## Distribution Agreement

In presenting this thesis as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis. I retain all ownership rights to the copyright of the thesis. I also retain the right to use in future works (such as articles or books) all or part of this thesis.

Signature:

______________________________ ____________________

**Seema P. Kini** **April 14, 2011**

# Pruritus: the skin equivalent of pain as measured by health utilities

By
Seema P. Kini
M.D./M.S.C.R.
Clinical Research

Suephy C. Chen, M.D., M.S.
Advisor

Thomas R. Ziegler, M.D.
Committee Member

John R. Boring, III, Ph.D.
Committee Member

John E McGowan, Jr., M.D.
Committee Member

Accepted:

Lisa A. Tedesco, Ph.D.
Dean of the James T. Laney School of Graduate Studies

April 15, 2011

# Pruritus: the skin equivalent of pain as measured by health utilities

By

Seema P. Kini

Bachelor of Arts

Advisor: Suephy C. Chen, M.D., M.S.

An abstract of:
A thesis submitted to the Faculty of the James T. Laney School of Graduate Studies of Emory
University in partial fulfillment of the requirements for the degree of Master of Science
in Clinical Research
2011

Abstract

# Pruritus: the skin equivalent of pain as measured by health utilities

By Seema P. Kini

## Abstract

***Objective*****:** To compare the quality of life impact of chronic pruritus to that of chronic pain using directly elicited health utilities

**Design**: Cross-sectional study

**Setting**: Convenience sample of patients attending the Emory Dermatology Clinic, Emory Spine Center, and Emory Center for Pain Management.

**Participants**: Adult men and women (≥18 years) experiencing chronic pain or pruritus for a minimum of 6 weeks

**Main Outcome Measure**: The mean utility score of subjects with chronic pruritus was compared to that of subjects with chronic pain. A regression analysis was performed to determine the impact of the primary predictor variable, symptom type, on the primary outcome variable, mean utility score (a measurement for quality of life impact)

**Results**: 73 subjects with chronic pruritus and 138 subjects with chronic pain were recruited. Mean (SD) utility among patients with pruritus was 0.874 (0.27) compared to 0.767 (0.31) for subjects with pain ($p<0.001$). After controlling for symptom severity, duration, and demographic factors, only symptom severity (-0.03, $p=0.048$) and single marital status (-0.12, $p= 0.02$) and not symptom type (0.05, $p= 0.43$) remained a significant predictor of mean utility score.

***Conclusions*****:** Chronic pruritus has substantial quality of life impact which may be comparable to that of pain. Symptom severity and support networks are important factors in determining the extent of quality of life impact. Addressing support networks in addition to developing new therapies may improve the quality of life of itchy patients.

# Pruritus: the skin equivalent of pain as measured by health utilities

By

Seema P. Kini

Bachelor of Arts

Advisor: Suephy C. Chen, M.D., M.S.

An abstract of:
A thesis submitted to the Faculty of the James T. Laney School of Graduate Studies of Emory
University in partial fulfillment of the requirements for the degree of Master of Science
in Clinical Research
2011

# I. Introduction

Pruritus (the medical term for itch) is a primary mechanism by which the nervous system processes and encodes noxious stimuli. Several studies have attempted to demonstrate that chronic pruritus has a significant effect on health-related quality of life (QoL).[1-3] Specifically, patients may experience a debilitating course including the development of symptoms of depression, global distress and impairment of sleep.[3]

Despite the reported widespread and debilitating effect of chronic pruritus, there is an overall paucity of research regarding this symptom in comparison to other chronic conditions such as pain. Chronic pain and pruritus share many similarities: both are complex, subjective symptoms that have been associated with the development of symptoms of depression and the impairment of activities of daily living and sleep.[4-6] However, unlike chronic pruritus, pain syndromes have been well studied in health-services and outcomes research resulting in a better understanding of this complex condition and the development of novel treatments.

Given the similarities between these two symptoms, we believe that chronic pruritus has significant QoL impact comparable to that of pain. To assess the extent of this impact, the purpose of this study was to measure health utility scores—numeric health economic measures that represent a subjective level of satisfaction with a certain health state— in subjects with pain and pruritus in order to compare the QoL impact of these two health states.

## II. Background

### IIa. Pruritus

Pruritus is a common symptom in dermatology and a key symptom in systemic diseases such as renal, hematologic, and neoplastic disorders. Acute pruritus is the desire to scratch for a limited period of time ranging from seconds to a week, whereas chronic pruritus may persist for weeks, months, or even years although no consensus on the exact time course or definition of chronic pruritus currently exists. Chronic pruritus is often not amenable to treatments for acute pruritus such as anti-histamines, anti-leukotrienes, and immunosuppressives and may result in a debilitating course.

Although few large-scale epidemiological studies have been performed to determine the prevalence of chronic pruritus, there is evidence to suggest it is a common problem: a Norwegian community based study found the prevalence of pruritus to be 8.4% in the general adult population. [7] Similarly, a cross-sectional study of skin disease in France found that pruritic cutaneous conditions may affect upwards of 20-30% of the French population. [8] The epidemiology of chronic pruritus in the general medical and dermatology populations is not well documented either and may be underestimated. Pruritus is particularly common in dermatological conditions such as atopic dermatitis and psoriasis with pruritus reported to be a symptom of psoriasis in over 70% of patients. Similarly, in the recent International Dialysis Outcomes and Practice Patterns Study (DOPPS) of the more than 18,000 patients on hemodialysis, moderate to extreme pruritus was experienced by 42% of patients.[9]

There is also data to indicate that chronic pruritus has a profound effect on QoL. The aforementioned French study found that 40% of individuals with pruritus described their disease as debilitating. [8] Additionally, a study of pruritus in German and Ugandan patients found that patients in both populations exhibited an impaired QoL secondary to their pruritus. [10] Of the studies exploring the burden of disease of pruritus, there has been little attention directed to what factors may drive QoL impact. However, a study by Zachariae *et al*, found that pruritus severity was a significant predictor of depressive symptoms, global distress, impairment of sleep and overall QoL in a sample of psoriasis patients.[3]

### IIb. Pruritus and pain

Pruritus and pain are both complex, unpleasant sensory and emotional experiences which appear to be inextricably linked. Under normal mechanisms, there is an antagonistic interaction between pruritus and pain: acute pruritus can be alleviated by nociceptive counter-stimuli (e.g. scratching). Conversely, inhibition of pain processing (e.g. spinal opioids) can generate pruritus and the blockade of spinal opioids can be used as an anti-pruritic therapy. Recently advances in the neural coding of pruritus have found the symptom to be mediated by a neuronal pathway distinct from the pain-processing pathway. Nevertheless, the sensations of itch and pain continue to be conceptualized as closely related. [11, 12]

The associations between pruritus and pain have mainly been studied from a neurobiological standpoint, but similarities between these two symptoms are also clinically relevant. Investigators of a large population based study in Norway sought to determine possible associations between chronic pruritus and pain. The authors concluded that women were more frequently affected by chronic pain and pruritus and that individuals affected most by their symptom reported an increased frequency of depression and overall poorer well being. [13] These findings underscore the potential contribution of psychosocial and affective dimensions contributing to the overall QoL impact of these two symptoms.

### IIc. Health-related quality of life (QoL) in dermatology

Health-related quality of life (QoL), a patient's assessment of his or her QoL within the specific context of health, is an increasingly important concept in both clinical medicine and research. This concept is particularly important in dermatology where few cutaneous diseases affect survival, but virtually all have the potential to impact QoL.

### IId. Health utilities in dermatology

One way to measure QoL are health utilities, which account for patient preferences and are therefore able to fully capture disease burden. In other words, utilities represent the strength of a patient's desirability for a particular health outcome or health state. Utilities are numeric values expressed on a continuous scale anchored at death (utility=0) and perfect health (utility=1). Health utility scores closer to "0" indicate a greater burden of disease than do scores closer to "1". [14] Utilities allow for comparison of disease burden across many different diseases and are used in cost-utility analyses in the calculation of quality adjusted life years (QALYs). A comprehensive catalog of dermatology utilities published by Chen *et al*. found the mean utility for subjects with pruritus to be 0.915. The mean utilities for several specific diagnoses associated with chronic pruritus were psoriasis (0.907), atopic dermatitis (0.890), and mycosis fungoides (0.867).[15]

A commonly accepted method for measuring utilities is the time trade-off (TTO) method which provides the subject with a decision: living the rest of his or her life in their current health state or living for a shorter period of time with perfect health. In other words, subjects may exchange a portion of their future survival time in order to live in perfect health during a shortened lifespan. The TTO-derived utility is the ratio of the time remaining after the trade to the life expectancy of the individual. For example, a subject with a life expectancy of 75 years who was willing to give up 3 years to live without pruritus, would have a utility of 72/75, or, 0.96 for the health state of chronic pruritus. Simply put, this subject would be willing to forfeit 4% of their life expectancy to live without pruritus.

# III. Methods

The specific aim of this cross-sectional study analyzed as a cohort study was to determine the QoL impact of chronic pruritus as measured by health utilities and to compare the degree of this impact to that of subjects with chronic pain. The null nypothesis was that there was no significant difference in mean utility score between the pain and pruritus cohorts.

The Emory Institutional Review Board approved this cross-sectional study. The survey materials included paper-based questionnaires regarding demographics, clinical parameters, and symptom severity.

In addition to these paper-based surveys, each consenting subject completed a face to face time trade-off (FTF TTO) interview to assess the QoL impact of their symptom (pain or pruritus). The FTF TTO interview is a standard method with which to elicit health utilities.[16]

In the FTF TTO interview, a computerized utility instrument provided subjects with a decision: living the rest of their life in their current health state or living for a shorter period of time with perfect health. In other words, subjects could exchange a portion of their future survival time in order to live in perfect health during a shortened lifespan. The length of the period of time in perfect health was varied until the subject was indifferent about the decision. The mean utility score was then the ratio of time remaining after the trade to the total life expectancy of the individual. Through the FTF TTO method, we were able to enumerate subject preferences for life in their health state (i.e. chronic pain or pruritus).

Subjects were asked to compare health states via 3 TTO scenarios: 1) paralysis versus no paralysis, 2) all of their medical problems versus a life free from all of their medical problems and 3) all of their medical problems versus a life with all medical problems but without chronic pain or pruritus. We chose this method in order to encourage subjects to think about how their various medical problems, including their pain or pruritus, affected their lives. Interviewers were trained to provide a standardized brief introduction and to follow a general template for the three TTO scenarios. In each scenario, two health states were described: a reference health state (i.e. a patient's current health state with either chronic pain or pruritus) and a comparison health state (a theoretical health state where the subject would be in the best possible health but would forfeit a certain number years of life). The appendix details the elicitation method.

From June 2007 to April 2008, adult (>18 years) subjects experiencing chronic pain or pruritus for 6 weeks or longer were recruited from the Emory Spine Center and the Center for Pain Management or from the Emory Dermatology clinic, respectively. Potential subjects were recruited via flyers placed in their respective clinic offices or were informed of the study by their treating physician. Subjects who demonstrated an inability to speak or read English, or any other disability that would prevent the subject from completing both the paper questionnaires and the FTF TTO interview were excluded from participating in the study. Informed consent was obtained from all subjects prior to inclusion in the study.

### Survey Variables

Sociodemographic variables were limited to age, gender, race (Caucasian, non-Caucasian), marital status (married, single), education (high school or less, college, graduate school), and household income ($50,000 or less, $50-100,000, $100,000+). Clinical variables included symptom duration (<1 year, 1-5 years, 5-10 years, or greater than 10 years) and symptom severity. Symptom severity was assessed using a visual analogue scale from 0-10 which asked subjects to rate the severity of their symptom ‘over the past 6 weeks’, ‘at its worst’, ‘at its best’, ‘currently’, and ‘daily average’. The ‘daily average’ assessment of severity was used in statistical analyses in this study. The primary outcome variable was mean utility score as generated by the FTF TTO interview.

## Statistical Analyses

The independent sample t-test was used to compare differences in continuous variables and mean utility scores between the pain and pruritus groups. The Chi-squared test was used to compare differences in categorical variables. Generalized linear modeling was used to develop a predictive model to assess the effect of symptom type (pain or pruritus) on the primary outcome variable, mean utility score, after adjusting for demographics and other clinical variables. Multi-collinearity was assessed by analyzing variance inflation factors for each covariate of interest. All tests were two-sided and a $p<0.05$ was required for statistical significance. All analyses were performed using SAS software (version 9.1; SAS Institute, Cary, North Carolina).

## Power Analysis

Rather than power for an equivalence study, we assumed a minimum effect size that would be meaningful between the two sets of utilities. Power was calculated with the goal of detecting at least a 0.10 difference in mean utility score (deemed as a clinically significant difference[17]) between the pain and pruritus groups. We assumed a two-sided t-test, with a common standard deviation of 0.300, an alpha of 0.05, and 80% power to estimate the need for 125 individuals per group. To power our regression analysis, we used the rule of thumb of 10 subjects per independent variable. With the 9 anticipated variables, we would need 90 subjects.

# IV. Results

## Demographics and Characteristics of Pain and Pruritus Cohorts

138 subjects with chronic pain were recruited from the Emory Spine Center and Center for Pain Management. In this group, the mean (SD) age was 55 (16) years, the majority were female (62%), and overwhelmingly (80%) Caucasian. 73 subjects with chronic pruritus were recruited from the Emory Dermatology Clinic where the mean (SD) age was 55 (17), 58% were female and 74% were Caucasian. In both groups, the median duration of symptoms was 6 months to 1 year and almost half of subjects characterized the severity of their symptoms as ‘moderate’. A greater proportion of subjects in the pain group, however, characterized their symptom as severe (36% vs. 28%).

Demographic characteristics of participants and the distribution of symptom severity (mild, moderate, and severe) among the pain and pruritus groups are displayed in **Table 1**. Continuous variables are reported as means with standard deviations (SD) and categorical variables are reported as proportions. There were no differences in demographic characteristics between the two groups with the exception of symptom severity with a significantly higher proportion of subjects in the pain cohort classifying their symptoms as “severe” (p<0.001). The mean (SD) utility score among subjects with pruritus was 0.874 (0.27) compared to 0.767 (0.31) for subjects with pain. This difference was clinically significant (p<0.001).

### Multivariate Regression: Primary Outcome Variable, Mean Utility Score for Pain and Pruritus Cohorts

We report the parameter estimates of the regression model with mean utility score as the primary outcome variable in **Table 2**. Single marital status (-0.12, p, 0.02) and symptom severity (0.03, p, 0.048) remained significant predictors of symptom utility score after controlling for other subject characteristics. Race trended toward significance (p,= 0.07). Neither symptom (pain or pruritus) type, nor symptom duration were significant predictors of mean symptom utility score.

## V. Discussion

This study of subjects with chronic pruritus and pain has several important findings. First, our data suggests that chronic pruritus carries considerable burden of disease, as measured by health utilities. In this study, the mean utility score of subjects with chronic pruritus was 0.874 indicating that the average subject was willing to forfeit 13% of their life expectancy in order to live without pruritus. Previously reported health utilities for other dermatological conditions include bullous diseases (0.640) and mycosis fungoides (0.867), and acne vulgaris (0.938).[15]

Second, our results from this small study indicate that chronic pruritus may have a QoL impact comparable to that of chronic pain. In our univariate analysis, subjects with chronic pruritus had a significantly greater mean utility score (0.867) for their symptom compared to subjects with chronic pain (0.767). At first glance it would seem that patients with chronic pain carry a considerably greater burden of disease than those with chronic pruritus. We feel that this is likely due to a greater proportion of subjects characterizing their symptom as 'severe' in the pain cohort compared to the pruritus cohort ($p<0.001$). Additionally, on multivariate analysis, after controlling for demographic and clinical variables, symptom type (pain or pruritus) was not a significant predictor of the primary outcome variable, mean utility score. This finding suggests that chronic pruritus carries considerable burden of disease—a burden that may be comparable to that of chronic pain.

Indeed, the primary determinants of mean utility score, and thus degree of QoL impact, on multivariate modeling were symptom severity (-0.03, p, 0.05) and marital status (-0.12, p, 0.02). Specifically, greater pruritus severity and single marital status were associated with a lower mean utility score (i.e. worse QoL). It may initially seem peculiar that marital status was a stronger measure of effect than symptom severity. However, on closer analysis, this finding is consistent with epidemiological research indicating that social relationships (with marital status as a proxy measure) may be protective of morbidity by aiding in economic well-being, healthier lifestyles, lower stress, and social support.[18-20]. Previous studies have had similar findings: a cross-sectional study of individuals with chronic pain and pruritus by Dalgard, *et al*. found that those individuals most affected by their symptoms tended to be younger, female, were more depressed and reported significantly poorer well-being.[13] Together, these findings underscore the importance of the psychosocial and affective dimensions associated with patient symptoms. The role of support groups to link patients with similar symptoms and the use of pruritus-specific QoL instruments to track improvements in patient defined endpoints may have a profound effect on reducing burden of disease.

In this study, the median duration of symptoms for both the pain and pruritus cohorts was 6 months to 1 year. While symptom severity and marital status were found to significantly contribute to overall mean utility score, symptom duration (0.06, p, 0.27) was not a significant predictor of mean utility score in the multivariate regression model. This may be due to an adaptation phenomenon where patients experiencing chronic illnesses or disabilities are motivated to find ways to accommodate their symptom. Consequently, an actual patient's ratings of their own QoL is often much higher than healthy individuals not experiencing the disease state of interest would otherwise have imagined.[21, 22]

## Limitations

Our study has several limitations. As with all survey-based studies, this study is subject to response, recall, and selection biases. Since subjects in both pain and pruritus cohorts were recruited from Emory University, a tertiary referral center, this population may include highly motivated patients with more severe disease than those found at a non-academic center. Similarly, patients who are severely affected may have been more likely to participate. Both of these biases, however, would result in an *overestimation* of burden of disease (i.e. lower mean utility score) and for the purposes of comparison would affect both the pain and pruritus cohorts similarly.

One limitation of the TTO technique is that subjects are asked to give up years at the end of life, which might be valued less, and therefore the results may be biased upward. Nevertheless, the TTO method is increasingly accepted as a standard method with which to elicit health utilities because of its greater feasibility, higher discriminative power, and better face validity than other methodology.[14] Finally, this study did not assess the potential contribution of other co-morbidities such as mood states (e.g. depression, anxiety) that have been previously reported to contribute to the overall poorer well-being experienced by patients with chronic itch and pain.[3, 13]

Despite these limitations, the aim of this study was to provide greater insight into the burden of chronic pruritus and to compare the QoL impact of this symptom to that of chronic pain.  To our knowledge, this study is the first to use a true measure of disease burden, health utilities, to assess the scope of QoL impact in patients with chronic pruritus. With health utilities, subjects are giving up something of value in the TTO: time. This currency is relevant to other health conditions as well. Consequently, our study provides a model with which to compare common debilitating symptoms that are best self-reported and have very few objective findings such as nausea, heartburn, neuralgias, and dysesthesias.

## Conclusions

Overall, our data support previously published results indicating that patients with chronic pruritus carry significant burden of disease. [8, 10, 13] This study provides preliminary evidence which future studies may build upon by incorporating larger and more general populations of subjects and by assessing the contribution of mood states (e.g. depression, anxiety) to the QoL impact of pruritus. Our results highlight the use of support networks for patients to discuss and commiserate, in addition to the development of new therapies, may improve the QoL of itchy patients.

## References

1. Zachariae R, Zachariae C. Psychological symptoms and quality of lfie of dermatology outpatients and hospitalized dermatology patients. Acta Derm Venereol 2004; 84:205-12.

2. Yosipovitch G, Goon A, Wee J, Chan Y, *et al*. The prevalence and clinical charactieristics of pruritus among patients with extensive psoriasis. Br J Derm 2000; 143:969-973.

3. Zachariae R, Zachariae C, Lei U, Pedersen A. Affective and Sensory Dimensions of Pruritus Severity: Associations with Psychological Symptoms and Quality of Life in Psoriasis Patients. Acta Derm Venereol 2008; 88:121-127.

4. McDermott A, Toelle T, Rowbotham D, Schaefer C, *et al.* The burden of neuropathic pain: results from a cross-sectional survey. Eur J Pain 2006;10:127-135.

5. Becker N, Olsen A, Sjoren P, Eriksen J. Pain epidemiology and health related quality of life in chronic non-malignant pain patients referred to a Danish multidisciplinary pain center. Pain 1997;73:393-400.

6. Skevington S. Investigating the relationship between pain and discomfort and quality of life using the WHOQOL. Pain 1998;76:395-406.

7. Dalgard F, Svensson A, Holm J, Sundby J. Self-reported skin morbidity in Oslo: associations with sociodemographic factors in cross-sectional study. Br J Dermatol 2004;151:452-7.

8. Wolkenstein P, Grob J, Bastuji-Garin S. French people and skin diseases: results of a survey using a representative sample. Arch Dermatol 2003;139(12):1614-1619.

9. Pisoni R, Wikstrom B, Elder S, Akizawa T. Pruritus in haemodialysis patients: international results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Nephrol Dial Transplant 2006;21(12):3495-3505.

10. Weisshaar E, Apfelbacher C, Jager G, Zimmerman E, *et al.* Pruritus as a leading symptom: clinical characteristics and quality of life in German and Ugandan patients. Br J Derm 2006;155:957-964.

11. Davidson S, Giesler G. The multiple pathways for itch and their interactions with pain. Trends Neurosci 2010;33(12):550-558.

12. Sun Y, Zhong-Qiu Z, Xio-Li M, Yin J, *et al*. Cellular Basis of Itch Sensation. Science. 2009(5947):1531-1534.

13. Dalgard F, Dawn A, Yosipovitch G. Are itch and chronic pain associated in adults? Results of a large population survey in Norway. Dermatology 2007;214:305-309.

14. McCombs K, Chen SC. Patient preference quality measures in dermatology. Dermatol Ther. 2007;20:102-109.

15. Chen SC, Bayoumi A, Soon S, Aftergut K, *et al*. A catalog of dermatology utilities: a measure of the burden of skin diseases. J Investig Dermatol. 2004;9:160-168.

16. Van Osch S, Wakker P, van den Hout W, Stiggelbout A. Correcting biases in standard gamble and time trade off utilities. Med Decis Making 2004;24: 511-517.

17. Furlong W, Feeny D, Torrance G, Barr R, *et al*. Guide to Design and Development of Health-State Utility Instrumentation. Center for health economics and Policy Analysis 1990;Working paper series 90-9.

18. House J, Landis K, Umberson D. Social relationships and health. Science. 1988; (241):540-545.

19. Holt-Lunstad J. Is there something unique about marriage? The relative impact of marital status, relationship quality, and network social support on ambulatory blood pressure and mental health. Ann Behav Med. 2008;35:239-244.

20. Berkman L. The role of social relations in health promotion. Psychosom Med. 1995;57:245-254.

21. Damschroder L, Zikmond-Fisher B, Ubel P. The impact of considering adapation in health state valuation. Soc Sci & Med. 2005;61(2):267-277.

22. Menzel P, Dolan P, Richardson J, Olsen J. The role of adaptation to disability and disease in health state valuation: a preliminary normative analysis. Soc Sci & Med. 2002; 55(12):2149-2158.

# TABLES

## Table 1: Demographics

| | | **Pruritus (n=73)** | | **Pain (n=138)** | | **p-value**** |
|---|---|---|---|---|---|---|
| Demographic | | n | % | N | % | |
| | Male* | 31 | 42% | 52 | 38% | |
| | Caucasian* | 54 | 74% | 112 | 80% | |
| | Married* | 54 | 74% | 91 | 66% | |
| | Age, mean (SD) | 55 | 17 | 55 | 16 | |
| Symptom Severity | | n | % | N | % | |
| | mild | 18 | 24% | 22 | 16% | |
| | moderate | 34 | 47% | 65 | 47% | |
| | severe | 21 | 28% | 50 | 36% | <0.001 |
| Utility, mean (SD) | | 0.874 | 0.27 | 0.767 | 0.3 | <0.001 |
| Utility by severity | | | | | | |
| | mild | 0.932 | 0.19 | 0.867 | 0.23 | |
| | moderate | 0.906 | 0.19 | 0.829 | 0.27 | |
| | severe | 0.706 | 0.41 | 0.656 | 0.34 | |

*****Chi-squared test, all other Student’s t-test

**Those p-values not listed $\geq 0.05$

**Table 2: Multivariate linear regression for primary outcome variable, mean utility score**

| Independent Variable | Coefficient | p-value |
|---|---|---|
| **Symptom type**<br>(0=pain, 1=itch) | 0.05 | 0.43 |
| **Severity group**<br>(1-3 mild, 4-6 moderate, 7-10=severe) | -0.03 | 0.048 |
| **Duration**<br>(<1 yr, 1-5 yrs, 5-10 yrs, >10 yrs) | 0.02 | 0.64 |
| **Gender** | 0.06 | 0.27 |
| **Age** | -0.001 | 0.56 |
| **Race**<br>(Caucasian, non-Caucasian) | -0.10 | 0.07 |
| **Marital Status**<br>(married, single) | -0.12 | 0.02 |
| **Education**<br>(High school or less, college, graduate school) | -0.01 | 0.9 |
| **Income**<br>($50,000 or less, $50-100,000, $100,000+) | 0.01 | 0.8 |

# Appendix

*Face to Face Time Trade-off (TTO) Elicitation Technique*

We presented a total of three health scenarios in order to allow subjects to think about how their medical conditions affected their life. The first scenario used paralysis as the reference health condition to familiarize subjects with the TTO elicitation technique. Following this scenario, two additional scenarios were used: 1) all medical problems and 2) life with all medical problems but without chronic pain or pruritus. The subject's hypothetical life expectancy was used as the time horizon in the computerized utility instrument. An example of the TTO task with paralysis as the reference health condition is provided below.

In this example, the subject is a 50 year old female with chronic pruritus secondary to her psoriasis. She has an average life expectancy of 80 years. Out interviewers were given a script and instructed to guide the subject as follows:

**Interviewer**: Imagine you are paralyzed from the neck down. Your first choice is whether you want to live the rest of your life for 30 years with paralysis or live without paralysis for 30 years and give up nothing. Which do you prefer or are the choices the same?

**Subject**: I choose option B where I would live 30 more years without paralysis.

**Interviewer**: Your next choice is whether you want to live the rest of your life for 30 years with paralysis or live without paralysis for 0 years and give up 30 years of life. In other words, you'd die this year without any pain or suffering. Which do you prefer or are the choices the same to you?

**Subject**: I do not want to die now. I choose option A and would rather live 30 more years without paralysis.

**Interviewer**: Your next choice is whether you would want to live for the rest of your life paralyzed for 30 years or live without paralysis for 29 years and give up 1 year of life. Which do you prefer or are the choices the same to you?

**Subject**: I would want to give up 1 year of life to have 29 years without paralysis. I choose option B.

**Interviewer**: Your next choice is whether you want to live the rest of your life paralyzed for 30 years or live without paralysis for 28 years and give up 2 years of your life. Which do you prefer or are the choices same to you?

**Subject:** I would give up 2 years of my life to live without paralysis. I choose option B.

A converging ‘ping pong’ technique was used by the computerized utility instrument to titrate down to the subject’s point of indifference. The iterations for each scenario were continued until subjects found the two choices equally good.