . The utility score of patients with low disease activity was significantly greater than those with moderate to severe disease activity (0.89 ± 0.12 vs 0.72 ± 0.19 , $p<0.001$). The HAQ-DI (unstandardized $\beta = -0.167$, 95%CI: -0.218 to -0.116, $p<0.001$) and PASI (unstandardized $\beta = -0.006$, 95%CI: -0.009 to -0.003, $p<0.001$) were found to be significant related factors for utility. These results indicated that Thai patients with PsA had relatively high health utility. However, most included patients were in remission or had low disease activity. The HAQ-DI and PASI showed a strong predictors of patients' health utility.

Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease associated with psoriasis, manifesting most commonly as peripheral arthritis, dactylitis, enthesitis, spondylitis, and nail plate abnormalities¹. The incidence of PsA is 3.6–7.2 per 100,000 person-years, while the prevalence ranges from 6–41% in patients with psoriasis². PsA has a negative impact on health-related quality of life (HRQoL) and healthcare resource utilization³. Early identification and early treatment are important for improving long-term outcomes⁴.

Patients with PsA could experience severe impairment of physical function, occupational incapability and negative psychosocial affects. PsA with mild disease, usually involves a few joints, has minimal impact on the patients' HRQoL. Moderately severe and severe PsA shows a significant impact on the daily tasks of living and physical functions^{5,6}. It may also impact the patients' physical and mental well-being and limit treatment responses⁷. Many patients could hardly perform the simple tasks of living due to severe pain. Physical disability is substantial in these patients⁶.

Treatment of PsA should aim to ameliorate the activity and severity of both joint and skin inflammation. Medical treatments of PsA include non-steroidal anti-inflammatory drugs (NSAIDs), intra-articular corticosteroids, and disease-modifying anti-rheumatic drugs (DMARDs). DMARDs can reduce joint and/or skin symptoms and prevent disease progression. These agents may be classified as conventional

synthetic DMARDs (csDMARDs) and biologic DMARDs (bDMARDs)⁸. Evidence indicates that such treatments can improve the physical signs and symptoms of PsA, as well as the patients' HRQoL⁹.

In economic evaluation, HRQoL may be measured as utility, which refers to the individual preference to his/her health status. For PsA, estimation of health utility is valued from both physical disability and severity of skin disease. A previous systematic review¹⁰ has shown that the Health Assessment Questionnaire Disability Index (HAQ-DI) and the Psoriasis Area and Severity Index (PASI) are important tools for estimating health utility in patients with PsA. A previous study in Thai patients with PsA did not include PASI in the analysis model, causing incomprehensive estimation of utility and related factors¹¹. Therefore, this study aimed to estimate health utility and its related factors which incorporating both rheumatologic and dermatologic clinical factors in Thai patients with PsA.

Material And Methods

Study design and patient enrollment. This cross-sectional study was conducted to determine the health utility and its relationship with disease activity, HAQ-DI and PASI scores in Thai patients with PsA. All PsA patients diagnosed according to the classification criteria for PsA (CASPAR) criteria¹² were invited to participate in this study. These patients had their outpatient regular rheumatology clinics visit at three university affiliated hospitals between January and April 2020. Those who were unable to communicate or denied participating were excluded.

Study protocol. All the subjects received detailed information about the purpose and procedure of the study and agreed to participate in writing. All patients gave their written informed consents before entering the study. Approval to conduct this cross-sectional study was obtained from the Central Research Ethics Committee (CREC) of Thailand in 2019 (certificate number: COA-CREC004/2020). All the methods were performed in accordance with the Declaration of Helsinki, the relevant guidelines and regulations. **Sample size estimation.** A previous study on health utility in PsA patients reported mean and SD of 0.5 and 0.3, respectively¹³. Using the above mean and SD, and the 95%CI of true mean of 0.5 ± 0.05 (error = 0.05), the sample size of this study was calculated to be 138.

Data collection. All eligible patients were invited to participate in this study. Baseline characteristics of participants were collected by a medical record review performed by rheumatologists. Participants were face-to-face interviewed for their current clinical status including their health utility, physical disability, and skin lesion activity by a trained research nurse or a rheumatologist. A structured data collection and interview form was developed. It consisted of four parts including 1) baseline characteristics; sex, age, health insurance, types of PsA, current disease activity (measured by clinical Disease Activity Index for Psoriatic Arthritis (cDAPSA))¹⁴, deformity, co-morbidity, and PsA treatment, 2) the Thai version of the EQ-5D-5L for patients' health utility, 3) the Thai version of HAQ (Thai HAQ) for physical disability, and 4) PASI for the severity of psoriatic skin lesions. All collected data was verified by RS, PD, and UP. Rheumatologists who were responsible for data collection were asked for any incomplete data to ensure the data validity.

Outcome Measures. Health utility and physical disability scores were determined by the Thai version of the EQ-5D-5L, and Thai HAQ, respectively¹⁵. The PASI questionnaire was used to determine the severity of the psoriatic skin lesions, the PsA disease activity, and the global assessment of the disease activity by the physicians, respectively.

The EQ-5D-5L¹⁶ was used for assessing the patients' health-related utility. It consists of five dimensions including mobility, self-care, usual activities, pain/ discomfort, and anxiety/depression. Each dimension has one question with five response levels. Patients' responses from the EQ-5D-5L questionnaire were converted to the utility scores based on the Thai algorithms, which had been elicited from 1,207 general population living in 12 provinces from all regions of Thailand¹⁷.

The Thai HAQ was used for determining functional disability. It consists of eight domains including dressing and grooming, arising, eating, walking, hygiene, reach, grip, and activities¹⁵. The 4-point difficulty level of the individual items from each domain is ranked from 0 (no difficulty) to 3 (unable to do). The highest score from each domain was then summed and averaged to a single disability index. The HAQ-DI scores range from 0–3, with higher score reflects greater disability.

The PASI questionnaire¹⁸ was used for determining the severity of psoriatic skin lesions in such patients. It consisted of four domains including percentages of skin involvement and the severity of skin lesions assessed by 3 clinical signs: erythema score, infiltration score, and desquamation score¹⁸. The PASI score was calculated using an equation reported in the original study. For each body section; (head, upper limb, lower limb and trunk), the percentage of affected skin area by psoriasis was estimated on a scale from 0 to 4 according to erythema score, infiltration score and desquamation score, then converted to a grade, ranged from 0 to 6¹⁸.

Statistical analyses. Baseline characteristics were presented as frequencies for categorical variables and means ± standard deviation (SD) for continuous variables. Kruskal-Wallis test was used to test the differences of the HAQ-DI, PASI, and health utility among disease activity (remission, low, and moderate-to-severe). Dunn's pairwise comparison with Bonferroni correction was used to test the differences of each comparison when significant difference was observed among disease severity. Spearman rho correlation was performed to relate utility score and VAS.

Two steps regression approach was applied to determine relationship of health utility and its related factors. Univariate linear regression was performed to relate patients' health utility and its factors. Factors with *p*-value < 0.10 in the univariate analysis and variables of interests from the literature relating to health utility (age, cDAPSA, HAQ-DI, and PASI) were selected for multivariate linear regression using a forward selection. Factors with *p*-value < 0.05 in the multivariate analysis indicated significant relationship with patients' health utility. Variance inflation factor (VIF) was used to assess multicollinearity among independent variables, while adjusted R² was used to determine model's goodness-of-fit. All analyses were performed using STATA version 15.0.

Results

Patient Characteristics. Since the outbreak of COVID-19, the management plan of all hospitals has been substantially altered. Physicians' appointments have to be postponed for those without urgent visits to the hospitals. Consequently, we decided to terminate the patient enrollment into this study in April 2020.

All invited patients agreed to participate in this study (100%). A total of 84 patients with their average age of 51.2 ± 12.5 years were included in the study. Forty-nine (58.3%) were female, 67 (79.8%) had remission or low disease activity, 54 (64.3%) had no deformity. Only one patient (1.2%) did not receive any specific treatment while the remaining received either csDMARDs or bDMARDs. Among the three healthcare schemes, the patients were under the Universal Health Coverage Scheme (UHCS), the Civil Servant Medical Benefit Scheme (CSMBS) and the Social Security Scheme (SS) in 31 (36.9%), 30 (35.7%) and 13 (15.5%), respectively (Table 1). They received csDMARDs in 65 (77.4%) [methotrexate in 61 (72.6%), sulfasalazine in 21 (25.0%), leflunomide in 19 (22.6%), and cyclosporine in 7 (8.3%)] and bDMARDs in 18 (21.4%) [etanercept in 6 (7.1%), infliximab in 5 (6.0%), secukinumab in 5 (6.0%), and guselkumab in 3 (3.6%)] (Table 1).

Table 1
Baseline characteristics of the studied patients

Patient characteristics	Number (%) (N = 84)	
Gender		
Female	50	(59.5)
Male	34	(40.5)
Age (Mean±SD)		(51.2±12.5)
<60 years	62	(73.8)
≥60 years	22	(26.2)
Healthcare scheme		
UHCS	31	(36.9)
CSMBS	30	(35.7)
SSS	13	(15.5)
Others	10	(11.9)
Type of psoriatic arthritis		
Peripheral arthritis	14	(16.7)
Peripheral arthritis+Axial disease	14	(16.7)
Peripheral arthritis+Dactylitis and/or enthesitis	25	(29.8)
Peripheral arthritis+Axial disease+Dactylitis and/or enthesitis	28	(33.3)
Axial disease	1	(1.2)
Axial disease+Dactylitis and/or enthesitis	1	(1.2)
Dactylitis and/or enthesitis	1	(1.2)
Disease activity		
Remission	20	(23.8)
Low	47	(56.0)
Moderate	12	(14.3)
Severe	5	(6.0)
Deformity		
No	54	(64.3)
Yes	30	(35.7)

Patient characteristics	Number (%) (N = 84)	
Co-morbidities		
Hypertension	31	(36.9)
Dyslipidemia	31	(36.9)
Diabetes mellitus	12	(14.3)
Treatments*		
Conventional synthetic DMARDs	65	(77.4)
Methotrexate	61	(72.6)
Sulfasalazine	21	(25.0)
Leflunomide	19	(22.6)
Cyclosporin	7	(8.3)
Azathioprine	3	(3.6)
Chloroquine	1	(1.2)
Biologic DMARDs	18	(21.4)
Etanercept	6	(7.1)
Secukinumab	5	(6.0)
Infliximab	5	(6.0)
Guselkumab	3	(3.6)
Ixekizumab	1	(1.2)
No specific treatment	1	(1.2)

Abbreviations: CSMBS: Civil Servant Medical Benefit Scheme; DMARDs: disease modifying antirheumatic drugs; SSS: Social Security Scheme; UHCS: Universal Health Coverage Scheme; *some patients receive more than one medication.

Physical disability, disease activity, and health utility. The HAQ-DI indicated that most patients were able to perform self-care activities without a need for assistance in terms of dressing and grooming of 74 (88.1%), arising of 48 (57.1%), eating of 56 (67.5%), walking of 63 (75.0%), hygiene of 66 (78.6%), reach of 45 (53.6%), grip of 55 (65.5%), and activities of 63 (75.0%). The average HAQ-DI score was 0.49 ± 0.60 in which the average score for patients with remission, low, and moderate to severe disease activity was 0.20 ± 0.28 , 0.36 ± 0.47 , and 1.17 ± 0.71 , which showed a statistically significant difference ($p < 0.001$) (Table 2). Additional subgroup analyses demonstrated the significant differences between low and moderate to severe disease activity ($p < 0.001$), and between remission and moderate-to-severe disease activity

($p<0.001$). However, the difference was not observed between patients with low disease activity and those in remission ($p=0.301$).

Table 2
The HAQ-DI and PASI in patients with psoriatic arthritis

	No assistance (%)	Need a special device (%)	Need help from another person (%)	Need both (%)
HAQ-DI				
Dressing and grooming	74 (88.1)	8 (9.5)	2 (2.4)	0 (0)
Arising	48 (57.1)	20 (23.8)	10 (11.9)	6 (7.1)
Eating	56 (67.5)	9 (10.8)	11 (13.3)	7 (8.4)
Walking	63 (75.0)	12 (14.3)	8 (9.5)	1 (1.2)
Hygiene	66 (78.6)	8 (9.5)	9 (10.7)	1 (1.2)
Reach	45 (53.6)	23 (27.4)	9 (10.7)	7 (8.3)
Grip	55 (65.5)	11 (13.1)	10 (11.9)	8 (9.5)
Activities	63 (75.0)	13 (15.5)	7 (8.3)	1 (1.2)
Disease activity	Mean±SD HAQ-DI score		p-value	
Overall	0.49±0.60			
Remission	0.20±0.28		<0.001	
Low	0.36±0.47			
Moderate to severe	1.17±0.71			
PASI score	(n, %)			
<10	73 (86.9)			
10-15	3 (3.6)			
>15	8 (9.5)			

Abbreviations: HAQ-DI: Health Assessment Questionnaire Disability Index; PASI: Psoriasis Area and Severity Index; SD: Standard deviation

The average PASI score was 5.31 ± 9.60 in which 73 (86.9%) had a PASI score <10 (Table 2). The average PASI score for patients with remission, low, and moderate-to-severe disease activity was 2.94 ± 6.01 , 5.34 ± 9.78 , and 7.99 ± 12.08 , respectively. The average PASI score for each HAQ-DI level of physical disability was not statistically significant different ($p=0.06$) (Table 3).

Table 3
Relationship of disease activity and PASI scores in patients with PsA

Disease activity	PASI score \pm SD	p-value
Overall	5.31 \pm 9.60	
Remission	2.94 \pm 6.01	0.06
Low	5.34 \pm 9.78	
Moderate to severe	7.99 \pm 12.08	

Abbreviations: PASI: Psoriasis Area and Severity Index; SD: Standard deviation

The average utility score measured by EQ-5D5L was 0.87 \pm 0.15. Forty-six (54.8%) had no problem in mobility, 70 (83.3%) in self-care, 54 (64.3%) in usual activities, 51 (60.7%) in anxiety but 45 (53.6%) had slight problem in pain/discomfort. The average utility was statistically significant ($p<0.001$) among the three groups categorized by disease severity. The utility of patients with low disease activity was greater than those with moderate to severe disease activity (0.89 \pm 0.12 vs 0.72 \pm 0.19). Patients in remission had the highest quality of life than those in other disease activities based on the greatest reported health utility score of 0.92 \pm 0.10. The results from VAS were similar to utility score measured by EQ-5D5L (Table 4). Spearman rho correlation analysis indicated that utility score and VAS are significantly correlated ($p<0.001$, rho = 0.548; Fig. 1).

Table 4
Number and percentage of patients in the 5 domains of utility scores

EQ-5D-5L	Dimensions, n(%)				
	Mobility	Self-care	Activity	Discomfort	Anxiety
Levels					
No problem	46 (54.8)	70 (83.3)	54 (64.3)	24 (28.6)	51 (60.7)
With slight problems	23 (27.4)	10 (11.9)	23 (27.4)	45 (53.6)	24 (28.6)
With moderate problems	10 (11.9)	3 (3.6)	5 (6.0)	13 (15.5)	7 (8.3)
With severe problems	5 (6.0)	1 (1.2)	2 (2.4)	2 (2.4)	1 (1.2)
Unable to perform/ with extreme problems	0 (0.0)	0 (0)	0 (0)	0 (0)	1 (1.2)
Utility					
Overall	0.87±0.15				
Remission	0.92±0.10		<0.001*		
Low disease activity	0.89±0.12				
Moderate to severe disease activity	0.72±0.19				
VAS					
Overall	77.10±16.33		<0.001*		
Remission	83.50±18.49				
Low disease activity	78.17±14.59				
Moderate to severe disease activity	66.65±13.96				
Abbreviations: EQ-5D-5L: EuroQoL; SD: Standard deviation. *Tested by Kruskal-Wallis					

Subgroup analysis found that the utility was significantly different between patients with low and moderate-to-severe disease activity ($p<0.001$) and between those in remission and moderate-to-severe disease activity ($p<0.001$). However, the difference was not significant between patients with low disease activity and those in remission ($p=0.306$).

Health utility and its related factors. Univariate analysis indicated that cDAPSA, HAQ-DI score, and PASI score were significantly related factors of health utility ($p<0.05$). No significant relationship were found

for age, gender, deformity, type of PsA, diabetes, hypertension, dyslipidemia, and history of receiving bDMARDs (Table 5).

Table 5
Two steps regression analysis model findings

Variable	Univariate analysis		Multivariate analysis (Adjusted R ² = 0.5899)*		
	Unstandardized beta coefficient (95%CI)	p-value	Standardized beta coefficient	Unstandardized beta coefficient (95%CI)	p-value
Gender	Reference	.299	N/A	N/A	N/A
Male	-0.036				
Female	(-0.103 to 0.032)				
Age	-0.002 (-0.005 to 0.001)	.106	-0.007 (-0.002 to 0.002)	-0.000 (-0.002 to 0.002)	.937
cDAPSA	Reference	.405	0.048	0.007	.781
Remission	-0.299 (-0.101 to 0.411)	<.001	-0.076 -0.012	(0.045 to 0.060) (-0.094 to 0.713)	.782
Low disease activity					
Moderate-to-high disease activity	-0.203 (-0.291 to -0.118)				
HAQ-DI	-0.180 (-0.219 to -0.142)	<.001	-0.664	-0.167 (-0.218 to -0.116)	<.001
PASI	-0.005 (-0.008 to -0.002)	.003	-0.299	-0.006 (-0.009 to -0.003)	<.001
Deformity	Reference	.345	N/A	N/A	N/A
No	-0.033				
Yes	(-0.102 to 0.359)				
Type of PsA	Reference	.914	N/A	N/A	N/A
Peripheral +/- Dactylitis and/or enthesitis	-0.010 (-0.183 to 0.172)	.574			
Axial +/- Dactylitis and/or enthesitis or Dactylitis and/or enthesitis alone	-0.192 (-0.087 to 0.048)				
Peripheral + Axial +/- Dactylitis and/or enthesitis					

Variable	Univariate analysis		Multivariate analysis (Adjusted R ² = 0.5899)*		
	Unstandardized beta coefficient (95%CI)	p-value	Standardized beta coefficient	Unstandardized beta coefficient (95%CI)	p-value
Diabetes	Reference	.610	N/A	N/A	N/A
No	0.024				
Yes	(-0.070 to 0.119)				
Hypertension	Reference	.427	N/A	N/A	N/A
No	-0.027				
Yes	(-0.096 to 0.040)				
Dyslipidemia	Reference	.479	N/A	N/A	N/A
No	-0.024				
Yes	(-0.093 to 0.044)				
Receiving bDMARDs	Reference	.252	N/A	N/A	N/A
No	-0.455				
Yes	(-0.124 to 0.033)				

Abbreviations: cDAPSA: clinical Disease Activity Index for Psoriatic Arthritis; bDMARDs: biologic disease modifying anti-rheumatic disease; HAQ-DI: Health Assessment Questionnaire Disability Index; PASI: Psoriasis Area and Severity Index; PsA: Psoriatic arthritis. *Final model indicates the adjusted R² of 0.5899 with the variance inflation factor ranged from 1.09 – 2.45; mean VIF as 1.70)

Multivariate analysis revealed that only HAQ-DI score (unstandardized β = -0.167, 95%CI; -0.218 to -0.116, $p<0.001$), and PASI score (unstandardized β = -0.006, 95%CI; -0.009 to -0.003, $p<0.001$) remained significant factors for patients' health utility, while cDAPSA was not significant for both low and moderate-to-high disease activity (Table 5). According to standardized beta coefficient, HAQ-DI score was the most influencing factor for patients' health utility (standardized β = -0.664) followed by PASI score (standardized β = -0.299). Adjusted R² of the final model was 0.5899 with VIF ranged from 1.09 – 2.45.

Discussion And Conclusions

This study found that PsA patients with remission or low disease activity significantly had lower HAQ-DI scores compared to those with moderate-to-severe disease activity. The majority of PsA patients had low PASI scores meaning that our samples had slightly skin lesion. The HAQ-DI score and PASI score had reverse relationship to patients' health utility based on the negative sign of beta coefficient.

Our findings showed relatively high utility possibly due to 80% of PsA patients in this study being in remission or having low disease activity. This was in line with a Thai study which reported high utility in patients with low cDAPSA¹¹.

Our findings were similar to a previous study from the United Kingdom¹⁹ which found that patients' health utility was associated with HAQ-DI and PASI scores. However, the magnitudes of effect were slightly different. The UK study reported unstandardized β of HAQ-DI as -0.298, while that of PASI was -0.004, while those for our study were -0.167 and -0.006, respectively. The differences meant that decreases in HAQ-DI and PASI score in Thai patients had less impact on overall health utility than patients in the United Kingdom.

The magnitude of reduction in HAQ-DI score in this study was also in line with a report from Canada²⁰, which found that reduction of the HAQ-DI by approximately 0.13 point resulted in a clinically significant perception of clinical improvement by the patients. This finding reflected a meaningfully better HR-QoL.

The HAQ-DI might vary in patients with different joint diseases. The average HAQ-DI in Thai PsA in this study (0.49 ± 0.60) was lower than that reported in Spanish population (0.76 ± 0.67)²¹. This might be due to several reasons where differences in patients' characteristic were the main reason. Difference in cultures might influence in the perception of the disease. In Thailand, family supports are very common, and patients are looked after by their own family members, which might indirectly affect the patients' self-care activities, resulting in lower HAQ-DI scores. Lastly, the Thai healthcare systems allow patients to easily get access to the primary care units upon their needs, for example, the village health volunteers could reach out the patients at home.

Our study was different from a previous Thai study¹¹ which reported the association of health utility and its related factors in Thai patients with PsA. The previous study was conducted in a university hospital in Bangkok, a capital of Thailand, while our study was conducted in three university hospitals. Two hospitals are located in Bangkok and another hospital is located in the northern part of Thailand. We believe that our study was better represent characteristics of Thai PsA patients. Another important difference was that the previous study did not incorporate PASI score in the study which was found to be significant related factors for patients' health utility in this study. This study was more comprehensive in terms of the factors used in the analysis because we incorporated factors from both rheumatologic and dermatologic clinical factors.

Since this study found a strong relationship between the HAQ-DI, PASI, and health utility, we suggest that the HAQ-DI and PASI instruments should be incorporated in routine monitoring practice. The HAQ-DI and PASI can be used to estimate health utility score which is an important input for further cost-effectiveness study.

Several limitations should be addressed in this study. Although this study planned to collect the data from the three large university hospitals located in Thailand, but the number of the patients could not be

reached as calculated sample size which was due to the outbreak situation of COVID-19. Next, this study required multi-setting interviews, which might be a subject of inter-rater variability. However, exhaustive site visits and monitoring were performed to train the data collectors to ensure their understandability of study methodology. This would minimize inter-rater variability in this study. As the healthcare system among Asian countries are difference, therefore, generalization of this finding to other Asian countries should be used with cautioned.

In conclusion, patients with PsA in Thailand showed relatively high utility scores. However, most included patients were in remission or had low disease activity. Patients in remission or with low disease activity had higher health utility than those with moderate-to-severe disease activity. The HAQ-DI and PASI were strong predictors of the patients' health utility. Therefore, both HAQ-DI and PASI instruments should be used in routine monitoring practice for patients with PsA as its scores can be applied to estimate health utility score.

Declarations

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Conflict of interest

All authors declare no conflict of interest.

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Figures

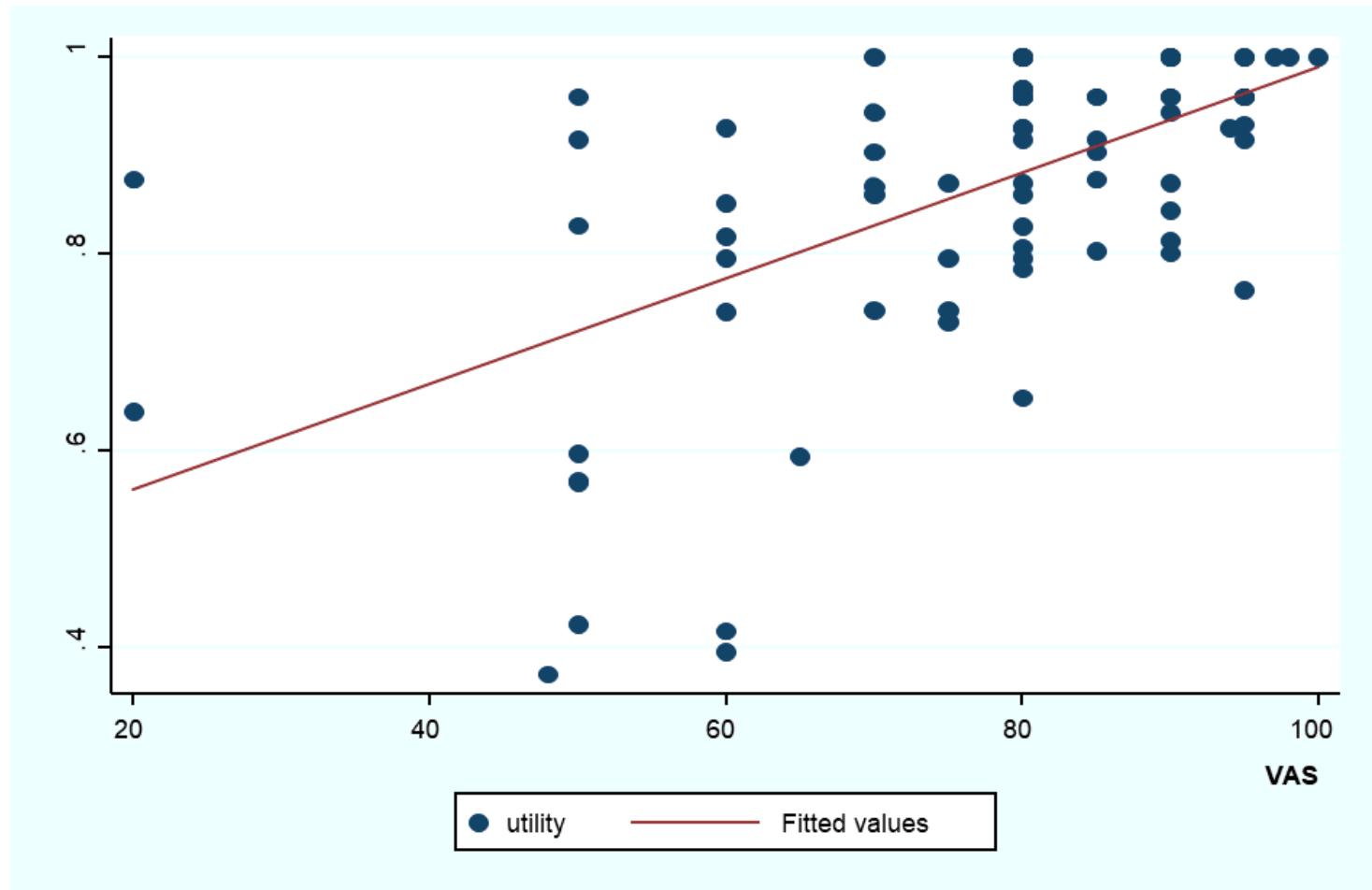


Figure 1

A correlation between utility and visual analog scale (VAS).